# Critical Review Form
## Meta-analysis

Does the Addition of Dexamethasone to Standard Therapy for Acute Migraine Headache Decrease the Incidence of Recurrent Headache for Patients Treated in the Emergency Department? A Meta-analysis and Systematic Review of the Literature, *Acad Emerg Med* 2008; 15: 1223–1233

**Objective:** "To critically appraise the existing literature and to provide recommendations for patient care regarding the use of dexamethasone for the prevention of headache relapse in patients with acute migraine headache in the ED." (p. 1224)

**Methods:** The authors conducted a well-described electronic search of MEDLINE, EMBASE, CINAHL, LILACS, and the Cochrane Central Register of Controlled Trials, along with Clinical Trials.gov for the period 1950 – May 2008. Additionally, they reviewed 7-years of scientific abstracts from ACEP, AAEM, and SAEM. Inclusion criteria for individual studies included: blinded randomized clinical trials, diagnosis of acute migraine with ED-initiated therapy including dexamethasone adjuvant therapy added to a control group, and outcomes including self reported moderate or severe headache at 24- to 72-hours. No language restrictions were applied.

Two authors independently performed the electronic searches, abstracted data, assessed inclusion criteria, and assigned quality scores using the Jadad score. Discrepancies were resolved by consensus opinion from a third author. Individual trial characteristics were assessed following the CONSORT statement and the QUOROM statement. Criteria for migraine headache diagnosis had to follow the International Headache Society guidelines. Various non-validated 4- and 5-element headache severity scores were reported and the meta-analysis authors decided a priori to include the worst 2- or 3-categories of each scale as their primary end point.

Using a random-effects model to provide the most conservative estimate of treatment effect, the authors calculated pooled risk ratios with 95% Confidence Intervals. Heterogeneity was assessed with the Cochrane's Q-test, tau-square, and $I^2$ statistic. Publication bias was assessed with the

funnel plot, Egger regression asymmetry test, and the Begg adjusted rank correlation test. Finally the authors conducted an influence analysis by sequentially removing various studies from the meta-analysis before re-computing the treatment effects.

| Guide | Question | Comments |
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| I | ***Are the results valid?*** | |
| 1. | Did the review explicitly address a sensible question? | Yes – can adjuvant therapy with dexamethasone for ED migraine patients reduce the recurrence of moderate to severe migraines within 1- to 3-days. |
| 2. | Was the search for relevant studies details and exhaustive? | Absolutely. In addition to well-described searches of multiple electronic databases without language restrictions, the authors included hand-searches of relevant bibliographic and scientific abstracts along with personally contacting several original investigators. |
| 3. | Were the primary studies of high methodological quality? | Yes. "All seven of the included trials had a final Jadad score of 5, (the highest score) indicating acceptable methodology with respect to randomization, blinding, and description of withdrawals and dropouts." (p. 1225) |
| 4. | Were the assessments of the included studies reproducible? | Unknown since the authors do not report a Kappa analysis of raw agreement for potential article selection or quality assessment (Jadad) score. |
| **II.** | ***What are the results?*** | |

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| 1. | What are the overall results of the study? | • MEDLINE search identified 2611 articles without additional articles identified by the other electronic engines. 37 articles were examined in full detail with three additional articles identified by review of their bibliographies. Nine scientific abstracts were also identified.<br>• Of these 37 articles, 25 were excluded as case reports (10) review articles (7) chronic headaches (3) or other unrelated topics (Fig 1, p. 1226). Ultimately five published RCTs and two scientific abstracts were included in this meta-analysis.<br>• The median dose of dexamethasone used was 15mg (range 8 to 24 mg) with six intravenous trials and one oral trial.<br>• The seven trials included 742 patients.<br>• Random-effects model favored dexamethasone (RR = 0.87, 95%; CI 0.80 – 0.95) with pooled absolute risk reduction .97% (NNT = 10; 95%; CI 6 – 30)<br>• No evidence of *publication bias* by Funnel plot (Fig 3, p. 1229). Beggs test (Z-score 0, p = 1.0), or Egger regression (t for bias 0.19, p = 0.86).<br>• No significant heterogeneity using Cochrane's Q ($\chi^2$ = 411, p = 066), tau-square ($\tau^2$ = 0.00) or $I^2$ (0%).<br>• Dexamethasone side-effects were inconsistently collected and not completely reported, but were suggested in 6% of the population. All reactions (tingling, flushing, and nausea) were transient, resolving without additional therapy.<br>• These results were unaltered by influence analysis (RR range changing to 0.86-0.90) even when excluding the trial with the most influence and the oral trial. |
| 2. | How precise are the results? | Precise enough to incorporate into practice – see CI's above. |
| 3. | Were the results similar from study to study? | Yes. "There was no evidence of publication bias, nor was there evidence of significant statistical heterogeneity." (p 1226) |

| *III.* | ***Will the results help me in caring for my patients?*** | |
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| 1. | How can I best interpret the results to apply them to the care of my patients? | "A single dose of dexamethasone, administered with standard anti-migraine therapy, would be expected to reduce the rate of moderate or severe recurrent headache at 24 to 72 hours in approximately 1 out of 10 patients." (p. 1230) |
| 2. | Were all patient important outcomes considered? | No assessment of QOL or ED recidivism. Also, no assessment of 1-day outcome in important subsets: treatment <24-hours after symptom onset, females, tendency for migraine recurrence, dexamethasone dose. |
| 3. | Are the benefits worth the costs and potential risks? | Yes, if appropriate subsets at high risk for migraine recurrence can be identified to optimize the risk/benefit ratio. |

## Limitations

1) **No reporting of study assessment reproducibility.**
2) **No analysis of important subsets = treatment <24 hours, dexamethasone dose > 15 mg, gender, primary ED migraine therapy (anti-emetic vs. NSAID vs. narcotic vs. other), or prior history of early migraine recurrence.**

## Bottom Line

**Well-conducted meta-analysis suggesting that a single ED dose of IV or PO dexamethasone (mean 8 mg) in International Headache Society defined migraine headache, in conjunction with other routine abortive therapy, can diminish moderate to severe migraine recurrence within 3-days (NNT = 10) without significant side-effect risks. Future trials are needed to identify the optimal dose, as well as ED migraine patient subsets most likely to benefit from acute prophylactic therapy.**