Critical Review Form
Therapy

Kravitz J, Dominici P, Ufberg J, Fisher J, Giraldo P. Two days of dexamethasone versus 5 days of prednisone in the treatment of acute asthma: a randomized controlled trial. Ann Emerg Med. 2011 Aug;58(2):200-4.

Objectives: **"to compare the time needed to return to normal activity and the frequency of relapse after acute exacerbation of asthma between patients receiving 2 days of oral dexamethasone versus 5 days of oral prednisone." (p. 200)**

Methods: **This prospective, randomized controlled trial was conducted at two urban EDs (Albert Einstein Medical Center and Temple University Hospital) between 2004 and 2007. Adult patients between 18 and 45 years of age presenting with asthma exacerbation (with a diagnosis of asthma for at least 6 months prior) who had a peak expiratory flow rate < 80% predicted on arrival were eligible for inclusion. Exclusion criteria included use of oral corticosteroids in the previous 4 weeks, COPD, CHF, pneumonia, sarcoidosis, pregnancy, breastfeeding, tuberculosis, systemic fungal infection, allergy to corticosteroids, or diabetes. Patients were also excluded if they were admitted to the hospital for their asthma exacerbation. A consecutive sample of eligible patients was enrolled.**

Patients were randomized to receive either 2 daily doses of oral dexamethasone or 5 daily doses of oral prednisone, the first dose to be given during the emergency department visit. Patient data was collected by research associates using a standard collection form. Patients were then followed up by telephone call 2 weeks after the ED visit. Outcomes included number of days to return to normal daily activities, number of times albuterol was used in the week after the ED visit, and rate of relapse (repeat ED visit, visit to primary care physician, or admission to the hospital for worsening asthma symptoms).

Out of 1756 patients screened for eligibility, 285 were randomized (129 to dexamethasone and 128 to prednisone). There were 25 patients lost to follow-up in the dexamethasone group and 32 in the prednisone group, leaving 104 and 96 patients in each group for the final analysis, respectively.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	Yes. Patients were randomized in a 1:1 fashion to either receive two daily doses of dexamethasone or five daily doses of

		prednisone.
2.	Was allocation concealed? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	Uncertain. "A computerized randomization table maintained by the pharmacy department was used to assign patients to one of 2 treatment arms." (p. 201) Although the exact mechanism by which allocation (based on the computer generated table) was performed, this seems likely to be adequate to prevent subversion of the randomization process.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. The authors make no mention of crossover between the groups and did not assess for medication compliance, but it would appear that an intention to treat analysis was used.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to age, gender, initial peak flow testing, number of recent ED visits, and number of hospital admissions in the last year. The number of patients requiring intubation (10% vs. 16%) or ICU admission (17% vs. 26%) in the past year was slightly higher in the dexamethasone group compared to the prednisone group, but this is unlikely to have affected the outcomes.
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	No. "Patients in the prednisone group received 5 medication packets labeled 1 through 5, each containing 60 mg of prednisone. Patients in the dexamethasone group received 5 identical medication packets; the first 2 contained 16 mg of oral dexamethasone in packets 1 and 2, with placebo doses in packets 3 through 5. Both the medications and the placebo doses were prepared in identical capsules by the hospital's pharmacy department so that neither the treating emergency physician nor the enrolling research staff could discern which study medication was administered." (p. 203)
2.	Were clinicians aware of group allocation?	No. See above.

3.	Were outcome assessors aware of group allocation?	No. See above.
4.	Was follow-up complete?	No. There were 57 patients lost to follow-up (22.2%), fairly evenly split between the two groups. While the even distribution of patients lost to follow-up makes attrition bias somewhat less likely, a loss to follow-up this high is concerning.
II.	**What are the results ?**	
1.	How large was the treatment effect?	• Patients in the dexamethasone group were more likely to return to normal activity within 3 days of ED visit compared to the prednisone group: 90% vs. 80%; absolute risk reduction 10%, 95% CI 0% to 20%. • There was no significant difference in rates of hospital admission (ARR 2% 95% CI -6% to 2%), repeat ED visit (ARR 1%, 95% CI -5% to 8%), or any primary care visit (ARR 2%, 95% CI -3% to 8%). • The number of albuterol doses needed per day did not differ between the two groups.
2.	How precise was the estimate of the treatment effect?	See above.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	Likely yes. This study enrolled adult patients seen in one of two large, urban, US EDs for asthma exacerbation with reduction of peak flow to less than 80% predicted who were discharged from the ED. These patients are likely similar to many patients seen in our ED for asthma who are discharged home, and the results would likely be applicable to our patients (external validity).
2.	Were all clinically important outcomes considered?	Uncertain. The authors did a poor job of defining their outcomes and do not appear to have done so *a prioi*. They did not define a primary outcome and appear to have adjusted their outcomes somewhat to demonstrate the efficacy of dexamethasone.
3.	Are the likely treatment benefits worth the	Yes. Despite the limitations noted (loss to

	potential harm and costs?	follow-up, lack of a primary outcome, failure to define outcomes *a priori*) it would appear that a two-dose regimen of oral dexamethasone is as safe and likely as effective as a 5-day course of prednisone, with the benefit of being completely more easily and hence possibly improving medication compliance.

Limitations:

1. **The study suffered from significant loss to follow up, increasing the risk of attrition bias.**

2. **The authors did not assess medication compliance during the study, which may have affected outcomes.**

3. **No primary outcome was defined; the outcomes assessed do not appear to have been well-defined *a priori* and may have been adjusted to bolster the supposition that oral dexamethasone is safe and effective. The study does not appear to have been registered with clinicaltrials.gov and one must wonder whether the outcomes were chosen to fit the hypothesis.**

Bottom Line:

This small, randomized controlled trial of two doses of oral dexamethasone compared to five doses of oral prednisone for outpatient management of mild to moderate asthma exacerbations essentially found a slight increase in the proportion of patients with return to normal activity at 3 days (ARR 10%, 95% CI 0% to 20%) with no difference in albuterol use or relapse. The primary limitation of this study was the lack of well-defined outcomes *a priori*, raising the possibility of data mining to find an outcome that benefited the dexamethasone group.