



ORIGINAL RESEARCH CONTRIBUTION

A Cost-effectiveness Analysis of Dexamethasone Versus Prednisone in Pediatric Acute Asthma Exacerbations

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Abstract

Objectives: The objective was to evaluate the cost-effectiveness of dexamethasone versus prednisone for the treatment of pediatric asthma exacerbations in the emergency department (ED).

Methods: This was a cost-effectiveness analysis using a decision analysis model to compare two oral steroid options for pediatric asthma patients: 5 days of oral prednisone and 2 days of oral dexamethasone (with two dispensing possibilities: either a prescription for the second dose or the second dose dispensed at the time of ED discharge). Using estimates from published studies for rates of prescription filling, compliance, and steroid efficacy, the projected rates of ED relapse visits, hospitalizations within 7 to 10 days of the sentinel ED visit, direct costs, and indirect costs between the two arms were compared.

Results: The rate of return to the ED per 100 patients within 7 to 10 days of the sentinel ED visit for the prednisone arm was 12, for the dexamethasone/prescription arm was 10, and for the dexamethasone/dispense arm was 8. Rates of hospitalization per 100 patients were 2.8, 2.4, and 1.9, respectively. Direct costs per 100 patients for each arm were \$20,500, \$17,200, and \$13,900, respectively. Including indirect costs related to missed parental work, total costs per 100 patients were \$22,000, \$18,500, and \$15,000, respectively. Total cost savings per 100 patients for the dexamethasone/prescription arm compared to the prednisone arm was \$3,500 and for the dexamethasone/dispense arm compared to the prednisone arm was \$7,000.

Conclusions: This decision analysis model illustrates that use of 2 days of dexamethasone instead of 5 days of prednisone at the time of ED visit for asthma leads to a decreased number of ED visits and hospital admissions within 7 to 10 days of the sentinel ED visit and provides cost savings.

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Asthma is the most common chronic condition affecting children and a prominent chief complaint in pediatric emergency departments (EDs).¹ Current standard of care in the ED includes systemic steroids for those patients who fail to respond promptly or completely to short-acting beta-agonist therapy.² Systemic steroids have been shown to reduce airway inflammation, decrease rates of hospitalization, and decrease the number of repeat visits to the ED.^{3–6} Traditionally, the most commonly prescribed systemic

steroid regimen is a 5-day burst of oral prednisone/prednisolone.^{4,5,7} However, several recent studies have shown that a 2-day course of dexamethasone has comparable efficacy to a 5-day course of prednisone/prednisolone for acute asthma management.^{3,6,8,9}

Compliance with oral systemic steroids after ED discharge is often a challenge for patients and families.¹⁰ Factors contributing to poor compliance include prolonged course of therapy, socioeconomic factors, underappreciation of severity of symptoms, and concern about medication side effects.^{3,10–12} Dexamethasone is an attractive alternative to prednisone/prednisolone because it has a significantly longer duration of metabolic effect and thus requires fewer doses to achieve similar results. Prior studies have examined both one- and two-dose dexamethasone regimens compared to longer courses of prednisone/prednisolone. Most recently, Kravitz et al.⁹ published a randomized controlled trial of adult asthmatics that showed similar efficacy with a 2-day course of dexamethasone compared

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to 5 days of prednisone with regard to the number of days required to return to normal activity. Four pediatric-specific studies exist. Qureshi et al.⁶ demonstrated that 2 days of dexamethasone provided similar efficacy to 5 days of prednisone with respect to ED relapse rates and symptom presence 10 days after treatment. Gordon et al.⁸ compared a single dose of intramuscular dexamethasone to 5 days of oral prednisolone and found similar changes in asthma score, 4-day follow-up asthma score, admission rates, and unplanned physician visits within 4 days of the initial event. Altamimi et al.³ compared a single dose of oral dexamethasone to a 5-day course of prednisone. While they were unable to achieve statistical power in this study, their results suggest similar efficacy between the groups with respect to days needed to return to baseline. Most recently, Greenberg et al.¹³ found no difference in 10-day relapse rate between randomized groups receiving either two doses of dexamethasone or five doses of prednisone.

The purpose of this study was to use previously published data to create a decision analysis model to compare oral dexamethasone to prednisone/prednisolone for the treatment of acute asthma exacerbations in the pediatric ED. We hypothesized that two doses of oral dexamethasone would be cost saving and result in fewer relapse ED visits and subsequent hospitalizations when compared to five doses of prednisone/prednisolone among pediatric asthma patients treated in and discharged from the ED.

METHODS

Decision Analysis

We constructed a decision analysis model to represent two systemic steroid options for pediatric asthma cases seen in the ED for acute exacerbation (Figure 1). Once the model was created, we surveyed the literature to obtain data on the assumptions needed for the decision tree (Table 1). Assumptions for this analysis included percentage of patients expected to fill prescriptions (45%),¹⁴ expected medication compliance rate (64%),¹⁰ and expected rates of relapse to the ED within 7 to 10 days of the initial event (6.3% for systemic steroid users, 17.4% for nonsystemic steroid users).¹⁵ The studies referenced in our model primarily involved urban children's hospitals, although the hospital admission rate reference included U.S. and Canadian hospitals with a mix of privately and publically insured patients. Based on published literature, we assumed that two doses of dexamethasone has equivalent clinical efficacy to five doses of prednisone.^{6,9,13} Using the 6.3% ED relapse rate with systemic steroid compliance¹⁵ and a 17.4% ED relapse rate for patients who do not take any systemic steroids, we calculated a 11.85% relapse rate for those who only take one dose of dexamethasone (assuming one dose provides half the efficacy of two doses), 15.18% for one dose of prednisone, 12.96% for two doses of prednisone, 10.74% for three doses of prednisone, and 8.52% for four doses of prednisone. To calculate the percentage of patients who would take the full 5 days of prednisone/prednisolone and those who would not complete the full course, we assumed that

64% would take the full five doses¹⁰ and then divided the remaining 36% by 4 to get 9% for each of the remaining compliance options. For dexamethasone, we conducted the analysis two ways. First, we assumed that a prescription would be provided for the second dose of dexamethasone (the dexamethasone/prescription analysis), and then we assumed the second dose would be dispensed at the time of ED discharge (the dexamethasone/dispense analysis), precluding the need for patients to fill a prescription. We included previously published expected hospitalization rates of 23% for each relapse requiring a visit to the ED.¹⁶ After all estimates were placed in the model, a hypothetical cohort of 100 children with asthma being discharged from the ED to home was introduced into each arm of the analysis. We then calculated and compared ED relapse rates and subsequent hospitalizations in each arm.

Cost-effectiveness Analysis

The purpose of the cost-effectiveness analysis was to evaluate the cost-effectiveness and/or potential cost savings attributable to improved compliance with systemic steroids in the 2-day dosing dexamethasone arm compared to the standard 5-day dosing prednisone/prednisolone arm. The primary analysis is from the perspective of the health care system and includes only direct costs related to health care utilization. Direct costs include the cost of the systemic steroids, ED relapse visits, and hospitalizations. The 2010 *Red Book: Pharmacy's Fundamental Reference* was used for steroid cost.¹⁷ Because systemic steroids used in acute asthma exacerbations are dosed based on weight, we introduced three separate cohorts of children into each arm of the model. First, we introduced a cohort of 2-year-olds at the 50th percentile for weight (12 kg), then a cohort of 8-year-olds at the 50th percentile for weight (25 kg), and finally, a cohort of 18-year-olds at the 50th percentile for weight (70 kg). Final results represent the average cost of the three age groups. For the 2-year-old cohort and the 8-year-old cohort, medication costs were based on 4 mg/mL compounded dexamethasone liquid for the dexamethasone dose given in the ED, the cost of a dexamethasone tablet to crush at home for the home dose, and the total cost of prednisolone 15 mg/5 mL solution for the prednisone/prednisolone arm. For the 18-year-old cohort, the costs of both dexamethasone and prednisone tablets were used for their respective groups. A 40% discount to medications given in the ED was applied to account for discounted hospital purchase prices. South Carolina Medicaid data were used to estimate the cost of asthma-related ED visits (\$237) and asthma-related hospitalizations (\$ 6,192). All costs are in 2010 dollars (Table 1).

To extend the analysis to the societal level, indirect costs secondary to missed parental work days were included. We first calculated expected missed school days and then translated that data into missed parental work days. For each ED relapse visit, we assigned 1 day of missed school and then multiplied this by a factor of 0.5, assuming that half of the ED visits take place after-school hours, for a total of 0.5 missed school days. For hospital admission calculations, we used 2006 Health Care Cost and Utilization Project

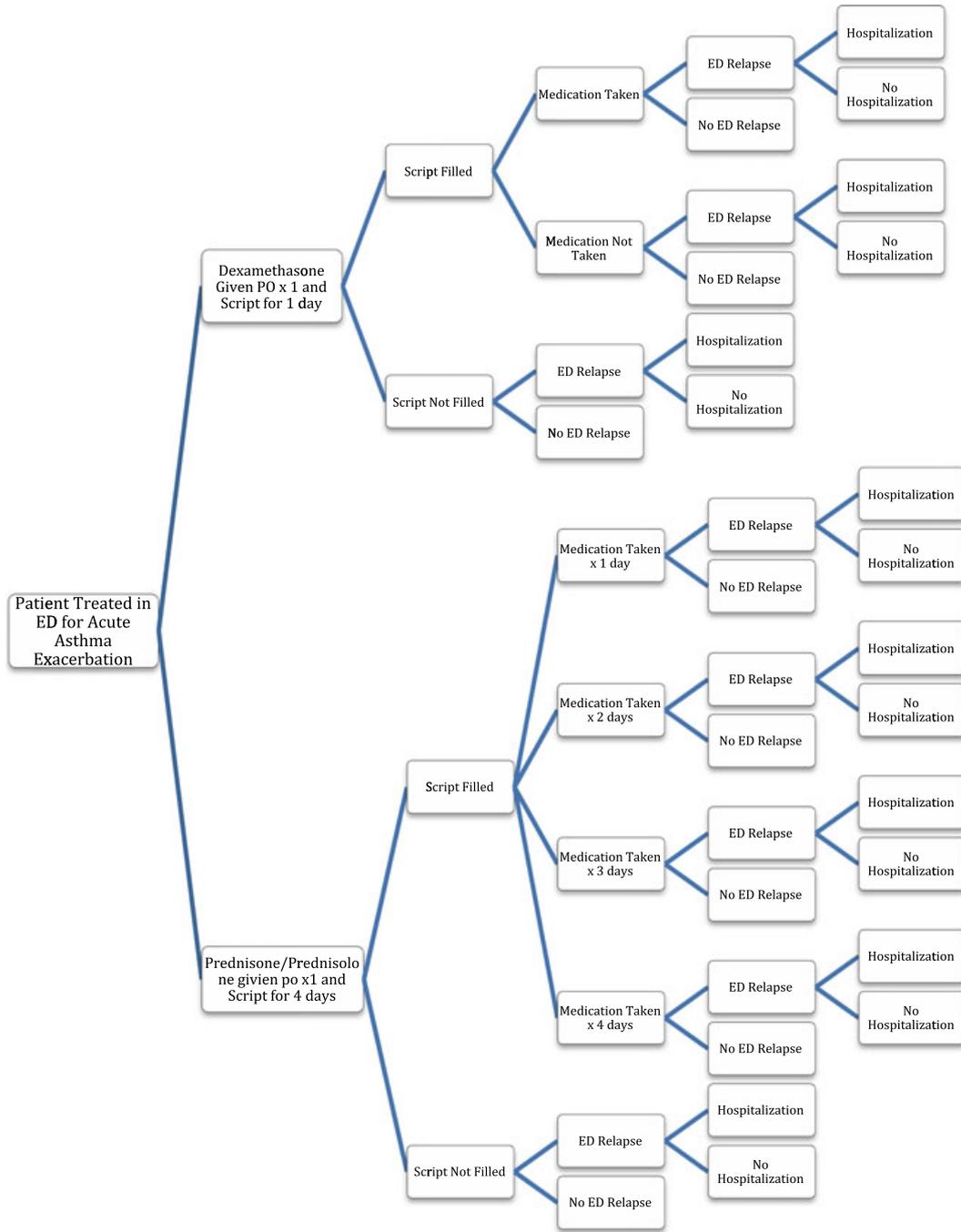


Figure 1. Decision analysis for systemic steroid use in the ED. ICS = inhaled corticosteroids.

mean length of stay per pediatric asthma admission of 2.2 days, which translates into 3 days of missed school. We then used a ratio of missed school days: missed parental work days of 1:0.82, a factor taken from previously published parental reports of missed school days and missed parental work days per year secondary to having a child with asthma.¹⁸ Using data from the Bureau of Labor Statistics, we then applied a median hourly wage of \$15.95 to calculate indirect costs due to missed parental work per asthma visit.¹⁹ Total indirect costs per ED visit and hospital admission were \$52 and \$319, respectively.

Sensitivity Analysis

We performed a sensitivity analysis to determine the stability of our model. We varied selected model assumptions thought to contribute most to our model by 20% bidirectionally. These included the ED relapse rate, admission rate, ED visit cost, medication compliance rate, and prescription fill rate. Additionally, we simultaneously varied the ED relapse rate and admission rate as these variables had the strongest effect on the model results. All analyses were conducted with Excel 2010 (Microsoft Corp., Redmond, WA).

Table 1
Key Assumptions for Decision Analysis

Assumption	Rate	Reference
Prescription fill rate	45%	Cooper and Hickson ¹⁴
Medication compliance	64%	Butler and Cooper ¹⁰
ED relapse rate with systemic steroids	6.3%	Rowe et al. ¹⁵
ED relapse rate without systemic steroids	17.4%	Rowe et al. ¹⁵
Hospital admission rate	23%	Pollack et al. ¹⁶
Compounded dexamethasone cost per mg	\$0.25/mg*	The Red Book 2010 ¹⁷
Prednisolone cost per mg	\$0.13/mg	The Red Book 2010 ¹⁷
Prednisone 20-mg tablet cost	\$0.40	The Red Book 2010 ¹⁷
Hospital medication discount	40%	
ED visit cost	\$237	South Carolina Medicaid Data
Hospital admission cost	\$6,192	South Carolina Medicaid Data

*All costs in 2010 dollars.

Table 2
Decision/Cost-effectiveness Analysis Results* for Both Systemic Steroid Delivery Systems Applied to Cohort of Pediatric Asthma Patients Treated in the ED for Acute Exacerbation

	ED Relapse Visits/100 Patients	Hospital Admissions/ 100 Patients	Direct Cost/ 100 Patients	Direct + Indirect Cost/ 100 Patients
Dexamethasone × 2 doses (prescription given for 2nd dose)	10	2.4	\$17,200	\$18,500
Dexamethasone × 2 doses (second dose dispensed in ED)	8	1.9	\$13,900	\$15,000
Prednisone/prednisolone × 5 doses	12	2.8	\$20,500	\$22,000

*Data assume 7- to 10-day follow-up period and do not include sentinel ED visit cost. Medication costs represent the average across children ages 2, 8, and 18 years. Results are presented in 2010 dollars.

RESULTS

When compared to the standard 5-day prednisone/prednisolone burst, our model predicts that the 2-day dexamethasone therapy results in a decreased number of ED relapse visits and subsequent hospital admissions over the 7- to 10-day period following the initial ED visit. Additionally, we found that both dexamethasone options are less expensive than the prednisone/prednisolone option when comparing both direct medical costs alone (\$3,300 cost savings per 100 patients for dexamethasone/prescription and \$6,600 cost savings for dexamethasone/dispense) and when including indirect costs in the analysis (\$3,500 cost savings per 100 patients for dexamethasone/prescription and \$7,000 for dexamethasone/dispense; Table 2).

Results of the sensitivity analysis show stability of our model, with a consistent prediction of cost savings for the dexamethasone arm. After adjusting model inputs 20% bidirectionally, ED relapse rate and admission rate had the greatest influence on the model's cost savings. This tornado diagram (Figure 2) represents savings when comparing the dexamethasone/prescription cohort to the prednisone/prednisolone cohort.

DISCUSSION

We created a decision analysis model to compare the two most commonly used steroid dosing regimens used

to treat acute asthma exacerbations in the pediatric ED. Our model predicts that two doses of oral dexamethasone is not only more effective clinically, but also provides a substantial cost savings when compared to the standard 5-day course of oral prednisone/prednisolone. The majority of the benefit seen in the dexamethasone arm is attributed to improved compliance due to shorter treatment length. Our model predicted two fewer "bounce-back" visits to the ED, 0.4 fewer admissions, and a total cost savings of \$3,500 per 100 patients treated in the ED for acute asthma exacerbations for the dexamethasone/prescription cohort and 3.8 fewer bounce-back visits to the ED, 0.9 fewer admissions, and a total cost savings of \$7,000 per 100 patients for the dexamethasone/dispense cohort.

Oral dexamethasone has several marked advantages over oral prednisone/prednisolone that make it an attractive alternative for the treatment of asthma exacerbations. These advantages include markedly increased half-life, excellent bioavailability, and palatability.^{9,20} Palatability and decreased number of needed doses (due to duration of metabolic effect) have been cited as reasons why the use of dexamethasone has been thought to markedly increase patient and family compliance with medication dosing.⁷ As previously mentioned, several studies have reported equivalent clinical outcomes between patients treated with dexamethasone and those treated with prednisone with regard to asthma scores, relapse physician visits, and

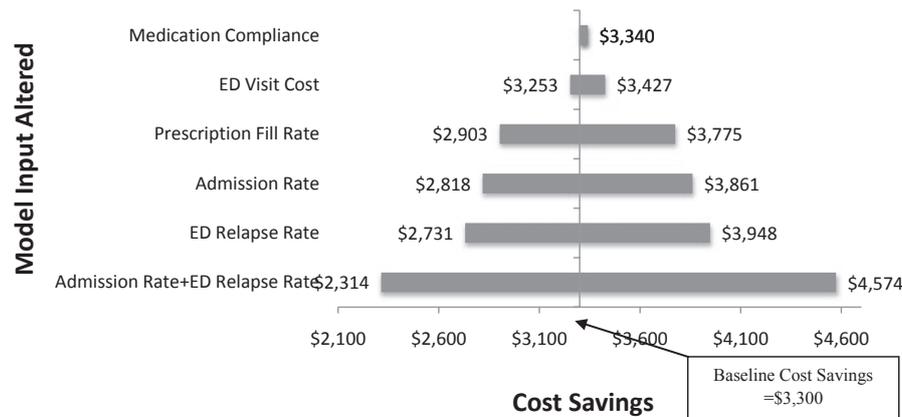


Figure 2. Tornado diagram for sensitivity analysis of predicted cost savings per 100 patients if using dexamethasone instead of prednisone/prednisolone. Sensitivity analysis used a 20% bidirectional variation in model assumptions and accounts for cost-savings comparing dexamethasone/prescription to prednisone/prednisolone.

hospitalization rates.^{3,6,8,13} To our knowledge, we are the first to report a cost savings attributed to the use of the two-dose dexamethasone regimen. With the increasing number of annual visits to the ED and primary care physician for asthma,¹ this potential cost savings to the patient, family, and health care system is substantial. For example, from 2005 to 2007 there were 640,000 pediatric asthma ED visits in the United States,²¹ translating to a potential cost savings of \$22 to \$44 million.

Recent studies have suggested that one dose of oral dexamethasone may be as effective as two doses of oral dexamethasone and/or a 5-day course of oral prednisone.^{3,8} While there is not yet sufficient evidence to support this statement definitively, using our model we are able to demonstrate that the cost savings would be amplified if these regimens are proven to be clinically equivalent.

LIMITATIONS

While we are unable to truly predict what will happen after an ED visit for asthma, decision analysis models take the best current evidence to make reasonable assumptions to inform decisions that can have significant clinical and financial effects. While these assumptions may not precisely reflect real-world findings, the effect of the model assumptions on the projected outcomes were carefully tested by sensitivity analysis, and the results were consistent. The data used in our model are based on studies from 2001 to 2004,^{10,14,16} as well as a Cochrane review from 2007.¹⁵ Although it would be ideal to have more recent data for our model, the assumptions used represent the most accurate data available at this time. Because there have not been any substantial changes to recommended asthma care over this time period, we feel that the assumptions used in our model are valid. The health care utilization costs used in this analysis are taken from South Carolina Medicaid data and may not accurately represent costs in other areas of the United States or costs for other payer populations. In addition, rates of prescription filling and medication compliance have been shown to

vary with demographic characteristics and are also likely positively correlated with the quality of asthma education. Subtle variations such as these may not have been completely accounted for in the sensitivity analyses. Our estimates regarding indirect costs (missed parental work days and parental salary) may under- or overestimate the societal cost. We believe that subtle variations in these estimates would not affect the conclusions of our study. We assumed that one dose of dexamethasone is only half as effective as two doses. This is a conservative approach and most likely underestimates the efficacy of one dose of dexamethasone, therefore underestimating the benefit of the dexamethasone arm of the decision analysis. We did not account for any additional cost of dexamethasone compounding, although our hospital pharmacy reports the charge for compounded dexamethasone is equivalent to the charge for dexamethasone tablets.

CONCLUSIONS

This decision analysis model provides evidence that the use of two doses of oral dexamethasone is both clinically more effective and cost saving when compared to a 5-day course of prednisone/prednisolone for the treatment of acute asthma exacerbations in the pediatric ED. Additionally, dispensing the second dose of dexamethasone at the time of ED discharge leads to a more substantial cost savings. While our model also predicts additional savings with single-dose dexamethasone, future studies are needed to confirm equivalent efficacy of this treatment strategy. In the meantime, this analysis strongly supports the routine use of two doses of oral dexamethasone in lieu of five doses of prednisone/prednisolone.

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