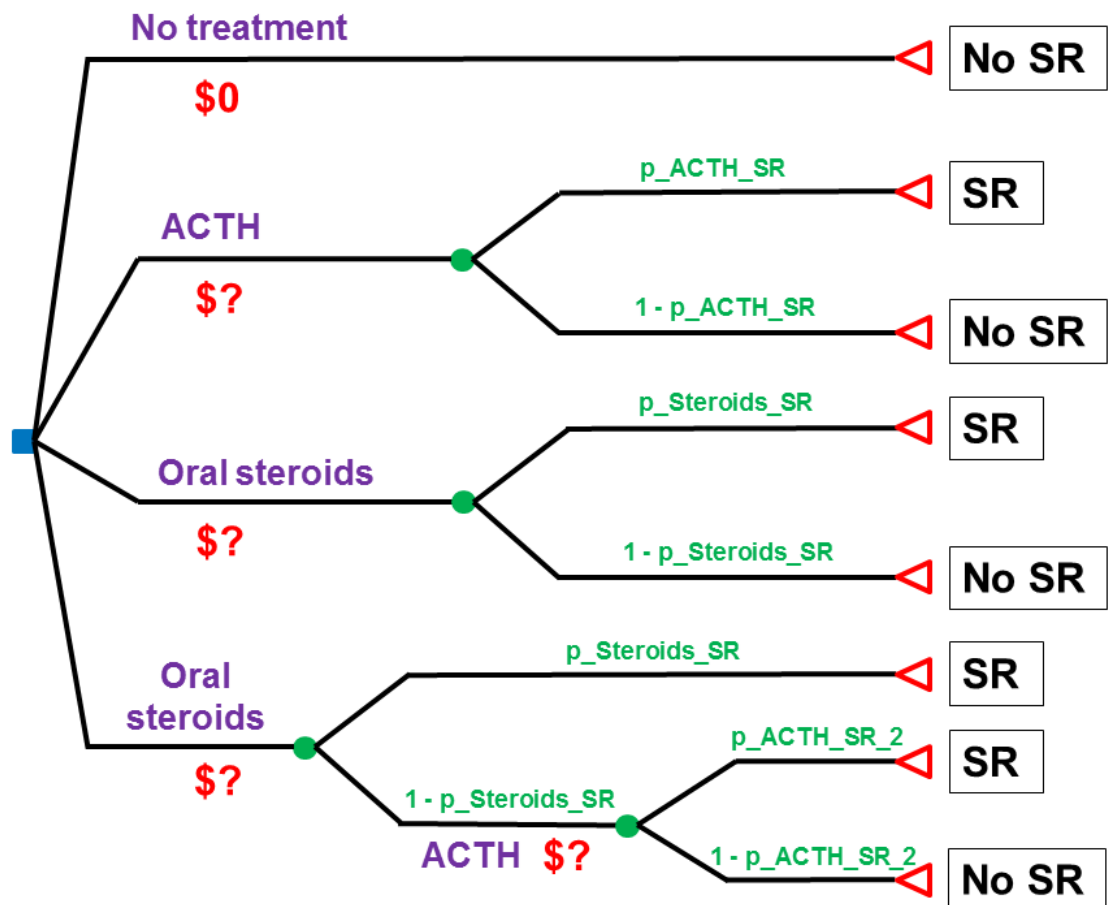


STEP-WISE STRATEGY: ORAL PREDNISOLONE \pm ACTH

Background. Adrenocorticotrophic hormone (ACTH) is several orders of magnitude more expensive than oral steroids in the USA, leading to access difficulties and delays in obtaining the medication¹. If one assumes that ACTH is marginally more effective than oral steroids, a potential strategy is a step-wise treatment: use oral prednisolone initially, but switch to a trial of ACTH if there is no spasms resolution in 2 weeks (prednisolone \pm ACTH). This or similar approaches have been previously proposed in the literature^{2,3}.



Decision tree for the comparison of individual treatments with the strategy oral steroids \pm ACTH. The caregivers of a patient with infantile spasms may consider intramuscular ACTH or oral

steroids as initial treatments or they may also consider oral steroids for 2 weeks and, if not effective, switch to ACTH. The “No treatment” option is as a zero-cost point of comparison with assumed zero effectiveness.

Legend: **ACTH:** Adrenocorticotrophic hormone. **No SR:** No spasms resolution. **SR:** Spasms resolution. **\$:** USA dollars. **?:** While the cost of “No treatment” was assumed to be zero (in the short term), the cost of ACTH and steroids need to be estimated as we did in our meta-analysis.

Probabilities: **p_ACTH_SR:** Probability that ACTH achieves spasms resolution as first treatment. **p_ACTH_SR_2:** Probability that ACTH achieves spasms resolution as second treatment (after failure of oral prednisolone). **p_Steroids_SR:** Probability that steroids achieve spasms resolution.

Data for the analysis. There is limited data on the effectiveness of ACTH after failure of prednisolone. There is some evidence that the rate of remission with first and second treatments are similar ⁴. The effectiveness of ACTH after failure of a prior treatment is based on very limited number of cases and ranges widely from 0.21⁵ to 0.6 ⁴.

Cost-effectiveness. We present the cost-effectiveness analysis for the prednisolone±ACTH strategy based on two different assumptions:

-Assuming independent probabilities, that is, that the effectiveness of ACTH after failure of oral steroids is similar to the effectiveness of ACTH on naïve patients ⁴.

-Assuming that the effectiveness of ACTH after failure of oral steroids is much lower (approximately, 0.21) than the effectiveness of ACTH on naïve patients ⁵.

Cost-effectiveness: Assumption of independent probabilities. Assuming that the effectiveness of ACTH is approximately 0.7 both as initial treatment and after failure of the initial prednisolone, and entering the data in the cost-effectiveness App for strategies at

https://bchis.shinyapps.io/cost_effectiveness_strategies/ yields the following results:

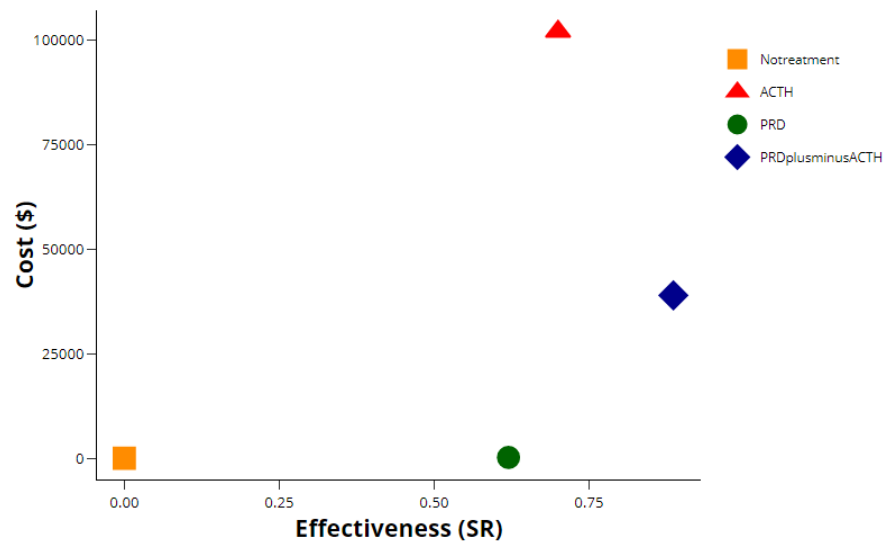
COST-EFFECTIVENESS TABLE

Names	Cost	Effectiveness	IE	IC	ICER
No treatment	0.00	0.00	0.00	0.00	NA
Prednisolone	171.00	0.62	0.62	171.00	275.81
PRDplusminusACTH	38965.96	0.89	0.27	38794.96	145845.71

*Strategies that are not cost-effective disappear from the table

Legend: IE: incremental effectiveness. IC: incremental cost. ICER: incremental cost-effectiveness ratio.

COST-EFFECTIVENESS PLOT



These results showed that ACTH was no longer cost-effective because it costed more than prednisolone±ACTH and it was less effective. The cost-effectiveness figure above showed this graphically: ACTH costed more and was less effective than prednisolone±ACTH. ACTH was “dominated”, that is, above the efficiency frontier line that would connect Notreatment, PRD, and PRDplusminusACTH.

Cost-effectiveness: Assumption of low effectiveness of ACTH as second treatment. Assuming that the effectiveness of ACTH is approximately 0.7 as initial treatment but that its effectiveness decreases to approximately 0.21 if used after failure of prednisolone and entering the data in the cost-effectiveness App for strategies at https://bchis.shinyapps.io/cost_effectiveness_strategies/ yields the following results:

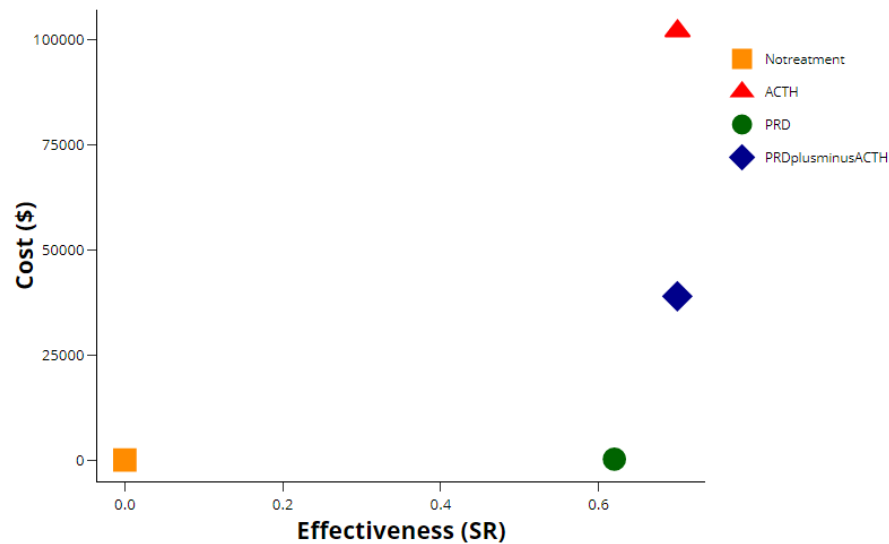
COST-EFFECTIVENESS TABLE

Names	Cost	Effectiveness	IE	IC	ICER
No treatment	0.00	0.00	0.00	0.00	NA
Prednisolone	171.00	0.62	0.62	171.00	275.81
PRDplusminusACTH	38965.96	0.70	0.08	38794.96	486152.38
ACTH	102092.00	0.70	0.00	63126.04	315630200.00

*Strategies that are not cost-effective dissappear from the table

Legend: IE: incremental effectiveness. IC: incremental cost. ICER: incremental cost-effectiveness ratio.

COST-EFFECTIVENESS PLOT



These results showed that, under that assumption, ACTH was still cost-effective, but at an ICER of \$315,630,200 per case of spasms resolved. The cost-effectiveness figure above showed this graphically: ACTH provided a slight incremental effectiveness compared to PRDplusminusACTH, but at a prohibitive incremental cost.

Conclusion. If one considers the prednisolone±ACTH step-wise treatment strategy, ACTH is either not cost-effective or in practice not cost-effective because its ICER is prohibitive.

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