

Translating Best Evidence Into Best Care

EDITOR'S NOTE: Studies for this column are identified using the Clinical Queries feature of PubMed, "hand" searching *JAMA*, *JAMA Pediatrics*, *Pediatrics*, *The Journal of Pediatrics*, and *The New England Journal of Medicine*, and from customized EvidenceUpdates alerts.

EBM PEARL: DIAGNOSIS RESULTS: PRE-TEST PROBABILITY (PTP): The PTP is the patient's disease-frequency estimate prior to performing the diagnostic test. The PTP and the diagnostic test characteristics (sensitivity and specificity or likelihood ratios) are required to calculate the post-test probability of disease. The best PTP estimate source is your local population's disease prevalence. If you do not know or are unsure, you can ask a local expert (for that particular disease). The next best approach may be to use the disease prevalence cited in a study of the diagnostic test you are interested in using. It would be important to ascertain that your patient population is not significantly different from the study's patient population. In any case, without the PTP, you will not be able to calculate the post-test probability.

LITERATURE SEARCH PEARL: BOOLEAN LOGIC: Boolean logic (named after George Boole, a nineteenth-century mathematician) in the context of searching the medical literature, refers to operators (AND, OR, NOT, all upper case in PubMed) that combine search terms to retrieve sets of citations. AND retrieves citations containing both search terms; OR retrieves citations containing one or both of the search terms. The NOT operator excludes citations containing the search term. If none of the Boolean operators are used, AND is the default operator in PubMed. PubMed operationalizes the search from left to right. Parentheses may be used to retrieve specific sets of citations. For example, bronchiolitis AND albuterol OR epinephrine will retrieve citations that contain both the bronchiolitis and albuterol search terms, as well as citations that contain the search term epinephrine (with and without the other search terms). Searching bronchiolitis AND (albuterol OR epinephrine) will retrieve citations that include bronchiolitis and at least one of albuterol and epinephrine.

—Jordan Hupert, MD

Early return to physical activity post-concussion associated with reduced persistent symptoms

Grool AM, Aglipay M, Momoli F, Meehan WP 3rd, Freedman SB, Yeates KO, et al. Association Between Early Participation in Physical Activity Following Acute Concussion and Persistent Postconcussive Symptoms in Children and Adolescents. *JAMA* 2016;316:2504-14.

Question Among children who are post-concussive, is early participation in physical activity, versus delayed participation, associated with fewer persistent post-concussive symptoms (PPCS)?

Design Prospective cohort study.

Setting Pediatric Emergency Research Canada network emergency departments.

Participants Children, age 5-18 years old.

Intervention Early versus no physical activity 7 days post concussion.

Outcomes PPCS.

Main Results Early physical activity demonstrated a lower risk of PPCS compared with no physical activity, (unadjusted) absolute risk reduction 18.9% (95%CI, 14.7%-23.0%); number needed to treat (NNT) 6 (95% CI, 5-7). Propensity score matching demonstrated similar results, NNT 9 (95% CI, 6-18).

Conclusions Early activity participation is associated with a lower PPCS rate.

Commentary This was a very well designed, large, multi-center cohort study that accounted for many factors that may affect recovery. A few days of rest in the initial days after a concussion, followed by gradual resumption of activities of daily living is the typical recommendation following concussion.¹ The physical activity that was measured in this study was physical activity at 7 days post injury. However, it is not known when these individuals initiated activity and if a few days of rest were included. Physical activity/rest was self-reported and, as the authors mention, the frequency, intensity, timing, type, and duration of activity were not known. Objective measurement of activity following concussion will enable a greater understanding of how these variables related to activity may affect recovery from concussion.² It is also important to consider cognitive rest, although there are currently no valid and widely accepted measures for cognitive rest. The results of this study are in keeping with current recommendations of reintroduction of activities of daily living after the initial few days following injury, including physical and cognitive activity.³ This is an excellent study that supports a more active approach to treatment during the initial 7 days following concussion, which is in keeping with current recommendations from the 5th International Consensus Meeting on Concussion in Sport.

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Ultrasound skin marking increases lumbar puncture success in infants

Neal JT, Kaplan SL, Woodford AL, Desai K, Zorc JJ, Chen AE. The Effect of Bedside Ultrasonographic Skin Marking on Infant Lumbar Puncture Success: A Randomized Controlled Trial. *Ann Emerg Med* 2016 Nov 14. pii: S0196-0644(16)31063-0. [Epub ahead of print.]

Question Among infants requiring lumbar puncture, what is the therapeutic efficacy of ultrasound (U/S) skin marking, compared with no U/S skin marking, in successful completion of lumbar puncture?

Design Randomized controlled trial.

Setting Pediatric emergency department, east coast US.

Participants Infants younger than 6 months of age.

Intervention U/S guided site marking or not.

Outcomes Successful first-attempt lumbar puncture.

Main Results U/S guided site marking demonstrated a higher first-attempt success rate: number needed to treat (NNT) 4 (95% CI, 3-10). The success rate within 3 attempts was also higher in the U/S group: NNT 4 (95% CI, 3-7).

Conclusions U/S guided lumbar puncture increased successful first attempt rate.

Commentary Despite the efforts of the “just-in-time” curriculum published by Kessler D et al,¹ the rate of procedural failure of lumbar punctures in infants remains high, so the results of this randomized controlled trial are extremely encouraging. The study methods were well thought out and the researchers considered the pertinent variables and limitations. There are several points that warrant additional analysis. First, the clinicians were provided with skin markings, measurements, and pictures of the spinal canal. It is not clear if the clinicians altered their technique based on the markings or on the information gleaned from spinal visualization. We recently published a similar investigation in which we concluded that lumbar puncture success was improved by marking a safe depth on the needle prior to the procedure, not the skin markings.² The benefit of U/S is likely multifactorial, but it may be important to discern which factor plays the greatest role to create the optimal procedural protocol. Second, while limiting clinicians to 3 procedure attempts was clinically reasonable, a repeat sonogram to detect the presence of

a hematoma in the “failed” patients may have allowed for additional attempts in the intervention arm and yielded better outcomes. Finally, although there was no difference in antibiotic use or hospital length of stay, the U/S arm was not only more successful, but also required fewer repeat procedures. Thus, widespread adaptation of the U/S technique should be considered, and future studies should assess its effect on disposition and overall healthcare resource utilization.

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Hormonal therapy with vigabatrin is superior to hormonal therapy alone in infantile spasms

O’Callaghan FJ, Edwards SW, Alber FD, Hancock E, Johnson AL, Kennedy CR, et al. Safety and effectiveness of hormonal treatment versus hormonal treatment with vigabatrin for infantile spasms (ICISS): a randomised, multicentre, open-label trial. *Lancet Neurol* 2017;16:33-42.

Question Among babies with infantile spasms (IS), what is the therapeutic efficacy of hormonal therapy with vigabatrin, compared with hormonal therapy alone, in spasm resolution?

Design Partially randomized controlled trial.

Setting 102 hospitals (Australia [3], Germany [11], New Zealand [2], Switzerland [3], and the UK [83]).

Participants 377 babies with IS.

Intervention Prednisolone or intramuscular tetracosactide depot with or without vigabatrin.

Outcomes Spasm resolution (no spasms between day 14-42 from trial entry).

Main Results Hormonal therapy with vigabatrin was superior to hormonal treatment alone: number needed to treat 7 (95% CI, 5-19) for spasm resolution.

Conclusions Hormonal therapy with vigabatrin is superior to hormonal therapy alone in IS.

Commentary Improving outcomes for rare diseases requires multicenter collaboration. This large randomized trial demonstrates that with time and collaboration (102 hospitals), improvement in treatment of IS can occur. Prior research from this group was not able to determine a difference between oral steroids and adrenocorticotrophic hormone (ACTH).¹ There is no consensus on which hormone treatment is most effective² and clinical care guidelines allow for the use of both.³ Side stepping this issue by allowing family choice in hormone

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