

## Translating Best Evidence into Best Care

**EDITOR'S NOTE:** Studies for this issue were identified using the Clinical Queries feature of PubMed, “hand” searching *JAMA Pediatrics*, *Pediatrics*, and *The Journal of Pediatrics*, and from customized EvidenceUpdates alerts.

**EBM PEARL: PUBLICATION BIAS:** Publication bias, one of the systematic review/meta-analysis-study methodologic validity issues, typically occurs when there is a nonrandom surplus of studies detecting, versus not detecting, statistical significance. Among reasons why “negative” studies may not be published, the most common are researchers and editors declining to publish negative studies. Conclusions drawn from publication-biased systematic reviews/meta-analyses tend to overestimate the effect size. Publication bias may be detected using both statistical and visual means. The funnel-plot method is a visual method, graphing the standard error of each study (y-axis) versus the effect size (x-axis), with higher standard error closer to the x-axis. The larger studies gather at the top of the plot and tend to group together close to the summary effect size. The smaller studies tend to have more scatter at the bottom of the plot. The result is an inverted funnel shape. If the funnel shape is not symmetric (missing some studies on the negative-result side), one presumes some studies were not published. Publication bias may be avoided by requiring registration prior to study initiation. The study by Soomro et al (see piece by Rössler and Faude on page 277 regarding *Am J Sports Med* (2015). pii: 0363546515618372) employed funnel-plot analysis to assess publication bias.

**LITERATURE SEARCH PEARL: DOCPHIN:** Docphin ([www.docphin.com](http://www.docphin.com)) is a free, personalized health-information, RSS (really simple syndication)-type network, aggregating information from journals and news sites. The “phin” in Docphin stands for personalized health information network. Physicians developed Docphin in 2010, to cull useful, specialty-specific, up-to-date information from the vast and expanding medical literature. At sign up, users can choose specialty (pediatrics is included) and university. The latter has the advantage of one-click access to full-length articles. If your university is not listed, you can request that Docphin add it. Docphin collects information from Twitter feeds and various news sites to keep you up-to-date on what your patients may be reading.

—Jordan Hupert, MD

### Adolescent injury prevention programs associated with sports-related injury reduction

Soomro N, Sanders R, Hackett D, Hubka T, Ebrahimi S, Freeston J, et al. The Efficacy of Injury Prevention Programs in Adolescent Team Sports: A Meta-analysis. *Am J Sports Med*. 2015 Dec 16. pii: 0363546515618372.

**Question** Among adolescents, what is the efficacy of injury prevention programs (IPP), compared with routine practice, in preventing sports-related injury?

**Design** Systematic review, meta-analysis.

**Setting** Amateur and club handball, basketball, and soccer teams.

**Participants** Boys and girls, average age range 11-20 years.

**Intervention** IPPs.

**Outcomes** Injury reduction rate (IRR).

**Main Results** The pooled overall IRR point estimate was 0.60 (95% CI, 0.48-0.75) controlling for hours of risk exposure, and 0.68 (95% CI, 0.54-0.84) when additionally controlling for publication bias.

**Conclusions** IPPs enhance injury reduction among adolescent sports programs.

**Commentary** Exercise-based injury prevention programs have proven to be effective in different youth team sports.

The results of several original studies provide good evidence and clearly demonstrate clinically meaningful reductions in injury rates. The responsible mechanisms still are not completely understood. They potentially relate to improvements in neuromuscular performance and proprioceptive capacity. Therefore, multimodal programs including different exercises (eg, strengthening, balancing, plyometrics) can be recommended. Whereas many studies on injury prevention in adolescents and adults have been conducted, data concerning younger children are lacking. An earlier meta-analysis on injury prevention in youth sports<sup>1</sup> included (among others) 8 out of 10 studies included in the study by Soomro et al. Given the similar databases, not surprisingly, the preventive effects (about 40% injury reduction) are comparable. Furthermore, another recent meta-analysis included randomized studies only and focused on lower extremity and knee injuries.<sup>2</sup> In general, one could ask whether multiple subsequent meta-analyses of very similar data pools and rationales are indicated and whether this enlarges the knowledge base.<sup>3</sup>

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## Autism and antidepressant use in pregnancy

Boukhris T, Sheehy O, Mottron L, Berard A. Antidepressant Use During Pregnancy and the Risk of Autism Spectrum Disorder in Children. *J Pediatr* 2016;169:76-80.

**Question** What is the association of antidepressant use during pregnancy with development of autism spectrum disorder (ASD) in the offspring?

**Design** Analysis of the prospectively assembled Quebec Pregnancy/Children Cohort database.

**Setting** Quebec, Canada.

**Participants** All pregnancies January 1, 1998, to December 31, 2009.

**Intervention** Antidepressant exposure during pregnancy.

**Outcomes** ASD among children exposed during pregnancy.

**Main Results** Antidepressant use during the second and/or third trimester was associated with an increased ASD risk; adjusted hazard ratio, 1.87 (95% CI, 1.15-3.04).

**Conclusions** Antidepressant use during the second and/or third trimester increases the risk of ASD in children, even after controlling for maternal depression.

**Commentary** Autism is a highly heritable disorder, one whose heritability overlaps substantially with other brain diseases. So, it should be no surprise that children of mothers with mood disorders are at increased risk for ASD. However, the apparent recent increase in prevalence has prompted a search for environmental contributors to risk, from air pollution to medications. The cohort study by Boukhris et al is one of at least 5 papers since 2011 investigating antidepressant exposure and ASD.<sup>1-5</sup> They find – in contrast with the majority of prior reports – a risk increase from ~0.7% to ~1.2% among children of mothers treated with antidepressants. This result reflects a total of 31 children with ASD exposed to antidepressants during the second or third trimester. Why the discordance among studies? One concern is confounding by indication – the indication for the antidepressant (ie, a brain disease) is actually the risk source. Controlling for the presence of maternal depression does not completely address this risk. Who are these other women receiving antidepressants? Indeed, the report by Boukhris et al strongly suggests that children of mothers receiving multiple antidepressants (ie, mothers likely to have more severe or difficult-to-treat illness) are at even greater risk. Once again, this suggests that the risk likely tracks with the heritable disease, not the treatment for it. In two case-

control studies from our group, we did not detect an ASD risk increase with antidepressant use after controlling for aspects of maternal illness.<sup>2,3</sup> On the other hand, psychotherapy exposure during pregnancy did increase substantially ASD risk. Short of implicating psychotherapy, this suggests the illness – not the treatment – is the source of risk.

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## Brace treatment in radiograph-negative, suspected Salter-Harris 1 ankle fractures

Boutis K, Plint A, Stimec J, Miller E, Babyn P, Schuh S, et al. Radiograph-Negative Lateral Ankle Injuries in Children: Occult Growth Plate Fracture or Sprain? *JAMA Pediatr* 2016;170:e154114.

**Question** Among children with radiograph-negative lateral ankle injury, how does the functional recovery among those with magnetic resonance imaging (MRI)-confirmed Salter-Harris type 1 fracture (SH1F) compare with those without a fracture?

**Design** Prospective cohort study.

**Setting** 2 emergency departments, one each in Toronto and Ottawa, Canada.

**Participants** Children aged 5-12 years with a clinically suspected SH1F.

**Intervention** Ankle MRI and removable brace and self-regulated return to normal activity.

**Outcomes** Primary: MRI-confirmed SH1F. Secondary: Activity Scale for Kids score at 1 month.

**Main Results** 3.0% (95% CI, 0.1% to 5.9%) demonstrated MRI-confirmed SH1F. At 1 month, the mean difference Activity Scale for Kids score of children with MRI-detected fibular fractures was not significantly different from those without fractures, -3.8% (95% CI, -1.7% to 9.2%).

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