Towards evidence based medicine for paediatricians

Edited by Bob Phillips

In order to give the best care to patients and families, paediatricians need to integrate the highest quality scientific evidence with clinical expertise and the opinions of the family. Archimedes seeks to assist practising clinicians by providing “evidence based” answers to common questions which are not at the forefront of research but are at the core of practice. In doing this, we are adapting a format which has been successfully developed by Kevin Macaway-Jones and the group at the Emergency Medicine Journal—“BestBets”.

A word of warning. The topic summaries are not systematic reviews, though they are as exhaustive as a practising clinician can produce. They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature. What Archimedes offers are practical, best evidence based answers to practical, clinical questions.

The format of Archimedes may be familiar. A description of the clinical setting is followed by a structured clinical question. (These aid in focusing the mind, assisting searching, and gaining answers.) A brief report of the search used follows—this has been performed in a hierarchical way, to search for the best quality evidence to answer the question. A table provides a summary of the evidence and key points of the critical appraisal. For further information on critical appraisal, and the measures of effect (such as number needed to treat, NNT) books by Sackett and Moyer may help. To pull the information together, a commentary is provided. But to make it all much more accessible, a box provides the clinical bottom lines.

Electronic-only topics that have been published on the BestBets site (www.bestbets.org) and may be of interest to paediatricians include:

- What is the use of smectite in acute diarrhoeal illnesses?
- Are the Ottawa ankle rules helpful in ruling out the need for x-ray examination in children?
- Can transcutaneous bilirubinometry reduce the need for serum bilirubin estimations in term and near term infants?
- What is the risk of cancer in a child with hemihypertrophy?

Bob Phillips, Evidence-based On Call, Centre for Evidence-based Medicine, University Dept of Psychiatry, Warneford Hospital, Headington OX3 7JX, UK; bob.phillips@doctors.org.uk

References
Are the Ottawa ankle rules helpful in ruling out the need for x-ray examination in children?

Report by
A Myers, K Canty, T Nelson, The Children’s Mercy Hospital and Clinics, 2401 Gillham Road, Kansas City, Missouri 64108, USA; amyers@cmh.edu
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The Ottawa ankle rules (OAR) are a set of guidelines to help the physician as to decision making regarding need for x-ray examination after ankle and mid-foot injury. A previous best evidence topic report examined whether these rules could be applied to children. At that time there was insufficient evidence to make a determination. This appraisal updates that topic.

Structured clinical question
In a child with history of ankle injury [patient] are the Ottawa ankle rules [test] reliable in eliminating the need for x-ray examination in some patients without the risk of missing fractures [outcome]?

Search strategy and outcome
Secondary sources
Cochrane—two trials that involved children were found in Central.

Primary sources
PubMed—(Clinical Queries) Ottawa ankle rules AND child.

One systematic review was found that included 27 studies, six of which were pertaining to children, two of which were the trials found in Central. Eight total prospective studies were found; six were those included in the systematic review plus two subsequent publications.

Search outcome
Eight relevant papers found. See table 1.

Commentary
The physical examination findings for the Ottawa ankle rules are as follows: tenderness over the lateral malleolus, inability to bear weight, and tenderness over the posterior distal tibia and fibula. A patient that exhibits one of these characteristics is deemed in need of x-ray examination. The OAR have been validated for use as a screening tool in adults who have sustained ankle or mid-foot injuries. Three considerations render the applicability of OAR to children less certain. Children may not be as reliable with regard to verbal history. Because Salter-Harris type I fractures, defined as a separation of bone >3 mm through the physes, more commonly accompany trauma in infants and children, point tenderness will generally be present. Further, a child must be able to walk freely prior to injury, in order for the OAR to be applied. Thus the OAR criteria will be positive and unnecessary radiographs may be obtained for an injury that will ultimately be treated the same as a sprain.

Main results
The overall sensitivity was calculated to be 97% with confidence limits of 93%–100%. The overall specificity was calculated to be 29% with confidence limits of 18%–40%.

An estimated prevalence of 12% was calculated based on the number of fractures in the studies divided by the total number of patients. The prevalence and likelihood ratio were then used to derive the PPV and NPV.

There was one article that showed five patients with negative results when applying the rules who ultimately had a fracture. All other articles had zero or 1 in this category. Using the Ottawa ankle rules has relevance in the clinical setting; as it is a tool that can be used to aid the clinician in decreasing unnecessary x-ray examinations. This may very well decrease patient care costs, as well as patient time spent in the acute care setting.

A small percentage of patients that are excluded from receiving x-ray evaluation based on the Ottawa ankle rules, will actually have a fracture. It is a low percentage of patients at 1.4%. These missed fractures will often be of little clinical significance, as many of them will represent the Salter-Harris I classification. While there may be no long term consequences to these missed fractures, each clinician must decide their comfort level in applying the rules to individual patients.

CLINICAL BOTTOM LINE
- These rules are meant to be applied to those patients who have the ability to walk prior to their injury, and can localise pain with verbal communication. (grade A)
- Negative results when applying the rules should help the physician to decrease x-ray usage without an increase in missed fractures. (grade A)
- For every 1000 patients that exhibit negative Ottawa ankle rules, 14 will actually have fractures. (grade A)

REFERENCES

10.1136/adc.2004.066647
<table>
<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Methods</th>
<th>Key results</th>
<th>Inclusion</th>
<th>Exclusion</th>
<th>Important notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boutis et al.</td>
<td>607 patients evaluated ages 3–16 years old</td>
<td>Blinded prospective study in 2 similar urban emergency departments with fellows and attending staff as participants. Instruction on the use of OAR was given by orthopedic surgeons prior to start of study</td>
<td>Sensitivity 100% (95% CI 0.96–1.00), Specificity 13% (95% CI 0.11–0.16)</td>
<td>Isolated ankle trauma within 72 hours of injury</td>
<td>Age &lt;3 years and &gt;16 years, preexisting musculoskeletal disease, coagulopathy, developmental delay, previous history of surgery or recent &lt;3 months injury of affected ankle or multi-system trauma</td>
<td>Patients were divided into low risk and high risk groups. Low risk consisted of isolated pain, tenderness, or both with or without oedema or ecchymosis of the distal fibula below the level of the joint line of the ankle. All other findings were classified as high risk. They also assessed the potential for reduction in radiographs when comparing the low risk clinical findings with those obtained by combining the Ottawa ankle rules</td>
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<tr>
<td>Chande</td>
<td>68 patients evaluated ages 2–18 years old</td>
<td>Prospective survey with 24 variables obtained by physicians; x rays were taken of all study participants with blinding of investigator as to results of x rays when applying OAR to evaluate for qualification of x ray</td>
<td>Sensitivity 100% (95% CI 0.77–1.00), Specificity 32% (95% CI 0.21–0.43)</td>
<td>All types of fractures</td>
<td>Open fractures, patients without follow up</td>
<td>Small sample size</td>
</tr>
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<td>Clarke and Turner</td>
<td>160 patients evaluated ages 0–18 years old</td>
<td>Prospective survey with 22 variables; x rays were taken on all patients with radiologists being blinded to survey results</td>
<td>Sensitivity 83% (95% CI 0.65–0.94), Specificity 50% (95% CI 0.41–0.58)</td>
<td>All types of fractures</td>
<td>Age &gt;18, intoxication, previous films, pregnancy, suspected physical abuse, open fractures, OI, metabolic disease, patient’s without phone contact, neurologic impairment</td>
<td>There was only case in a child &lt;5 years that was a true negative for rules and fracture, and no true positives</td>
</tr>
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<td>Cuello-Garcia et al.</td>
<td>111 patients evaluated ages 3–18 years</td>
<td>Prospective evaluation by paediatric nurses, third year residents, and attendings in the ER; OAR was applied, and x rays were obtained at physician discretion. Radiology was blinded to OAR results</td>
<td>Sensitivity 100% (95% CI 0.95–1.00), Specificity 6% (95% CI 0.01–0.11)</td>
<td>Salter-Harris II-V</td>
<td>Multiple trauma, &gt;7 days from event, changes in consciousness, bony disease, patients who came for reevaluation, Salter-Harris I fractures</td>
<td>Salter-Harris I fractures were not included; there were 18 of these total. Patients were followed up at one month with telephone calls, and none of the patients showed later complications or changes in the diagnosis</td>
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<td>Karpas et al.</td>
<td>190 patients evaluated ages 5–19 years</td>
<td>Blinded cross-sectional study that implemented OAR after two nurse training sessions</td>
<td>Sensitivity 96% (95% CI 0.82–0.99), Specificity 96% (95% CI 0.41–0.51)</td>
<td>Patients who presented within 48 hours of injury and all fractures</td>
<td>Open fracture, multiple traumas, developmental delay, referral with x ray, recurrent visits for the same injury in the last 2 weeks</td>
<td>Study included one patient with Salter-Harris I and negative rules</td>
</tr>
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<td>Libetta et al.</td>
<td>761 patients evaluated ages 1–15 years</td>
<td>A historical control group was included prior to the implementation of OAR in this prospective evaluation as a comparison to predict need for x ray</td>
<td>Sensitivity 98% (95% CI 0.95–1.00), Specificity 46% (95% CI 0.43–0.51)</td>
<td>Patients that had ability to walk prior to injury</td>
<td>Patients were excluded in August in order to give the staff one month to learn and implement the Ottawa ankle rules</td>
<td>Small number of children &lt;5 years old. Total of 57 children out of 761 patients. Mid-foot injuries were included in this study</td>
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<td>McBride</td>
<td>37 patients evaluated ages 9–15 years</td>
<td>Prospective survey looking at the ability of OAR to decrease need for x ray after instructing family practitioners in the ER setting on the use of these rules</td>
<td>Sensitivity 100% (95% CI 0.87–1.00), Specificity 28% (95% CI 0.14–0.39)</td>
<td>Fracture &gt;3 mm</td>
<td>Pregnancy, open injury, presentation &gt;1 week after injury, enrolment one time per patient</td>
<td>Small study, no children &lt;9 years old and only five were younger than 12 years old. This limited the issue of growth plate fractures</td>
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<tr>
<td>Plint et al.</td>
<td>670 patients evaluated ages 2–16 years</td>
<td>Patients were evaluated by staff and fellows trained in OAR at two hospital EDs; x rays were obtained based on each hospital’s practices. Data forms with physical exam findings were filled out prior to viewing the x ray. The principal investigator reviewed the data forms and made a decision regarding positive or negative OAR</td>
<td>Sensitivity 100% (95% CI 0.58–1.00), Specificity 27% (95% CI 0.11–0.42)</td>
<td>Present with injury within 48 hours, fractures &gt;3 mm</td>
<td>Salter-Harris I, nonsignificant fractures defined as &lt;3 mm, &lt;2 years old, multiple injuries, obvious open fractures, neurovascular compromise, diseases predisposing to fractures (OI), underlying disease with sensory/neural abnormalities (spina bifida), isolated injuries of the skin, patients returning for reassessment of the same injury, patients referred to the ED with x rays, intoxication</td>
<td>119 Salter-Harris I fractures, 32 nonsignificant fractures</td>
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Can transcutaneous bilirubinometry reduce the need for serum bilirubin estimations in term and near term infants?

Report by
S Thayyil, L Marriott, Addenbrookes Hospital, Cambridge, Addenbrookes Hospital, Cambridge, UK; sudhists@doctors.org.uk
doi: 10.1136/adc.2004.070292

While doing a discharge check on a 3 day old baby, a paediatric SHO notices mild jaundice and prepares to perform a serum bilirubin estimation (SBR). She explains this to the mother, who breaks into tears and asks why she would miss the level of jaundice without doing a blood test. The SHO discusses this with the neonatal consultant who mentions “We used to have a transcutaneous bilirubinometer when I was an SHO, but we stopped using it because it was inaccurate.”

A more sympathetic registrar gives you a recent review article on jaundice which indicates that the older generation bilirubinometers were shown to be inaccurate for clinical use; however, a newer version, the “SpectRx Bilicheck” may be more reliable. Bilicheck (BC) uses multiple wavelengths of light, and the manufacturer claims that the monitor is unaffected by skin pigmentation and other interfering factors.

You wonder if the Bilicheck could be safely used as a screening test for jaundice on the postnatal wards.

Structured clinical question
In term or near term healthy newborn babies [population] can transcutaneous bilirubinometry [test] when compared with serum bilirubin estimation [gold standard] accurately identify all cases of significant jaundice (i.e. >250 μmol/l)?

Search strategy and outcome
We searched PubMed under clinical queries and diagnosis using keyword “Bilicheck”, which identified three studies, all of which were of good quality. See table 2.

Commentary
We intended to use transcutaneous assessment on the postnatal ward as a screening test. It was important that the Bilicheck would not miss any significant jaundice. We arbitrarily chose 250 μmol/l (a level below which an intervention would be unlikely in term or near term babies after 24 hours). We wanted to determine if Bilicheck had a high sensitivity at this SBR level, so that babies would not need a blood test if Bilicheck value was less than 250 μmol/l. Bilirubin values were converted to SI units (μmol/l) (1 mg = 17.1 μmol/l) for easiness of comparison.

The review is confined to three good quality studies identified following a basic PubMed search. The first two studies compared Bilicheck with the internationally accepted gold standard for bilirubin estimation2-4 (that is, high performance liquid chromatography) and found that it was at least as good as laboratory method.

Even though all studies showed good correlation between the Bilicheck readings and laboratory values, it was more important to establish that no cases of significant jaundice would be missed when it is used as a screening test.

Considering bilirubin levels of >250 μmol/l as significant jaundice, it appears that Bilicheck can be used to exclude

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Table 2 Transcutaneous bilirubinometry in term and near term infants

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<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Study type</th>
<th>Outcome</th>
<th>Key results</th>
<th>Comments</th>
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<tr>
<td>Bhutani et al (2000)5</td>
<td>490 term and near</td>
<td>Prospective cohort</td>
<td>Sensitivity and specificity on comparison with gold standard bilirubinogram chart used</td>
<td>For picking up SBR &gt;256 μmol/l (95th centile)</td>
<td>Only 3.1% had SBR &gt;256 μmol/l Bilicheck was as accurate as standard laboratory measurement No babies with significant jaundice would be missed</td>
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<td>term (≥35 weeks,</td>
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<td>Sensitivity 100%, Specificity 88%</td>
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<td></td>
<td>&gt;2 kg) up to 4 days</td>
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<td>All babies with SBR &lt;40th centile had BC &lt;40th centile</td>
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<td>Gold standard = high performance liquid chromatography (HPLC)</td>
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<td>Rubaltelli et al (2001)6</td>
<td>Newborns &gt;30 weeks</td>
<td>Prospective cohort</td>
<td>Sensitivity and specificity on comparison with gold standard HPLC</td>
<td>All HPLC cut off 222 μmol/l, BC had a sensitivity and specificity of 93% and 73%, and while standard lab method had sensitivity and specificity of 95% and 76%</td>
<td>BC more accurate than standard lab SBR, especially at higher values Independent of race, gestation, and weight</td>
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<td>and &lt;28 days, 210</td>
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<td>At HPLC of 290 μmol/l BC and standard lab method had sensitivity and specificity of 90%/87% and 87%/83%</td>
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<td>infants in 6 European hospitals recruited</td>
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<td>HPLC as gold standard</td>
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<td>Samanta et al (2004)4</td>
<td>300 term and near</td>
<td>Prospective cohort</td>
<td>Sensitivity and specificity on comparison with gold standard</td>
<td>91% sensitivity and 66% specificity in diagnosing significant jaundice (i.e. &gt;250 μmol/l)</td>
<td>55% reduction in blood sampling would have occurred if Bilicheck was used as a screening tool. 5 babies with significant jaundice (&gt;250 μmol/l) were missed. But all the 5 had SBR &lt;300 μmol/l</td>
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significant jaundice and therefore reduce the number of serum bilirubin estimations. It is unlikely that the sensitivity of Bilicheck would be 100% in clinical practice; however, by using a low cut off for estimating serum bilirubin, the false negatives would be still well below the levels associated with neurotoxicity. Bilicheck has been shown to have similar efficacy in a wide range of ethnic groups.

Since we wanted to examine the use of Bilicheck in postnatal wards, this review is confined to only term and near term babies. There are insufficient data to support the routine use of Bilicheck on babies receiving phototherapy at present.

**REFERENCES**


**What is the risk of cancer in a child with hemihypertrophy?**

**Report by**

P Abraham, Barnsley Hospital NHS Foundation Trust, Gawber Road, Barnsley S75 2EP, UK; philipabrahamuk@yahoo.co.uk
doi: 10.1136/adc.2005.082792

You have a 4 year old girl with hemihyperplasia limited to the left leg in your clinic come for review. This child was originally referred to your clinic a few weeks back after her mother noticed leg length discrepancy when she bought a new pair of trousers. You notice asymmetry between the two legs, with the left leg larger and longer than the right. An orthopaedic surgeon was consulted, who ruled out a hip problem and suggested the possibility of hemihyperplasia of the left leg. There is an increased risk of cancer, especially of Wilm’s tumour in children with Beckwith-Wiedemann syndrome (BWS)/idiopathic hemihypertrophy (HH). Asymmetric overgrowth of unknown aetiology may involve the whole of one side of the body or it may be limited in extent to one limb or a side of the face. There may be associated asymmetric hypertrophy of internal organs. The reported incidence of hemihyperplasia is 1 in 86 000 live births.

Hemihypertrophy or hemihyperplasia is well known, but the exact risk is not well documented. Green and colleagues reported that only in one third of cases of children with Wilm’s tumour and hemihyperplasia, was the hyperplasia diagnosed more than a month prior to the discovery of the tumour. The case series by Choyke and colleagues concluded that children with BWS/HH may benefit from screening abdominal ultrasound scans at intervals of four months or less. The only multicentre prospective study looking at the risk of tumour development and follow up of children with hemihyperplasia was the one carried out by Hoyne and colleagues. In this study, of the total 168 children with isolated hemihyperplasia, 10 tumours developed in nine children (one child developed two tumours). Of these, six were Wilm’s tumour, two were adrenal cell carcinoma, and there was one each of hepatoblastoma and leiomysarcoma of the small bowel. Follow up protocols varied in different centres. Two children, an infant and a 5 year old, developed Wilm’s tumours at nine month and five months respectively after their previous abdominal ultrasound scan. This led the investigators to conclude that six months may be too long a screening interval, especially in early childhood.
Hence from the available evidence, the risk of tumour development in isolated hemihyperplasia is about 1 in 20 or approximately 5%. The best follow up plan on the basis of available evidence is that till the age of 6 years these children should have abdominal ultrasound scans at three monthly intervals. There is currently insufficient evidence to screen children above 6 years of age.

REFERENCES

Table 3  Follow up and outcome of children with hemihyperplasia

<table>
<thead>
<tr>
<th>Citation</th>
<th>Patient group</th>
<th>Study type</th>
<th>Outcome</th>
<th>Key results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hoyme et al (1998)³</td>
<td>168 children</td>
<td>Prospective multicentre study of incidence of neoplasia and follow up over 10 year period</td>
<td>Tumour development on follow up abdominal ultrasound</td>
<td>Tumour incidence 5.9% (95% CI 2.3%–8.2%) compared to 0.17% in general population; follow up protocol varied among respondents; mostly abdominal palpation 6–12 monthly and USS abdomen 6 monthly</td>
<td>Prospective multicentre study, over 10 year period. Relatively large number of patients (with a rare condition). No control group. Varied follow up protocols, varied duration of follow ups; tumour surveillance protocol suggested; abdominal USS 3 monthly till 6 years of age and 6 monthly afterwards until puberty.</td>
</tr>
<tr>
<td>Choyke et al (1999)⁵</td>
<td>74 children</td>
<td>Case series comparing late stage Wilm’s tumour in patients with BWS/HH who are screened with ultrasound scans (4 monthly) against those who are not screened</td>
<td>Follow up sonograms; tumour development</td>
<td>None of the screened (n = 14) had late stage (stage III or IV) Wilm’s tumour whereas 25 out of the 59 unscreened had late stage disease; benefit from sonograms at intervals of 4 months or less</td>
<td>Case series Both BWS and HH included in the study and hence difficult to correlate risk of tumour development and screening to isolated HH alone. Small sample size, especially the screened group.</td>
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</table>

CLINICAL BOTTOM LINE
- Risk of tumour development in children with isolated hemihyperplasia is 5.9%. (95% CI 2.3%–8.2%); approximately 5% or 1 in 20. (grade A)
- The best follow up plan for these children is to do abdominal ultrasound scans at three monthly intervals until the age of 6 years. (grade C)
- Further clinical trials are needed to find the benefit of screening children older than 6 years of age as there is currently insufficient evidence to justify screening these children.
Can transcutaneous bilirubinometry reduce the need for serum bilirubin estimations in term and near term infants?

S Thayyil and L Marriott

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