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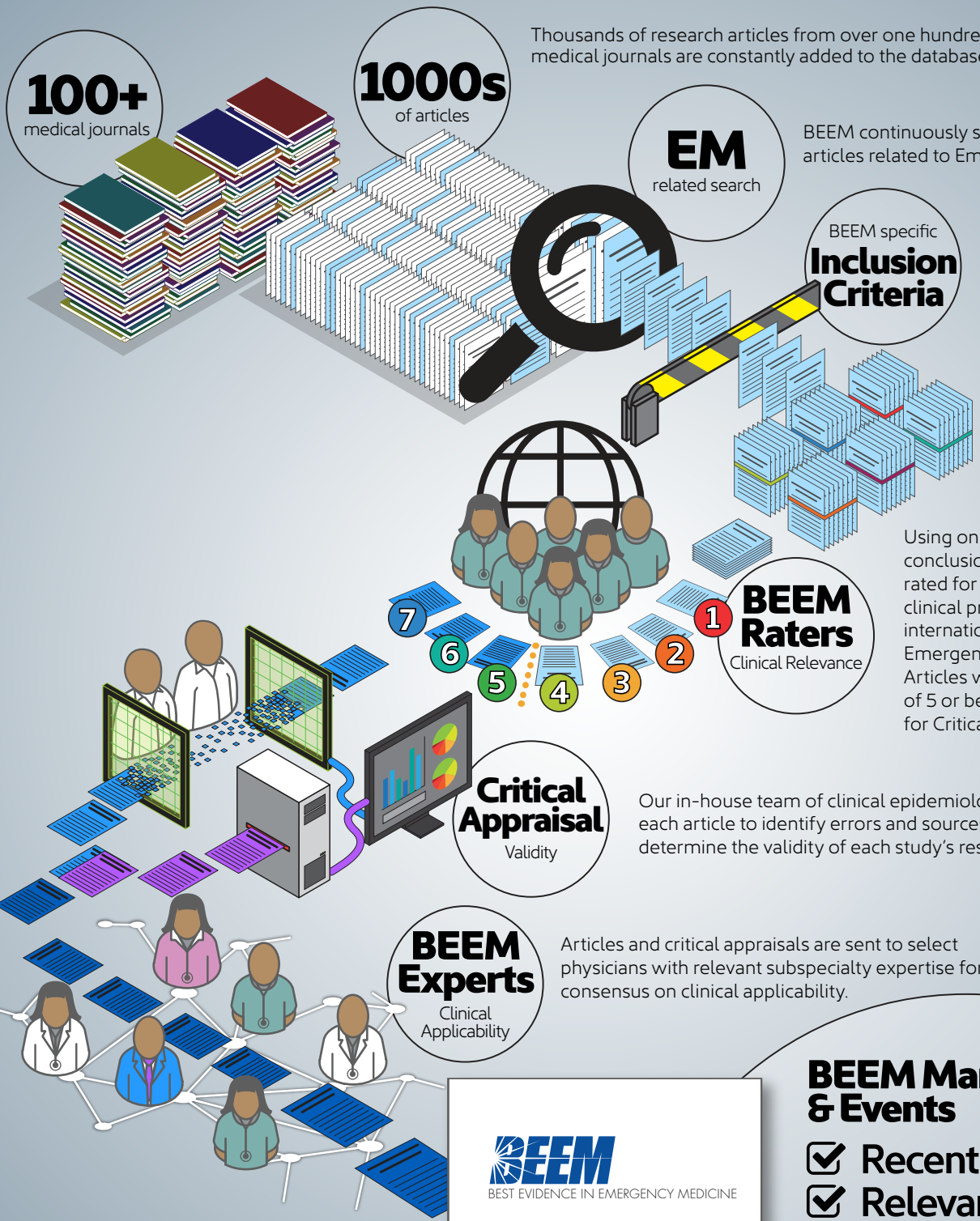
The BEEM Process

Identifying the Best Evidence



Thousands of research articles from over one hundred medical journals are constantly added to the database.

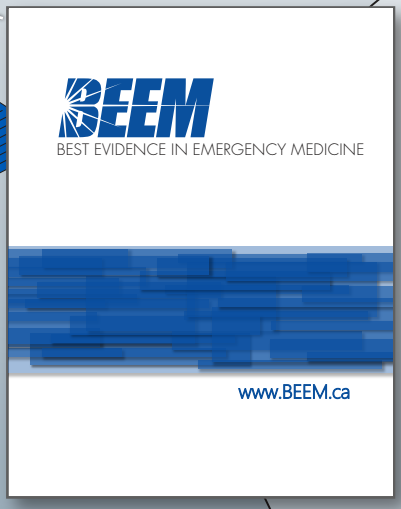
BEEM continuously scans for the latest articles related to Emergency Medicine.

Articles meeting the inclusion criteria are sorted by discipline and study design.

Using only their titles and conclusions, articles are rated for their relevance to clinical practice by BEEM's international network of Emergency Physicians. Articles with a median score of 5 or better are selected for Critical Appraisal.

Our in-house team of clinical epidemiologists appraises each article to identify errors and sources of bias and determine the validity of each study's results.

Articles and critical appraisals are sent to select physicians with relevant subspecialty expertise for consensus on clinical applicability.



BEEM Manual & Events

- ☑ Recent
- ☑ Relevant
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The best evidence-based guidance for clinical practice in Emergency Medicine

Best Evidence in Emergency Medicine (BEEM)

About BEEM

Founded in 2004, Best Evidence in Emergency Medicine (BEEM) is an international knowledge translation project and collaboration of academic emergency physician researchers and educators from around the world. The objective of BEEM is to find and appraise emergency medicine-related studies of the highest levels of evidence that have the most impact on emergency medicine clinical practice to provide emergency medicine practitioners with the best clinical evidence to optimize patient care.

The BEEM Process

BEEM conducts continuous multiple source searches of 1,000s of articles from more than 100 medical journals for research studies and clinical practice guidelines related to emergency medicine. Articles meeting the BEEM selection criteria (noted further below) are sent to BEEM Raters, a group of Emergency Physicians from around the world that assess each study on its clinical relevance using the validated and reliable BEEM Rater Score. BEEM's team of experts in health research methodology and biostatistics appraise the studies with the highest BEEM Rater scores, producing the highest quality and most reliable critical appraisals. In addition, emergency medicine experts from around the world are invited to write the BEEM Bottom Line, a summary of the impact of the original research study on emergency medicine practice.

The BEEM critical appraisal process allows for the most comprehensive article review. Because BEEM's editorial staff and authors have no ties to industry or conflicts of interest that bias them in their assessments, BEEM has no obligation to favorably appraise any article based on the sponsor, the author, or the primary journal. This results in the most recent, relevant, reliable, and unbiased single source of practice-changing clinical evidence for emergency physicians.

BEEM Article Selection Criteria

Therapy Study: randomized controlled trials of human patients, systematic reviews of randomized controlled trials of human patients, and clinical practice guidelines based on systematic reviews

Harm Study: randomized controlled trials of human patients, systematic reviews of randomized controlled trials of human patients, prospective cohort studies, and case control studies

Diagnostic Study: level five and demonstration of patient outcome efficacy

Clinical Practice Guidelines: based on systematic reviews

Clinical Decision/Prediction Rules: minimum level two (i.e., rules that can be used in various settings with confidence with accuracy)

Dear BEEM Attendee,

BEEM is a well-established conference that is designed to provide you with the highest levels of evidence for high impact articles related to the practice of Emergency Medicine. The sessions are categorized in different areas to cover a breadth of papers that include trauma, critical care, pediatrics, infectious diseases and cardiology to name a few. Each article is reviewed using the BEEM critical appraisal methodology to equip you with an unbiased critique.

During the conference, you will learn from experts in the field of Emergency Medicine and critical appraisal / methodology. You will have multiple opportunities to interact with the other participants as well as faculty. Please feel free to ask them any questions you have.

Sincerely,

Dr. Rahim Valani
Chair, BEEM

Dr. Suneel Upadhye
Co-Chair, Ski BEEM

Dr. Marcel Emond
Co-Chair, QueBEEM

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BEEM BITs

Research Question

What are the latest recommendations for ED low-risk abdominal pain?

BEEM Bottom Line

Why is this study important? Low risk recurrent abdominal pain (LRRAP) is a common and diagnostic resource-intensive/costly ED problem. Patients are often subjected to repeated imaging studies, and pain is treated invariably poorly.

What, if any, threats to validity are most likely to have an impact on the results and how? The paucity/absence of direct evidence to answer CPG PICOT questions leads to "Conditional" Recs that may not significantly influence ED practice.

How do the key results compare with the current evidence? The evidence base (published in accompanying scoping & systematic reviews) is very thin and lacking direct evidence to inform GRADE tables for CPG Recs. Conditions explicitly addressed in other specialty CPGs (eg. surgery, urology, gastroenterology, OBGyne, etc.) also excluded.

How should this study impact the care of ED patients? The current evidence for imaging and treating recurrent low risk abdominal pain is rather weak and indirect, although some clear inequities in imaging and analgesia rates are identified (women, black/Hispanic patients) which ideally should be rectified by use of standardized care-paths.

Study Summary

Article	Broder JS, Oliveira J E Silva L, Bellolio F, Freiermuth CE, Griffey RT, Hooker E, Jang TB, Meltzer AC, Mills AM, Pepper JD, Prakken SD, Repplinger MD, Upadhye S, Carpenter CR. Guidelines for Reasonable and Appropriate Care in the Emergency Department 2 (GRACE-2): Low-risk, recurrent abdominal pain in the emergency department. Acad Emerg Med. 2022 May; 29(5):526-560. Doi: 10.1111/acem.14495.
Design	Clinical Practice Guideline
Population	***Included:*** Adult patients with multiple ED visits recurring over a period of months/years, with similar clinical presentations. ***Excluded:*** Children, adults with abnormal vital signs, clinical findings significant for acute abdominal pathology, or other risk factors for serious abdominal disease. Also not intended for new/acute presentations with a only short-term recurrence. Patients not previously evaluated for similar abdominal pain in ED.
Scope of Recs	CPG intended for ED physicians/clinicians who evaluate adult patients with LRRAP. Recs targeted for ED physicians in USA with access to advanced diagnostic imaging, lab tests and specialty referral.

Key Recommendations (LoE = Level of Evidence)

Recommendation (Strength, LoE)
Recommendation 1: In adult ED patients with low-risk, recurrent, undifferentiated abdominal pain and prior negative computed tomography of the abdomen and pelvis (CTAP) within 12 months, there is insufficient evidence to accurately identify populations in whom repeat imaging can be safely avoided or routinely recommended in the ED. **(No recommendation) [No evidence]** ***Recommendation 2***: In adult ED patients with low-risk, recurrent, undifferentiated abdominal pain and a negative CTAP with IV contrast in the ED, we **suggest against ultrasound** unless there is concern for pelvic or biliary pathology. (**Conditional recommendation, against**) **[Very low certainty of evidence]** ***Recommendation 3***: In adult ED patients with low-risk, recurrent, undifferentiated abdominal pain, we **suggest screening for depression and/or anxiety** may be performed during the ED evaluation. **(Conditional recommendation, either) [Very low certainty of evidence]** ***Recommendation 4:*** In adult ED patients with low-risk, recurrent, undifferentiated abdominal pain, we **suggest an opioid-minimizing strategy** for pain control. **(Conditional recommendation, for) [Consensus, no evidence]**

BEEM Critique

Risk of bias assessment (amalgamated from AGREE-II/NEATS instruments)

	A1	A2
1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.	✓	✓
2. Financial conflicts of interest of guideline development group (GDG) members have been disclosed and managed.	✓	✓
3. The CPG development group includes all of the relevant multidisciplinary stakeholders, including clinicians, methodologists and patients/caregivers. **One very engaged patient participant, and board-certified psychiatrist with pain management experience.**	✓	✓
4. The CPG objectives, health questions, scope of relevant providers and target recipients of care are clearly defined.	✓	✓
5. Values/preferences of patients, caregivers, advocates and/or the public with experience with the clinical disease management has been sought/integrated into CPG development (reported clearly).	✓	✓
6. The search strategy for evidence is thoroughly developed and described. **2 published support SR's**	✓	✓
7. The criteria for selecting relevant studies/evidence are clearly described.	✓	✓
8. The quality, strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.). Summaries of evidence tables are provided.	✓	✓
9. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
10. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
11. The strength of recommendations is clearly reported, including confidence in underlying evidence.	✓	✓
12. Recommendations are clear and unambiguous, and easily identified in the CPG publication.	✓	✓
13. Different options for management for managing the health questions are clearly presented.	✓	✓
14. Experts externally reviewed the guideline prior to its publication.	✓	✓
15. The CPG describes a procedure to update the guideline.	X	✓
16. The CPG provides advice, tools and/or clinical pathways for easy adoption/adaptation into practice.	X	
17. The CPG describes barriers and facilitators to implement recommendations.	✓	✓
18. Performance metrics for monitoring implementation of recommendations for audit/feedback have been defined appropriately. **Unable to define QI PMs due to insufficient evidence.**	X	X
19. Resource implications for implementing CPG recommendations have been discussed.	✓	✓

A1 = S. Upadhye A2 = E. Lang

Funding and conflicts of interest

Funding	Reported; funding by Society for Academic Emergency Medicine (SAEM)
Conflict of interest	Reported; no conflicts of interested declared

Potential threats to viability

Development	*Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible?* Recs supported by 3 separate systematic reviews, and followed GRADE methods.
Presentation	*Well organized with easy to find recommendations?* Key Recs summarized at beginning of document.
Comprehensive	*Was the information to inform decision-making complete?* Yes; each Rec is fully discussed re: literature searches, benefits, harms, radiation risks and system/societal costs.
Clinical Validity	*Are the recommendations clinically sound and appropriate for the intended patients?* Yes; benefits and harms of following Recs discussed in context of individual patients, health care systems. "Low-risk" and "recurrent" groups defined with widest inclusive definitions to optimize equity concerns; higher-risk populations defined in Table 1.

Administrative details

Key words	Abdominal pain, analgesia, anxiety, computed tomography, depression, emergency department, low-risk, opioid, recurrent, ultrasound
Reference(s) Supporting evidence reviews, editorials.	1) Oliviera J. e Silva L, Prakken SD, Meltzer AC, Broder JS, Gerberi DJ, Upadhye S, Carpenter CR, Bellolio F. Depression and anxiety screening in emergency department patients with recurrent abdominal pain: An evidence synthesis for a clinical practice guideline. Acad Emerg Med 2021; PMID: 34665903 DOI: 10.1111/acem.14394 2) Carpenter CR, Griffey RT, Mills A, Doering M, Oliveira J eSilva L, Bellolio F, Upadhye S, Broder JS. Repeat computed tomography in recurrent abdominal pain: An evidence synthesis for guidelines for reasonable and appropriate care in the emergency department. Acad Emerg Med 2022; 29(5): 630-648. DOI: 10.1111/acem.14427 3) Carpenter CR, e Silva LOJ, Upadhye S, Broder J, Bellolio F. A candle in the dark: The role of indirect evidence in emergency medicine clinical practice guidelines. Acad Emer Med 2022; DOI: 10.1111/acem.14494.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	****Author (Methodologist) for this publication**
Eddy Lang MDCM CCFP(EM) FCAHS *Professor and Department Head, University of Calgary*	**No conflicts of interest**

Research Question

What are the most effective interventions to reduce low-value emergency department (ED) computed tomography (CT) scanning?

BEEM Bottom Line

Why is this study important? CT scans have been ordered with increasing frequency during ED visits thereby prolonging ED length-of-stay, increasing healthcare costs, increasing the risk of over-diagnosis/treatment, and radiation exposures, and without necessarily adding high-value information for patient care. This study reviews interventions to reduce low-value CT scanning.

What, if any, threats to validity are most likely to have an impact on the results and how? High heterogeneity of included studies precludes pooling of outcome measures into a summary effect estimate. Not all studies reported clinical balancing measures to fully explore consequences of CT scanning reductions (e.g., ED revisits, missed disease rates/complications, death).

How do the key results compare with the current evidence? This study is congruent with prior knowledge translation/ quality improvement (QI) studies (e.g., Choosing Wisely) where multimodal and multidisciplinary initiatives have the best likelihood of reducing low-value care.

How should this study impact the care of ED patients? ED initiatives to reduce low-value CT scanning should engage multiple (specialty) stakeholders and produce diagnostic pathways (with alternative test choices) using QI performance measures amenable to audit and feedback.

Study Summary

Article	Dunne CL, Elzinga JL, Vorobiechik A, Sudershan S, Keto-Lambert D, Lang E, Dowling S. A Systematic Review of Interventions to Reduce Computed Tomography Usage in the Emergency Department. Annals Emerg Med 2022; DOI:10.1016/j.annemergmed.2022.06.001
Design	Systematic Review; registered with the International Prospective Register of Systematic Reviews (CRD42020182896)
Population	***Included:*** All ED adult/pediatric patients undergoing diagnostic CT scanning ***Excluded:*** Observational studies without reduction interventions, or in/outpatients (not ED-based).
Intervention	ED-based interventions to reduce CT utilization
Comparison	Concurrent/historic cohorts not receiving reduction interventions
Outcomes	***Primary:*** Difference in CT scan proportions ***Secondary:*** Various subgroups defined *a priori*
Key Results	**149 studies included. Most studies from USA (78%), singles sites (74.5%) or tertiary care centers (75%). Majority of interventions aimed at reducing overall CT imaging (75.2%).** Single interventions 63.1%, multimodal 36.9%. Most studies targeted scans of the head (38.3%) or abdomen/pelvis (28.2%); Table 3. ***Primary (data not pooled):*** a) Highest impact single interventions = implementing diagnostic pathways [-86.4 to +8.6%] , increasing alternative test availability (e.g., US, blood, etc.) [-65.1 to -14.7%], and involving specialists in advanced decision-making [-63.0 to -14.7%]. b) Highest multimodal interventions = Diagnostic pathway + CDSS* [-100.0 to -7.7%], Pathway + CDSS + feedback [-66.3 to -7.9%] Higher CT relative reduction with multidisciplinary-led (vs ED-led alone) interventions (Fig 4A) CT reductions did not lead to a spike in adverse balancing measures reported (e.g., ED revisits/ readmissions, missed/delayed diagnoses, disease complications or death); reported in 43.6% of included studies. For ED length of stay reported (17.4% included studies), there was no difference 46.2%, decreased ED LOS (38.5%) or increased (15.4%).

*CDSS = computerized decision support systems

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Appendix Supp 1; English-language only.**	✓	✓
3. The search for studies was unbiased and reproducible. **Single searcher?**	?	?
4. The selection of studies was unbiased and reproducible. **Duplicate independent searches; agreement "moderate" for abstract & full-text screening (kappa 0.64 & 0.60 respectively).**	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **4 researchers**	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible. **GRADE – Use of Cochrane RoB (RCTs) or ROBINS-I (non-randomized studies); 4 independent ratings**	✓	✓
7. The quality of the primary studies is high.	X	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	X

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Reported; funding by Alberta Health Services Emergency Strategic Clinical Network 2020 systematic reviews grant. No role in study design, data collection/analysis, or manuscript preparations.
Conflict of interest	Reported; no conflicts of interest declared.

Potential threats to viability

Chance	None.
Selection bias	Authors used funnel plots/Egger tests to assess for possible publication bias; none detection.
Measurement bias	Majority of RCTs had "concerning" ROB, non-RCTs had "serious/critical" RoB.
Analysis bias	Random effects analyses for all outcomes. Heterogeneity high (I^2 75-90% for all interventions studied).
Confounding	Studies selected with missing data were excluded if unable to get relevant data from contacting corresponding author. Certainty of GRADE evidence "Very Low" for all interventions reviewed. Some studies may have been misclassified by category. Lack of balancing measures reported in 50% of studies. No information re: CT radiation dose reductions provided.

Administrative details

Key words	Computerized tomography, emergency department, reduced utilization
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc, FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**
Andrew Worster, MD, MSc Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University	**No conflicts of interest (ICMJE)**

Research Question

What is the safety & efficacy of a diagnostic algorithm using pretest clinical probability and D-dimer thresholds to exclude Deep Vein Thrombosis (DVT)?

BEEM Bottom Line

Why is this study important? This study refines low and moderate risk categories for DVT based on Wells scores + D-dimer results, and can help to avoid unnecessary ultrasound (US) scans and or oral anticoagulants (OAC).

What, if any, threats to validity are most likely to have an impact on the results and how? Some specific subgroups were under-represented, so firm conclusions cannot be drawn on these patients. The primary outcome results, however, are robust and reliable.

How do the key results compare with the current evidence? This work further solidifies the approach to the low risk (as determined by pretest probability [PTP] assessment) patient with negative D-dimer (<1000ng/ml), but couldn't reinforce the cutoff of <500mg/ml for moderate PTP patients due to lower outcome events in this subgroup. This reinforces prior risk stratification work for pulmonary embolism (PE) (Kearon 2019).

How should this study impact the care of ED patients? Applying the Wells criteria with appropriate D-dimer testing thresholds can allow clinicians to safely exclude DVT, reduce low-value US scans, and avoid unnecessary OAC.

Study Summary

Article	Kearon C, de Wit K, Parpia S, Schulman S, Spencer FA, Sharma S, Afilalo M, Kahn SR, LeGal G, Shivakumar S, Bates SM, Wu C, Lazo-Langner A, D'Aragon F, Desahies JF, Spadafora L, Julian JA, on behalf of the Designer D-Dimer Deep vein thrombosis (4D) Study Investigators. BMJ 2022;376:e067378 http://dx.doi.org/10.1136/bmj-2021-067378
Design	Prospective Diagnostic Mgt Study. Registered with ClinicalTrials.gov NCT02038530.
Population	***Included:*** Adult patients presenting to ED (or output clinics) with DVT signs/symptoms. ***Excluded:*** Patients with a known D-Dimer prior to clinical pre-test probability (PTP) assessment, already on oral anticoagulants (OAC) for >24hrs (any indications), prior DVT Dx, age <18yo, pregnancy, suspected pulmonary embolism (PE), expected mortality <90days, geographically inaccessible for follow-up, or venous US contrary to study protocol.
Exposure	DVT diagnostic (4D) algorithm
Comparison	N/A
Outcomes	***Primary:*** Incidence of symptomatic objectively verified VTE (proximal DVT, PE), or death at 90days. ***Secondary:*** Incidence of VTE in subgroups: Low PTP + DD<1000ng/ml, or Mod PTP + DDimer<500ng/ml. Overall death rate, US scans avoided by 4D algorithm.
Key Results	**1508 patients included for analysis; 58% female, mean age 60yo. Eight pts lost to follow-up (0.5%).** **Pretest Probabilities:** Low 529 (35%), Mod 649 (43%), High 330 (22%). **Prevalence of DVT:** Low PTP 2%, Mod PTP 12%, High PTP 27% ***Primary:*** 1275pts (85%) who had 4D exclusion of DVT and no OAC Rx, 8 had a subsequent DVT (0.6%, 95%CI 0.3-1.2%). **Upper limit 95%CI <u>below</u> pre-specified safety margin of 2% miss rate with 4D algorithm.** ***Secondary subgroups:*** 1) Low PTP + neg DDimer (<1000ng/ml), no OAC Rx (374pts): 1pt had a DVT in 90d (0.3%). 2) Mod PTP + neg DDimer (<500ng/ml), no OAC Rx (197pts): 0pts with DVT. 3) Low/Mod PTP + positive DDimer, no OAC Rx (414pts): 3pts with DVT (0.7%). 4) High PTP + neg US + D-dimer <1500ng/ml, no OAC Rx (148pts): 0pts with DVT. 5) 18 deaths during follow-up period; none attributed to VTE. ***Ultrasound Usage:*** Mean scans 4D algorithm = 0.72 per pt, vs 1.36 conventional algorithm. Absolute reduction = -0.64 scans per pt (relative difference 47%). %Difference in US needed with 4D vs conventional algorithm = -19.7% absolute, -24% relative.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were selected consecutively or randomly (i.e., without bias). **10 Cdn university clinical centres.**	✓	✓
2. The patients were representative of those with the problem.	✓	✓
3. The patients were sufficiently homogeneous with respect to prognostic risk.	✓	✓
4. The outcome criteria were clinically appropriate for the research question.	✓	✓
5. The outcome criteria were explicit. **Predefined outcomes criteria.**	✓	✓
6. The outcome criteria were applied without bias. **Blinded central adjudication.**	✓	✓
7. The follow-up was complete.	✓	✓
8. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Reported; Funding from CIHR & endorsed by CANVECTOR network. No role in study design, execution, data analysis nor publication.
Conflict of interest	Reported; no conflicts of interest declared.

Potential threats to viability

Chance	Sample size met for primary outcome; not met for some of the secondary subgroup analyses. Some physician discretion may have influenced patient enrollment.
Selection bias	Sample size 1500 met; no evidence of bias.
Measurement bias	None.
Analysis bias	Data-driven.
Confounding	Residual confounding as with all observational studies because of unknown prognostic factors that cannot be controlled for. All participating hospitals allowed to use their own D-dimer assays (after protocol revised away from a single standardized test).

Administrative details

Key words	Diagnostic algorithm, deep vein thrombosis, D-dimer, emergency department
Reference(s)	Kearon C, de Wit K, Parpia S, et al, PEGeD Study Investigators. Diagnosis of Pulmonary Embolism with d-Dimer Adjusted to Clinical Probability. N Engl J Med 2019;381:2125-34. doi:10.1056/NEJMoa1909159.

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc, FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**
Andrew Worster, MD, MSc *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**

Research Question

Does a scheduled follow-up telephone call 2 days after ED discharge reduce ED revisits at 7days?

BEEM Bottom Line

Why is this study important? Reducing emergency department (ED) revisits can reduce health systems costs, patient volumes, treatment delays and mortality. Interventions to reduce such visits, such as post-discharge telephone follow-up calls, can improve revisit rates and potentially improve compliance with follow-up plans and patient satisfaction.

What, if any, threats to validity are most likely to have an impact on the results and how? This is a nonrandomized trial conducted at a single, urban ED on a patient population with special social/housing insecurity needs while excluding those without telephone services. The results are subject to multiple biases as well as a high lost-to-follow-up rate.

How do the key results compare with the current evidence? Prior research on telephone follow-ups after ED discharge have shown mixed results on ED revisit rates, and potentially costly (Biese 2022). Targeting the proper ED transition care targets can lead to improved outcomes.

How should this study impact the care of ED patients? Timely follow-up calls after ED discharge can avoid near-future ED revisits.

Study Summary

Article	Fruhan S, Bills CB. Association of a Callback Program with Emergency Department Revisit Rates Among Patients Seeking Emergency Care. JAMA Netw Open. 2022 May 2;5(5):e2213154. doi: 10.1001/jamanetworkopen.2022.13154.
Design	Prospective QI Intervention cohort.
Population	***Included:*** All ED patients seen during study period & discharged from ED, left AMA or prior to formal discharge. ***Excluded:*** Patients without a valid telephone number, admitted to hospital, transferred to another inpatient facility/jail or left prior to ED triage or being seen by ED physician.
Exposure	Telephone follow-up call at 2 days.
Comparison	"Usual" post-discharge care.
Outcomes	***Primary:*** ED revisit within 7 days of index. ***Secondary:*** ED return visit within 72 hours, within 7 days resulting in hospital admission, and patient care perceptions (4 quality questions asked at 14 days) Subgroup: Responders at 2days vs all patients enrolled (including nonresponders). Exploratory analyses based on days of random calls, and past frequent ED users (3+ visits in past 6months).
Key Results	**15688 patient encounters during 10-week study period;** 10500 ED discharges, 186 left AMA, 262 left prior to final discharge. 4720 admitted/transferred/LWBS. 8110 patients recruited for 2d phone f/u; 4460 male (55%), mean age 40.5yo. Hispanic 41%, black 22%. English language 75%. Homeless/insecure housing 13%. **2d callback:** 2958 (36.5%) reached, 5152 pts (63.5%) did not. 328/2958pts requested a phone f/u, and 224 (68.3%) successfully reached. Interventions undertake for 115/224 = help with f/u appts (64%), meds support (32%), Dx/Tx treatments (62%) and discharge clarification (52%). **14d callback:** 8110pts contacted, 1876 successfully reached (21%), 1438 (77%) completed questions. ***Primary:*** Lower rates of ED return visits for those called at 2d vs non-called: - 72hr return rates: called 4.6% vs non-called 6.2% (p=0.03) - 7d return rates: called 7.6% vs non-called 10.3% (p=0.03) Call benefit retained after exploratory subgroup analysis for intervention day. Fewer ED revisits in those with 2d calls in the "frequent users" group: 72hrs OR 0.50 (95%CI 0.32-0.80) and 7d OR 0.49 (0.34-0.71). No significant difference in ED visits for non-frequent users' subgroup. ***Secondary:*** No difference of 2d calls on hospital admissions (regardless of prior ED visit frequency); Table 4. No significant difference for patient care perceptions; those reached were significantly more likely to understand the care received than those who didn't.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were selected consecutively or randomly (i.e., without bias). **Non-random days of intervention during study period.**	X	X
2. The patients were representative of those with the problem.	✓	✓
3. The patients were sufficiently homogeneous with respect to prognostic risk.	✓	✓
4. The outcome criteria were clinically appropriate for the research question.	✓	✓
5. The outcome criteria were explicit.	✓	✓
6. The outcome criteria were applied without bias.	✓	✓
7. The follow-up was complete.	X	X
8. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Reported; support by UCSF Hospital Liability grant. No role in project design, execution, data analysis, or manuscript preparation.
Conflict of interest	Reported; none declared.

Potential threats to viability

Chance	Calls on non-random days (1/3 of total study period); risk of biased sampling. Exclusion of those without telephones can introduce selection bias.
Selection bias	Single site sampling with predominantly urban indigent population with high frequency use (sampling bias).
Measurement bias	Very small proportion of those called for 2d follow-up eventually received direct ED clinician calls (7.6%); high attrition rates.
Analysis bias	*Are the results data- or hypothesis-driven? Is the model over fitted and not applicable?* N/A.
Confounding	Residual confounding as with all nonrandomized trials because of unknown prognostic factors that cannot be controlled for. Patients with insecure housing/telephone access are likely unable to access telephone follow-up benefits, and may use ED more frequently.

Administrative details

Key words	Emergency department, follow-up, revisits, telephone
Reference(s)	Biese et al, 2022. Emergency Department Care Transition Programs—Value-Based Care Interventions That Need System-Level Support. *JAMA Netw Open.* 2022;5(5):e2213160. doi:10.1001/jamanetworkopen.2022.13160.

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc FRCPC **No conflicts of interest (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Andrew Worster, MD, MSc **No conflicts of interest (ICMJE)** *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*

What is the efficacy of topical tranexamic acid (TXA) in epistaxis?

BEEM Bottom Line

Why is this study important? Effective treatments for bleeding problems are important, and tranexamic acid (TXA) has been used in a variety of clinical scenarios with benefit (e.g., trauma bleeding, menorrhagia, etc.). This review summarizes the evidence of TXA use in acute epistaxis.

What, if any, threats to validity are most likely to have an impact on the results and how? A limited search strategy could result in important missing information, although authors did assess for publication and missing/future studies bias. The summary measure (odds ratio) was generated combining the results of studies of different designs which, in part, explains the excessive heterogeneity reported.

How do the key results compare with the current evidence? This review supports prior ones that TXA may have benefit for treating anterior epistaxis. A recent positive RCT (Hosseinialhashemi et al, Annals Emerg Med 2022), that wasn't included in this review, also had TXA supportive results.

How should this study impact the care of ED patients? Use of topical TXA is effective in resolving acute anterior epistaxis during the index ED visit, and reduces risk of rebleeds at 24-72hrs post visit.

Study Summary

Article	Janapala RN, Tran QK, Patel J, Mehta E, Pourmand A. Efficacy of topical tranexamic acid in epistaxis: A systematic review and meta-analysis. Am J Emerg Med 2022 (51); 169-175. DOI: 10.1016/j.ajem.2021.10.043. PMID: 34763235
Design	Systematic Review with Meta-analysis; registered with PROSPERO (CRD42021253034).
Population	***Included:*** RCTs & observational studies (prospective & retrospective) with adult patients (>18yo), published in English language. ***Excluded:*** Non-full-text studies, conference abstracts, epistaxis due to vascular pathologies, surgery, etc.
Intervention	Tranexamic acid (TXA) for epistaxis.
Comparison	Usual care (placebo gel, anterior nasal packing with various solutions (lidocaine/epinephrine, saline, oxymetazoline, phenylephrine).
Outcomes	***Primary:*** Prevalence of bleeding cessation at first re-assessment point. ***Secondary:*** Recurrent bleeding 24-72 hrs, and at 7-8 days post ED Rx.
Key Results	**8 studies included (7 RCTs, 1 retrospective study); 1299 patients included (596 TXA – 46%, 703 controls – 54%).** ***Primary (6 studies; Fig 2 & 3):*** **Benefit for TXA** OR 3.5 (95%CI 1.3-9.7, p=0.014); I^2=86%. **ED-based studies (n=5): **Benefit for TXA** OR = 5.7 (2.6-12.3, p=0.001); I^2=70% ***Rebleed 24-72hrs (5 studies; 282pts TXA – 46%, 331pts control – 54%):*** **Benefit for TXA** OR = 0.37 (0.20-0.66, p=0.001). Fig 4A ***Rebleed 7-8d (5 studies; 483pts TXA – 47%, 543pts control – 53%):*** **No difference** OR = 1.24 (0.78-1.98, p=0.36); I^2=76%. Fig 4B

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Conf abstracts/other gray literature deliberately excluded. English only studies.**	X	X
3. The search for studies was unbiased and reproducible. **Duplicate independent screening.**	✓	✓
4. The selection of studies was unbiased and reproducible. **Duplicate independent selection.**	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **Independent, duplicate? Not specified.**	?	?
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high. **Low/minor risk of bias for included RCTs, high RoB for single observational study.**	?	?
8. The methods used to combine the included primary studies were reported and valid.	✓	X
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	X

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Reported; no funding for this study.
Conflict of interest	Reported; no conflicts of interest declared.

Potential threats to viability

Chance	Limited number of included studies may have contributed to heterogeneity. More studies needed to confirm TXA benefits definitively (14).
Selection bias	Tests for publication bias with Begg's/Egger's tests showing low likelihood of publication bias (0.35 & p=0.37 respectively). Prediction for missing/future studies by Orwin's Fail-Safe N test; need 14 more studies.
Measurement bias	Duplicate independent quality assessments using Cochrane Risk of Bias (RCTs) or Newcastle-Ottawa scales (observational studies).
Analysis bias	Combined results of studies of different design.
Confounding	Impractical to blind various interventions for clinicians, patients (e.g., topical Rx, packing, etc.).

Administrative details

Key words	Emergency department, epistaxis, nasal bleeding, tranexamic acid (TXA)
Reference(s)	Hosseinialhashemi M, Jahangiri R, Faramarzi A, Asmarian N, Sajedianfard S, Kherad M, Soltaniesmaeili A, Babaei A. Intranasal Topical Application of Tranexamic Acid in Atraumatic Anterior Epistaxis: A Double-Blind Randomized Clinical Trial. Annals Emerg Med. 2022 Jun 22: S0196-0644(22)00247-5. doi: 10.1016/j.annemergmed.2022.04.010.

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc FRCPC **No conflicts of interest (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Andrew Worster, MD, MSc **No conflicts of interest (ICMJE)** *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*

Research Question

What is the effectiveness of ketamine for acute sickle cell crisis pain?

BEEM Bottom Line

Why is this study important? Vaso-occlusive crises (VOC) is the most common complication of sickle disease, and lead to costly frequent ED visits, hospitalizations and higher risk of death. Effective analgesia reduces morbidity from same but recurrent opioid use for VOC can contribute to tolerance/hyperalgesia.

What, if any, threats to validity are most likely to have an impact on the results and how? Single site RCT may limit generalizability to other ED settings. Type I error is possible given the small sample size. The ketamine IV dose may have been low to detect superiority in this application, but this is a consistent dose with other low-dose ketamine ED acute analgesia studies (Balzer 2021). The primary outcome, numerical pain rating scale (NPRS) score over 2 h is a highly focused and subjective clinical outcome. The missing flow chart is a significant reporting oversight.

How do the key results compare with the current evidence? Non-opioid alternatives for ED analgesia are increasingly important in the era of the opioid epidemic, and having viable analgesics for acute pain conditions are important (Uwaezuoke 2018, AlShahrani 2021).

How should this study impact the care of ED patients? Ketamine IV is a useful analgesic for acute sickle cell VOC and is opioid-sparing in such patients.

Study Summary

Article	Alshahrani MS, Alsulaibikh AH, ElTahan MR, et al. Ketamine administration for acute painful sickle cell crisis: A randomized controlled trial. Acad Emerg Med 2021; doi: 10.1111/acem.14382
Design	Prospective randomized controlled trial (single site academic ED Saudi Arabia). Registered Clinicaltrials.gov: NCT03431285
Population	***Included:*** Adults >18yo with confirmed HbSS subtypes. ***Excluded:*** Pregnant or breast-feeding women, patients with body mass index of >40 kg/m2, known neurological disease, seizures, acute head or eye injury, psychiatric disorders, known cardiac diseases, known pulmonary diseases besides acute chest syndrome, renal disease, chronic liver disease, allergic to the study drugs, sepsis or septic shock, need for circulatory or ventilatory support, alcohol or drug abuse, or known chronic pain that is unrelated to SCD.
Intervention	Ketamine single-dose infusion (IVK) over 30min (0.3mg/kg in 100cc NS)
Comparison	Morphine single-dose infusion (IVM) over 30min (0.1mg/kg in 100cc NS)
Outcomes	***Primary:*** Mean difference in the numerical pain rating scale (NPRS) score over 2 h. NPRS was recorded every 30 min for a maximum of 180 min. ***Secondary:*** Cumulative dose of opioids, ED length of stay, hospital admission, change in vital signs, and drug-related side effects.
Key Results	Mean age 29.4yrs, mean NPRS 8.6 (ketamine) and 8.6 (morphine) at enrollment. Equal distribution gender, hydroxyurea use, HbSS genotypes, comorbidities, pre-analgesia, SpO_2 scores. ***Primary:*** NPRS Mean Diff ITT 0.13 (-0.34 to 0.60, p=0.625); per protocol 0.16 (-0.96 to 1.27, p=0.780) ***Secondary:*** Cumulative morphine dose MD 0.061 (0.038-0.083, p<0.001) favouring ketamine Rescue morphine doses MD 0.008 (-0.272 to 0.290), p=0.802) ED discharge time MD -3.99 min (-35.85 to 27.85, p=0.805) Hospital admission OR 0.71 (0.44-1.39, p=0.399) Dizziness IVK 5 (3.9%) vs IVM 3 (2.2%) Nausea IVK 4 (3.1%) vs IVM 0 Vomiting IVK 1 (0.8%) vs IVM 0 Sedation (RASS scale) MD -0.09 (p=0.324) MAP MD -1.41 (p=0.261) SpO_2 MD 0.15 (p=0.382)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	✓	?
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	?	?
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	X	X
10. The effect size of the primary outcome is clinically significant.	X	?

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	None (reported).
Conflict of interest	None (reported).

Potential threats to viability

Chance	Sample size calculated (n=260), enrollment exceeded (278). Patients pretreated with IV paracetamol or NSAID prior to enrollment; those with NPRS >5 enrolled.
Selection bias	Unclear consecutive sampling. Equal baseline group characteristics (Table 1).
Measurement bias	Block 1:1 randomization (groups of 6).
Analysis bias	ITT, Per Protocol, As Treated.
Confounding	All patients pretreated with IV paracetamol or NSAIDs, and then enrolled after initial failed pre-treatment.

Administrative details

Key words	Analgesia, ketamine, morphine, sickle cell vaso-occlusive crisis
Appraisers	S. Upadhye, A. Worster
Reference(s)	Uwaezuoke SN, et al. Vaso-occlusive crisis in sickle cell disease: current paradigm on pain management. J Pain Res 2018; 11: 3141-3150. doi: 10.2147/JPR.S185582. PMID: 30588066. Balzer N, McLeod SL, Walsh C, Grewal K. Low-dose Ketamine for Acute Pain Control in the Emergency Department: A Systematic Review and Meta-analysis. Acad Emerg Med 2021; 0:1-11. doi: 10.1111/acem.14159 Alshahrani MS, Alghamdi MA. Ketamine for sickle cell vaso-occlusive crises: A systematic review. Saudi J Med Med Sci 2021; 9: 3-9.

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**
Andrew Worster, MD, MSc *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**

Research Question

How accurate is the REDEEM risk score for assessing geriatric delirium?

BEEM Bottom Line

Why is this study important? Geriatric delirium is a common occurrence, with significant morbidity/mortality, and easily missed in ED (83%). It can be easily missed in its hypoactive form, so routine screening is recommended for all older ED patients in order to intervene early once detected.

What, if any, threats to validity are most likely to have an impact on the results and how? There may be some element of selection bias, as ED patients were screened at bedside nursing discretion. The derivation cohort is predominantly white, from a single site. Most of the predictor variables come from the triage information, but two clinical variables come from the MEDFRAT falls assessment, which may not be used in mainstream ED care (time & training to implement with ED nurses)?

How do the key results compare with the current evidence? This work builds on previous reviews, including a 2021 SR by the same authors, that provided predictor variables incorporated into this new risk stratification score.

How should this study impact the care of ED patients? Screening for potential delirium in older ED patients should be routinely done using the established DTS + bCAM sequence. Use of this REDEEM risk stratification score, however, requires further prospective validation prior to mainstream use.

Study Summary

Article	Silva LOJE, Stanich J, Jeffery MM, Mullan A, Bower S, Campbell RL, Rabinstein AA, Pignolo RJ, Bellolio F. REcognizing DElirium in geriatric Emergency Medicine: The REDEEM Risk Stratification Score. Acad Emerg Med 2021; doi: 10.1111/acem.14423.
Design	(Clinical Decision Rule)
Population	*Included:* ED patients aged ≥75yo who screened sequentially positive for delirium using DTS (Delirium Triage Screen) then bCAM (brief Confusion Assessment Method) tools. *Excluded:* Patients with stupor/comatose.
Predictor Variables	Combination of 10 variables; 7 triage, 3 early history taking
Comparison	Positive bCAM scores
Outcomes	*Primary:* Presence of delirium *Secondary:* N/A
Key Results	967 patients evaluated, 107 had delirium (11.1%); 75% hypoactive. Median age 83yo (IQR 79-88), 54% female, 98% white. ***REDEEM Score Performance***: Best cutoff at ≥11pts Sensitivity 84.1% (90/107 ED delirium patients, 95%CI 75.5-90.2%) Specificity 86.6% (745/860 non-ED delirium patients, 95%CI 84.1-88.8%). Overall accuracy 86.3% (835/967 patients, 95%CI 84.0-88.4%) AUC 0.901 (0.86-0.94) Lower cutoff ≥ 5 = Fewer false negatives; Sens 91.6% (98 of 107 ED delirium patients, 95%CI 84.2-95.8%). Lower overall accuracy 74.8% (723/967 patients, 95% CI 71.9% to 77.5%) Each score increment 1pt = 12% increase in delirium (OR 1.12, 1.10-1.14) Score increment 10pts = 3x increase (OR 3.11, 2.63-3.69)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those with the problem.	✓	?✓X
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	?	?✓X
3. All patients underwent the same clinical evaluation.	?	?✓X
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	✓	?✓X
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	X	?✓X
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	?	?✓X
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓	?✓X
8. All patient-important outcomes were considered.	✓	?✓X
9. The follow-up was complete.	✓	?✓X
10. The point estimates and respective precisions are clinically significant.	✓	?✓X

A1 = S. Upadhye A2 = (insert name here)

Funding and conflicts of interest

Funding	Funding from the Kern Society Innovation Fund (Mayo clinic), and NCATS grant. No study inputs from granting agencies.
Conflict of interest	None (reported)

Potential threats to viability

Chance	*Type I & II errors?* Single site retrospective study with predominantly white population.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Patients selected for delirium screening at discretion of ER bedside nurse (selection bias?)
Measurement bias	Most data elements extracted from EHR; missing data acquired from chart review (5.1% visits, kappa 0.80).
Analysis bias	*Are the results data- or hypothesis-driven? Is the model over fitted and not applicable?* Mimimal missing data (<4% overall) for falls rates (scored as 0) and some vital signs (imputed means from non-missing data). Use of LASSO logistic regression to prevent over-fitting of predictor variables.
Confounding	*Residual confounding as with all observational studies because of unknown prognostic factors that cannot be controlled for; Independent factors affecting the outcome; clinicians to comment.*

Administrative details

Key words	Delirium, emergency department, screening
Reference(s)	Silva LOJE, Berning MJ, Stanich JA, Gerberi DJ, Murad MH, Han JH, Bellolio F. Risk Factors for Delirium in Older Adults in the Emergency Department: A Systematic Review and Meta-Analysis. Annals Emerg Med 2021; 78: 549-565. https://doi.org/10.1016/j.annemergmed.2021.03.005

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI)
McMaster University

Research Question

What interventions are most effective to decrease ED opioid prescribing?

BEEM Bottom Line

Why is this study important? Although ED opioid prescribing has been trending downwards for a number of years, there is still evidence of over-prescribing and under-utilization of opioids, leading to potential diversion or misuse. This review summarizes interventions to reduce ED opioid prescribing.

What, if any, threats to validity are most likely to have an impact on the results and how? The majority of included studies are based upon US populations which limits generalizability. The significant heterogeneity between studies can threatens the validity of pooled results but random effects and sensitivity analyses showed overall robust results.

How do the key results compare with the current evidence? These results mirror review findings from post-surgical opioid prescription reduction strategies. Other data from ED studies is more variable, and heterogeneous.

How should this study impact the care of ED patients? Education/policy/guidelines (EPG) interventions are the most effective strategies to reduce ED opioid prescribing rates and quantities. The impact on patient outcomes is unknown.

Study Summary

Article	Daoust R, Paquet J Marquis M, Chauny JM, Williamson D, Huard V, Arbour C, Emond M, Cournoyer A. Evaluation of Interventions to Reduce Opioid Prescribing for Patients Discharged From the Emergency Department. A Systematic Review and Meta-analysis. JAMA Netw Open 2022 Jan 4;5(1):e2143425. doi: 10.1001/jamanetworkopen.2021.43425.
Design	Systematic Review/Meta-analysis of Prospective Trials; PROSPERO #: CRD42020187251
Population	*Included:* All intervention studies designed to reduce the opioid prescription rate and/or the quantity of opioids per prescription given to adults discharged from the ED (>18 years of age) for home pain management. *Excluded:* Case reports, case series. Pediatric patients, ED opioid analgesia administration, or populations with Substance Use Disorder, non-ED settings, opioid use for non-painful conditions, non-reporting of opioid rates/quantities were also excluded.
Intervention	Cochrane EPOC Taxonomy of Implementation Strategies categorized into interventions: 1) Education, policy or guidelines (EPG), 2) Prescription drug monitoring programs (PDMPs) with state laws, 3) Clinician peer comparison (CPC), 4) EMR quality changes (EMR-QC), or 5) Physical therapy (PT).
Comparison	N/A
Outcomes	*Primary:* Variation in the opioid prescription rate and/or quantity generated by the intervention. Interrupted time series (ITS) studies analyzed at 6mo. *Secondary:* Patients' level of pain relief, patients' satisfaction with their opioid prescription, and percentage of patients requiring additional opioid prescriptions. Planned sensitivity analyses based on study risk of bias, 1yr step change for ITS studies.

Key Results

63 intervention studies included. Most studies from USA (55; 87%), Australia 5, Canada 3; all published within last 10yrs.

39 pre/post intervention studies, 21 ITS studies, 2 cohort studies, 1 RCT.
Opioid Rx rate reported in 25 studies, quantity in 13 studies, both in 25 studies.

Overall Opioid Rx rate (51 studies): 46 studies reported reduced Rx rates (90%); 34 studies statistically significant.
ITS 6mo step change: -22.61% (95%CI -30.7 to -14.52%); I^2= 77%.
Other study designs: OR 0.56 (0.45-0.70); I^2 = 99%.

Overall Opioid Quantities (39 studies): 32 studies reported intervention-related reductions (82%); 17 studies statistically significant.
ITS 6mo step change: -8.64% (-17.48 to 0.20, not statistically significant); I^2=92%.
Other study designs: SMD 0.30 (-0.51 to -0.09); I^2 = 100%; small statistical significance.

Intervention Category	Opioid Rx Rates	Opioid Rx Quantities
EPG (n=21 studies)	ITS: −33.31% (−39.67%to −26.94%, I^2 = 0%) Other designs: OR, 0.47 (0.33-0.69, I^2 = 99%) rates	ITS: −15.38% (−24.51% to −6.25%, I^2 = 18%) Other: SMD −0.07 (−0.15 to 0.02, I^2 = 33%)
PDMP (n=19)	ITS: −11.18% (−22.34%to −0.03%, I^2 = 81%) Other: OR 0.61 (0.44-0.86, I^2 = 96%)	ITS: 3.62% (2.39-4.85%, I^2 = 0%) Other: SMD −0.37 (−0.58 to −0.15, I^2 = 95%)
EMR-QC (n=11)	Other: OR 0.94 (0.88-0.99, I^2 = 99%)	ITS: −11.65% (−29.30% to 5.99%, I^2 = 87%) Other: SMD −0.20 (−0.47 to 0.07, I^2 = 100%)
CPC (n=10)	Other: OR 0.46 (0.29-0.72, I^2 = 96%)	Other: SMD −0.51 (−1.10 to 0.08, I^2=100%)
PT (n=2)	Other: OR 0.98 (0.49-1.95, I^2 = 75%)	No data.

Secondary: No reporting of patient pain relief in any studies. Patient satisfaction with opioid scripts (4 studies): 1 low response rate (1.9%), 2 no impact, 1 slight gain (52% to 61%). No change in need for additional opioids (1 study).
Sensitivity: No change in results of interventions/categories at 1yr segmented ITS analysis. No difference when ITS studies with high RoB removed. Single RCT (low RoB, CPC intervention) did show significant reduced rate (-5.5%) and quantity (-8MEQ) reductions.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	X	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	X

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Supporting funds from Sacre-Coeur Hospital and OPUM grant funds. No industry funding.
Conflict of interest	Two authors have public grants supporting this work. No industry ties (reported).

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Majority of included studies from USA; generalizability to other jurisdictions?
Selection bias	*Limited/incomplete search, publication bias, etc.* Thorough search of multiple electronic databases, trial registries, gray literature, conference abstracts and reference lists for relevant studies; no language restrictions. Funnel plots for possible risk of bias, shown but Egger tests results non-significant.
Measurement bias	*Missing details on study selection; missing results of quality assessments.* Quality assessments used Cochrane ROBINS-I (ITS) or EPOC (RCTs, cohorts) tools. Abstracts auto-assigned high RoB. Quality appraisals: 10/21 studies had moderate risk of bias; all others were serious/critical RoB. Single RCT was low RoB, 2 cohorts high RoB.
Analysis bias	*Fixed vs. random effects, combined results of studies of different design.* High heterogeneity outcomes appropriately analyzed using random effects models.
Confounding	*List as reported.* Substantial differences in how interventions were designed, implemented, outcomes measured, and duration of follow-up. Risk of allocation bias in PT studies, as physician discretion used to allocate patients to PT or other treatments.

Administrative details

Key words	Opioid prescribing, interventions, emergency department
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc, FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Andrew Worster, MD, MSc
Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What ED interventions are beneficial to improve health outcomes in homeless patients?

BEEM Bottom Line

Why is this study important? Homeless patients suffer from more chronic illnesses, poorer health outcomes and access to primary care compared to housed citizens. They use the ED (frequently) for many primary care concerns, and may not benefit from continuity of care for chronic conditions. Getting such patients into stable housing and access to health services can optimize health outcomes and resource utilization.

Which, if any, threats to validity are most likely to have an impact on the results and how? Heterogeneity of ED interventions and inability to pool study results. Variable risk of bias associated with these challenging study designs.

How do the key results compare with the current evidence? Congruence with prior studies/reviews showing a benefit for early ED interventions to connect homeless patients with stable housing and essential community social services.

How should this study impact the care of ED patients? Intensive case management that focusses on stable housing and connection to primary care services can lead to optimal social/health outcomes. This will require sustained significant funding, resources, and interprofessional collaboration. The costs of such, however, may be offset by improved health outcomes and less ED utilization.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Formosa EA, Kishimoto V, Orchanian-Cheff A, et al. Emergency department interventions for homelessness: a systematic review. CJEM 2021, 23: 111-122. https://doi.org/10.1007/s43678-020-00008-4
Design	Systematic review of intervention trials. A priori decision NOT to meta-analyze results due to anticipated clinical and methodological heterogeneity.
Population	*Included*: Patients experiencing homelessness in >50% of study populations. *Excluded*: Studies with ED return visits and/or hospital costs
Intervention	Interventions initiated in the ED aimed at social determinants of health. All studies in North America.
Comparison	Usual care (not all studies).
Outcomes	Changes in housing status, substance use disorder variables, access to primary care.
Key Results	*13 studies included; 6 RCTs, 3 non-randomized studies, 4 pre/post interventional studies* Case-management with an emphasis on "housing first" resulted in successful housing in >90% recipients (8 studies). Case-management targeting substance use had variable results, from zero change in opioid risk to 70% alcohol use reduction.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	?	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	X	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	None.
Conflict of interest	None.

Potential threats to validity

Chance	None.
Selection bias	None.
Measurement bias	No raw data available from individual studies for quantitative analyses. Mixed results of quality assessments for study risk of bias. Small sample sizes for most studies.
Analysis bias	Short length of interventions make it difficult to ascertain sustainability of interventions (1-24mo).
Confounding	Practical limitations in conducting trials with homeless populations and relevant interventions (eg. Blinding). Heterogeneity in interventions and other study elements make it difficult to pool/aggregate study results.

Administrative details

Key words	Social health determinants, homelessness
Appraisers	Upadhye, S.
Reference(s)	Formosa EA, Kishimoto V, Orchanian-Cheff A, Hayman K. Emergency department interventions for homelessness: a systematic review. CJEM 2021, 23: 111-122. https://doi.org/10.1007/s43678-020-00008-4

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Is supplemental hearing assistance beneficial to ED geriatric patients?

BEEM Bottom Line

Why is this study important? The emergency department (ED) presents one of the most challenging listening situations in clinical medicine, especially for the older hearing-impaired patient. Poor communication is a barrier to care for older people with hearing loss (50% age >60, 66% age >70yo).

Which, if any, threats to validity are most likely to have an impact on the results and how? This pilot study isn't powered to detect small differences in the validated outcome instruments. Veterans' hospitals patients may benefit from different health care resources than regular public ED populations. Unblinding of professionals could have modified their approach to the patient with personal amplifier. Some potentially confounding differences in presence of family/caregivers and use of hearing aids in personal amplifier (PA) group.

How do the key results compare with the current evidence? As a first study on PA in the ED, these results correlate with similar study in other settings as reported in a review by Mamo et al.

How should this study impact the care of ED patients? The benefit of PA in the ED is mainly about decreasing "cognitive fatigue or competition". The listening efforts without PA can engage cognitive resources and competes with other cognitive tasks such as memory and language processing. The latter are prerequisite to a good understanding of the older patient health conditions or treatment. Further research, with possibly cheaper devices and other patient learning enhancement techniques, is warranted.

Study Summary

Article	Chodosh J, Goldfeld K, Weinstein BE, et al. The HEAR-VA Pilot Study: Hearing Assistance Provided to Older Adults in the Emergency Department. J Am Geriatr Soc. 2021 Apr;69(4):1071-1078. doi: 10.1111/jgs.17037. Epub 2021 Feb 11.
Design	Prospective, randomized controlled pilot study.
Population	*Included:* Adults $\geq$ 60, English speaking, Emergency Severity Index category 4 and 5 (3 on occasion) with high likelihood of discharge. Handicap Inventory (HHI-S)> 10 or self-reported hearing difficulties. *Excluded*: patients with unstable and life-threatening situation.
Intervention	Personal amplifier (Williams Sound Pocketalker 2.0 device) during ED length of stay (as early as possible).
Comparison	Standard care.
Outcomes	*Primary:* Three validated instruments (Hearing and Understanding Questionnaire (HUQ), Care Transitions Measures (CTM-3), Patient Understanding of Discharge Information (PUDI). *Secondary:* Return to ED (up to 30 days).

Key Results: *N* = 133 patients (Intervention=66, Control= 67). Males 98.3%, mean age 76.4yrs.

Sig.	*Outcome*	*Intervention*	*Control*	*ARR (95% CI)*	*NNT (95% CI)*
NS	Voices "clearer"	62/66	60/67	4.9 (-4.3; 13.7)	Not estimable
S	3-days RTED	2/66	6/67	6.2 (-1.9; 14.4)	NE
	30-days RTED	15/66	18/67	3.4 (-11.2; 17.8)	NE
SS	Understand without effort	50/66	38/67	19.0 (3.3; 34.7)	5
SS	Understand management of health	64/66	56/67	10.8 (1.4; 20.1)	9

ARR = absolute risk reduction (if the CI includes the value 0, there is no difference in risk between the groups and the NNT is not estimable); CI = confidence interval; *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A2	A3
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	X	X
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	X	X
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	?	?

A1 = M. Émond A2 = S. Upadhye ITT = intention to treat.

Funding and conflicts of interest

Funding	Private foundation & Veteran's merit award
Conflict of interest	None reported

Potential threats to validity

Chance	This is a single site study at a US Veterans Affairs Hospital, that may offer different resources/services compared to public hospitals, which may limit generalizability of results.
Selection bias	Using self-reported hearing difficulties as eligibility criteria and discharged patient could lead to a lower handicap group of patients.
Measurement bias	Unblinding of ED professionals could introduce a Hawthorne bias. Various clinical instruments were adapted for ED use, but not necessarily pre-validated; it is not clear what are minimal clinically important differences (MCID) for patients responding to these adapted scales in ED settings. Some surveys done post-discharge during a phone follow-up call.
Analysis bias	ITT, No power calculation – pilot study.
Confounding	Significant difference in presence of family/caregivers between groups (31.8% in intervention vs 17.9% controls), as was the use of hearing aids (54% intervention vs 39% controls).

Administrative details

Key words	Older patients; Hearing disabilities; Discharge instructions.
Appraisers	Emond, M; Upadhye, S.
Reference(s)	1. Vincent CA, Wears RL. Communication in the emergency department. Med J Aust. 2002;176(9):409-410. 2. Baevsky R. Sound levels in the emergency department setting. Acad Emerg Med. 2006;13(2):233. 3. Mamo SK, Reed NS, Nieman CL, Oh ES, Lin FR. Personal Sound Amplifiers for Adults with Hearing Loss. *Am J Med*. 2016;129(3):245-250.

Clinical Appraisal faculty

Marcel Émond MD MSc CCFP(EM) FRCP
Associate professor, Université Laval.
No conflicts of interest/Identify conflicts (ICMJE)

Suneel Upadhye, MD MSc FRPCP
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University.
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Is there a difference in ED imaging rates based on patient race/ethnicity?

BEEM Bottom Line

Why is this study important? Patient care equity in ED is paramount, yet is often lacking in various areas of care (eg. Analgesia, Dx testing, etc.). This study explores equity differences in ED imaging based on race/ethnicity.

Which, if any, threats to validity are most likely to have an impact on the results and how? Insert text here. Notes: Top 3 fatal flaws in order of priority. Explain in simple terms for clinician readers. Comment on GRADE. Notes:

How do the key results compare with the current evidence? The results of this review mirror other studies showing disparities in patient care based on race/ethnicity (eg. ED analgesia/opioid use). These results also seem to extend to imaging decisions for children, although the drivers for such decisions may be different between adults & children.

How should this study impact the care of ED patients? Unconscious implicit bias and other motivators may influence how ED practitioners manage their patients. It is critical for ED staff to be aware of unconscious/other biases in evaluating and treating patients, in order to optimize equitable patient outcomes.

Study Summary

Article Shan A, Baumann G, Gholamrezanezhad A. Patient Race/Ethnicity and Diagnostic Imaging Utilization in the Emergency Department. J Am Coll Radiol 2020; 18(6): P795-808. https://doi.org/10.1016/j.jacr.2020.12.016

Design Systematic review of observational studies exploring ethnicity/race associations with ED imaging.

Population *Included:* Imaging rates for ED adult and pediatric patients.
Excluded: Enter text here, separated by semicolons.

Intervention Imaging rates between white and non-white/Hispanic patients (various indications).

Comparison N/A

Outcomes *Primary:* Imaging rates in various ethnic/race groups.
Secondary: Subgroup analyses based on disease severity, triage levels, clinical scenarios (eg. Abdominal pain, chest pain, headache/head injury, etc.), adult vs. pediatric.

Key Results 42 studies included (41 US, 1 Canada). Sample sizes 155-2 million pts.

Sig.	*Outcome*	
NSS	Secondary	Mixed results on race/ethnicity differential imaging rates for head injury (adults & pediatric). Disease severity, triage level, insurance status not necessarily associated with differential imaging rates. No imaging differences amongst adults with stroke. Less associations with differential utilization of US, MRI (various indications).
SS	Primary	71% of included studies reported various degrees of decreased imaging rates for non-white and Hispanic patients (10-50% less likely); OR range 0.21-0.92. Adult black patients less likely to receive ED imaging relative to Hispanics (depending on clinical condition). Strong association of decreased imaging for non-white/Hispanic/black children across various clinical conditions (abdo pain, trauma). Strong associations with differential utilization of CT, Xray.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	X	X
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	?	X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	X	✓
7. The quality of the primary studies is high.	?	X
8. The methods used to combine the included primary studies were reported and valid.	X	?
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	?

A1 = S. Upadhye A2 = G. Ghate

Funding and conflicts of interest

Funding	None declared.
Conflict of interest	None (reported).

Potential threats to validity

Chance	None?
Selection bias	Limited search of English language studies from 3 electronic databases. No analysis for publication bias. Nearly all studies conducted in USA (31/32).
Measurement bias	No quality assessments for included studies described/reported.
Analysis bias	Heterogeneity of classification categories of race/ethnicity in included studies. No quantitative reporting of imaging rates from individual studies, no pooled data analysis.
Confounding	Various biases associated with different study designs, survey samples, etc. Lack of information of provider-level decision-making, or on availability of primary care services for white vs non-white populations, language barriers/cultural differences or parental values/preferences for imaging children.

Administrative details

Key words	Diagnostic imaging, ethnicity/race, health equity, utilization.
Appraisers	Upadhye S, Ghate G.
Reference(s)	Shan A, Baumann G, Gholamrezanezhad A. Patient Race/Ethnicity and Diagnostic Imaging Utilization in the Emergency Department. J Am Coll Radiol 2020; 18(6): P795-808.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Gauri Ghate, MD FRCPC
Consultant ER, London Health Science Centre, London, ON
Assistant Professor, Western University
No conflicts of interest (ICMJE)

Research Question

What is the prevalence and impact of work-place violence (WPV) in the emergency department?

BEEM Bottom Line

Why is this study important? Workplace violence (WPV) in the ED is a serious threat to ED staff health and well-being.

Which, if any, threats to validity are most likely to have an impact on the results and how? Limited search, data abstraction & quality assessment cause uncertainty in the thoroughness and fidelity of analyses completed. Lack of universal definitions of different types of WPV can lead to classification heterogeneity.

How do the key results compare with the current evidence? The current results mirror similar past studies looking at WPV in different workplaces.

How should this study impact the care of ED patients? Workplace violence is a common and serious problem in the ED, against both nurses and physicians. There is an urgent need for more standardized research into WPV causes/instigators and solutions to mitigate risks of injury/burnout amongst ED staff victims.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Aljohani B, Burkholder J, Tran QK, et al. Workplace violence (WPV) in the emergency department: a systematic review and meta-analysis. Public Health 2021; 196: 186-197. DOI: 10.1016/j.puhe.2021.02.009
Design	Systematic review and meta-analysis of survey studies on WPV prevalence and causes.
Population	*Included:* Studies of adult patients with WPV against ED staff, and instigators of such ED WPV. *Excluded*: Studies not reporting WPV against ED staff, prehospital personnel. Also excluded studies reporting domestic violence prior to ED arrival, or involving drugs/alcohol/psychiatric illness. Case reports, editorials and opinion articles also excluded.
Intervention	N/A.
Comparison	N/A.
Outcomes	*Primary:* Prevalence of WPV violence. *Secondary:* Countries of origin, types of WPV, instigators, WPV victim professions (physicians, nurses, other).

Key Results *26 studies included - 5792 health care workers (HCWs) survey respondents.*

Outcome	*Studies*	*Prevalence (95% CI)*	*I^2*
Verbal violence (overall)	21	0.77 (0.72-0.82); physicians 0.74 (0.520-0.88), nurses 0.75 0.67-0.82)	97%
Patient instigator	13	0.24 (0.18-0.31); 0.28 (0.19-0.38) vs nurses, 0.15 (0.09-0.24) vs physicians	93%
Types of WPV	21	Verbal 72.5%, physical 18.1%, other 9.5% (stalking, sexual harassment)	
Overall instigators	13	Family members 52%, patients 27.2%, "others" 20.8% (other relatives/friends)	

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.
P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.
*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	X	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	?	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	?	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	?	?✓X	?✓X
7. The quality of the primary studies is high.	?	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	None (declared).
Conflict of interest	None (declared).

Potential threats to validity

Chance	None?
Selection bias	None or enter text here (incomplete search, publication bias, etc.). Limited search of electronic databases (PubMed, SCOPUS). Unclear data abstraction process/personnel.
Measurement bias	All studies based on surveys of health care worker WPV victims. No universal definition of abuse/assault/bullying between various studies. No quality assessment tools reported for included studies.
Analysis bias	Random effects models used for pooled data analysis, esp with high heterogeneity studies.
Confounding	Risk of recall bias when surveying victims for WPV experiences. Interpersonal bias based on different perceptions of threat/confrontation based on age/gender/race/other attributes, which may affect objective reporting of WPV incidents.

Administrative details

Key words	Instigator, healthcare workers, workplace violence.
Appraisers	Upadhye S,
Reference(s)	Aljohani B, Burkholder J, Tran QK, Chen C, Beisenova K, Pourmand A. Workplace violence in the emergency department: a systematic review and meta-analysis. Public Health 2021; 196: 186-197. DOI: 10.1016/j.puhe.2021.02.009

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Is D-Dimer reliable in ruling out venous thromboembolism (VTE) in pregnancy?

BEEM Bottom Line

Why is this study important? The diagnosis of venous thromboembolic events (VTE) which include DVT and PE, during pregnancy is challenging due to the increased physiological risk and overlap with normal pregnancy signs and symptoms. Inappropriate testing can subject the expectant mother to unnecessary stress, invasive / harmful procedures, and exposure to incorrect treatments.

What, if any, threats to validity are most likely to have an impact on the results and how? There were few studies included (4), but they are of high quality. Specificity is not reported for any individual/pooled studies, so one cannot calculate likelihood ratios (so estimates are susceptible to prevalence issues).

How do the key results compare with the current evidence? There are mixed guideline recommendations from Europe, USA, Canada, etc., on the use of a negative D-Dimer to rule out VTE in pregnancy, although the latest ESC guidelines endorse this strategy.

How should this study impact the care of ED patients? A negative D-Dimer, when combined with a low/intermediate/ indeterminate risk pre-test probability score (e.g. Geneva-R, YEARS, Wells), seems sufficient to rule out VTE in pregnancy.

Study Summary

Article	Bellesini M, Robert-Ebadi H, Combescure C, Dodionigi C, Le Gal G, Righini M. D-Dimer to rule out venous thromboembolism during pregnancy: A systematic review and meta-analysis. J Thromb Hemostas 2021; 19(10):2454-2467. doi: 10.1111/jth.15432.
Design	Systematic review of diagnostic tests
Population	*Included:* Pregnant women (adult age ≥18yo) with suspected VTE (DVT, PE) with low/intermediate/unlikely risk (based on CDR if applied). Studies included 2x2 tables to calculate Dx test parameters.
Index Test	D-Dimer (with/without pre-test probability assessment using a CDR). Cutoffs based on source study thresholds (majority 500ng/ml, 1 study used 1000ng/ml)
Reference Standard	Confirmatory imaging test (VQ scan, CTPA, pulmonary angiogram, lower limb CUS) or clinical follow-up at 3mo
Diagnoses of Interest	Acute symptomatic VTE in pregnancy (safety, diagnostic yield – Sens, NPV); subgroup analyses based on trimester/puerperium
Key Results	4 studies included, 836 patients analyzed. Suspected PE 3 studies, DVT 1 study. Overall proportion of included patients with negative D-Dimer 34.2% (15.9-55.1, I^2=98%) Three high-sensitivity ELISA/turbidimetry assays used, 1 SimpliRED latex agglutination. Three prospective Dx algorithm studies with PreTP stratification, 1 retro study (no PreTP). Overall weighted mean prevalence of VTE was 5.0% (95%CI 1.1-11.4%, I^2=90%). Pooled Sens: 99.5% (95-100) Pooled NPV: 100% (99.1-100) Diagnostic yield to r/o VTE = 34.2% (15.9-55.2, I^2=98%) Overall pooled "failure rate" of D-Dimer (1/312): 0.32% (0.06-1.8). Overall rate of 3mo VTE in untreated women with neg diagnostic algorithm: 0.2% (0.06-0.74). Insufficient data to complete sensitivity analyses based on trimesters/puerperium. Trend towards decreasing proportion of negative D-Dimer results with increasing gestational age. Unable to perform planned sensitivity analyses due to small number of included studies.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	✓	✓
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	✓	✓
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = K. Lin

Funding and conflicts of interest

Funding	Not reported
Conflict of interest	None (reported). Three authors in this SRMA are also on the largest study included.

Potential threats to viability

Chance	None
Selection bias	Electronic search used Medline & EMBASE only, supplemented with manual reference list searches, trial registries and questioning experts. No language restrictions. No publication bias analysis reported.
Measurement bias	Specificities for included studies not reported; unable to calculate neg likelihood ratios to account for prevalence issues.
Analysis bias	Planned subgroup analyses: PreTP assessment, DDimer type/cutoff, reference standards, retro/prospective designs, median QUADAS-2 scores. Overall high QUADAS-2 quality scores for included studies. High heterogeneity (I^2 = 90%), so random effects model used.
Confounding	The D-Dimer assays used in 2 of 4 included studies are no longer commercially available.

Administrative details

Key words	clinical probability, D-dimer, diagnostic strategy, pregnancy, pulmonary embolism
Appraisers	S. Upadhye, K. Lin
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Katie Lin, MD MPH FRCPC CCSC
Clinical Assistant Professor, Emergency Medicine/Department of Clinical Neurosciences, University of Calgary
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the efficacy of avoiding antibiotics in mild acute diverticulitis?

BEEM Bottom Line

Why is this study important? Prior dogmatic treatment of acute diverticulitis (AD) with antibiotics (for presumed infectious etiology) has been refuted with recent evidence of no benefit from antibiotics. In an era of antibiotic stewardship, any opportunity to reduce/eliminate low-value Abx is warranted.

What, if any, threats to validity are most likely to have an impact on the results and how? Lack of blinding deemed impractical for a multi-centre design; not likely to have affected admission, ED revisit rates or emergency surgery rates.

How do the key results compare with the current evidence? These results of this study are congruent with evolving guidelines that recently recommend avoiding antibiotics in mild uncomplications AD (Hall 2020). However, both groups in the DINAMO-study were given nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and omeprazole, none of which is recommended in diverticulitis guidelines. Hence, perhaps the trial's results are partly explained by use of these treatments and their actions on an inflammatory process and subsequent reduction in pain and/or fever.

How should this study impact the care of ED patients? For cases of mild, uncomplicated AD, it is safe to avoid empiric antibiotics and focus on analgesia only.

Study Summary

Article	Mora-Lopez L, Ruiz-Edo N, Estrada-Ferrer O, et al. Efficacy and Safety of Nonantibiotic Outpatient Treatment in Mild Acute Diverticulitis (DINAMO-study): A Multicentre, Randomised, Open-label, Noninferiority Trial. Annals Surg 2021 Nov 1;274(5):e435-e442. DOI: 10.1097/SLA.0000000000005031
Design	Multi-centre open label prospective noninferiority (NI) RCT. 15 colo-rectal surgery units in Spain. Trial registered at the ClinicalTrials.gov database (ID: NCT02785549) and the EU Clinical Trials Register database (EudraCT number: 2016-001596-75).
Population	*Included:* Adults aged 18-80 yo, modified Neff 0 AD on abdominal CT scan, no AD episode in the last 3 months, no antibiotic treatment for any reason in the last 2 weeks, no significant comorbidities*, immunocompetence, patient's written informed consent, adequate cognitive capacity, adequate family support, good symptom control at the ED and maximum 1 of the following: Temp <36.8°C or ≥38.8°C, WBC <4000/mL or >12,000/mL, HR>90 bpm, RR >20 rpm, CPR >15 mg/dL. **Significant comorbidities = complicated DM (with retinopathy, angiopathy, nephropathy), emergency assistance for a cardiogenic event in the last 3 months (AMI, angina, heart failure), decompensation of chronic liver disease in the last 3 months (Child≥B) and end-stage renal disease.* *Excluded:* Women in pregnancy/breastfeeding, age <18 years or > 80 years, allergy to any of the study drugs, modified Neff grade I or upper AD, AD episode in the last 3 months, inflammatory bowel disease, antibiotic treatment for any reason in the last 2 weeks, presence of significant comorbidities, immunodepression, absence of patient's written informed consent, inadequate cognitive capacity, inadequate family support, poor symptom control at the ED (VAS≥5) and/or systemic inflammatory response syndrome.
Intervention	Conservative analgesia = ibuprofen 800mg q8h alternating with acetaminophen 1g q8h for 7 days. No antibiotics.
Comparison	Analgesia above + Amox 875/clav 125mg q8h for 7 days.
Outcomes	*Primary:* Hospital admission *Secondary:* ED revisits, pain control, need for emergency surgery Assessment schedule: 2, 7, 30 and 90days.

Key Results	Median age 58yo, gender balance 42-50%, initial CRP different (not clinically important)	
480 enrolled (Int 242, Cont 238); LTFU 7.9% Int, 9.2% Cont	Hospital admissions:	Non-Abx was NI to Abx for overall admissions. Shorter admissions in the non-Abx group (3 vs 5 days, p=0.002).
	ED revisits:	No significant differences in ED revisit rates
	Pain control:	Higher levels of pain at 2d in Abx vs non-Abx group (MD 3.39, 6.96 to -0.18). No significant differences at later time points.
	Emergency surgery:	None in either group.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	X	X
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	X	X
6. All groups were treated equally except for the intervention.	✓	?
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	None (reported)
Conflict of interest	None (reported)

Potential threats to viability

Chance	Sample size calculated for a **7% NI margin** (previously researched/defined); recruiting goal exceeded.
Selection bias	Unclear consecutive sampling. Groups well balanced otherwise.
Measurement bias	Open-label design, lack of blinding of patients/surgeons. Unclear blinding of outcomes assessors at later follow-up times?
Analysis bias	ITT, Per Protocol for primary outcome.
Confounding	Lack of placebo in the Non-Abx arms (deemed impractical for multi-centre trial).

Administrative details

Key words	Mild acute diverticulitis, nonantibiotic, outpatient
Appraisers	S. Upadhye, A. Worster
Reference(s)	Hall J, Hardiman K, Lee S, et al., On Behalf Of The Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. The American society of colon and rectal surgeons clinical practice guidelines for the treatment of left-sided colonic diverticulitis. Dis Colon Rectum. 2020;63:728–747.

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc, FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Andrew Worster, MD, MSc
Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the benefit of pictorial ED discharge materials, compared to standard discharge advice?

BEEM Bottom Line

Why is this study important? Providing adequate discharge advice for patients leaving the ED is an essential activity to optimize patient outcomes. Use of pictorial materials may facilitate this process.

Which, if any, threats to validity are most likely to have an impact on the results and how? There are limited, and somewhat dated, studies examining the benefit of ED pictorial interventions. Limited generalizability as all included studies were US-based. No information provided on costs of production/implementation of ED pictorial discharge materials, which require multidisciplinary inputs.

How do the key results compare with the current evidence? There is limited evidence on the utility of ED pictorial discharge advice materials with which to compare these results.

How should this study impact the care of ED patients? Pictorial ED discharge materials increase comprehension, compliance and patient satisfaction. More research, with broad stakeholder inputs (including patients/caregivers) would likely make such materials more impactful.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Dermody S, Hughes M, Smith V. The Effectiveness of Pictorial Discharge Advice vs Standard Advice Following Discharge from the Emergency Department: A Systematic Review and Meta-Analysis. J Emerg Nurs 2021; 47: 66-75. https://doi.org/10.1016/j.jen.2020.07.005
Design	Systematic review and meta-analysis of randomized controlled trials (RCTs).
Population	*Included:* Adults/children sent home from ED with any type of pictorial information. *Excluded*: Other modes of communicating discharge information (texts, recordings, videos), non-ED settings, non-English languages used.
Intervention	Use of pictorial information for discharge advice (line drawings, pictures, photographs, paintings, cartoons).
Comparison	Standard written/verbal discharge information.
Outcomes	*Primary:* Patient/caregiver comprehension of discharge advice. *Secondary:* Compliance/adherence to discharge advice, patient satisfaction with ED visit/discharge advice, ED reattendance within 28days with same complaint.

Key Results *4 studies, 1397 patients included.* All studies conducted at US study sites (mixed rural/community/urban teaching hospitals).

Sig.	*Outcome*	*N/Studies*	*Outcome Measure (95% CI)*	*I^2*
NSS	ED visit satisfaction	1 study, 205 pts	RR 1.02 (0.92-1.14)	N/A
SS	Comprehension	3 studies, 389 pts	RR 2.53 (1.19-5.35) favouring pictorial ED discharge; results stable to sensitivity analysis	89%
	Compliance	2 studies, 298 pts	RR 1.44 (1.22-1.68) favouring intervention	0%
	Completed meds course	1 study, 93 pts	RR 1.72 (1.11-2.50) favouring intervention	N/A
	Satisfaction with discharge advice	1 study, 205 pts	RR 1.48 (1.28-1.71) favouring intervention	N/A

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	?	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	X	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	Graduate student funding as part of MSc course (SD).
Conflict of interest	None (reported).

Potential threats to validity

Chance	None?
Selection bias	Thorough search of all usual information sources; not reported if done by single author or independently by 2+. No reporting of publication bias assessment (too few studies to complete a funnel plot).
Measurement bias	Use of Cochrane Risk of Bias tool for quality assessments; most studies had moderate RoB.
Analysis bias	Fixed effects analyses for low heterogeneity studies (random if high). Results stable to sensitivity analysis (removal of 1 large trial). No reporting on 28d ED recidivism in any included studies.
Confounding	Pictorial advice provided as an adjunct to verbal/written discharge instructions, so the effect is additive, not as replacement. No reporting on costs of generating pictorial materials and implementation. US-based studies may not be generalizable to other ED settings internationally.

Administrative details

Key words	Emergency Dept discharge, pictorial discharge advice, pictograms.
Appraisers	Upadhye S,
Reference(s)	Dermody S, Hughes M, Smith V. The Effectiveness of Pictorial Discharge Advice vs Standard Advice Following Discharge from the Emergency Department: A Systematic Review and Meta-Analysis. J Emerg Nurs 2021; 47: 66-75. https://doi.org/10.1016/j.jen.2020.07.005

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Can ED physicians use bedside POCUS to diagnose acute cholecystitis?

BEEM Bottom Line

Why is this study important? Acute cholecystitis can be a challenging diagnosis in the ED. A validated ED risk score, using elements of history symptoms, physical examination signs, and bedside POCUS findings, can help make a definitive diagnosis.

Which, if any, threats to validity are most likely to have an impact on the results and how? There is concern about convenience sampling that could introduce a selection bias in test performance outcomes. Lack of reported blinding for final outcomes adjudication also introduces risk of classification bias.

How do the key results compare with the current evidence? As with other ED POCUS studies, the main elements of diagnostic POCUS test performance are strongly dependent on operator experience.

How should this study impact the care of ED patients? The Bedside SAC score may be useful to successfully rule out/in acute cholecystitis (without lab studies), but further validation is likely required to make this a level II/I CDR.

Study Summary

Article	Graglia S, Shokoohi H, Loesche MA, et al. Prospective validation of the bedside sonographic acute cholecystitis score in emergency department patients. Am J Emer Med 2021; 42: 15-19. https://doi.org/10.1016/j.ajem.2020.12.085
Design	Validation of a previously derived clinical prediction or decision rule.
Population	*Included:* Adults (≥ 18years) in ED with suspected cholecystitis and being considered for RUQ POCUS. *Excluded*: Known diagnosis, pregnant, prisoners, declined/unable to give consent, non-English speaking, unable to complete follow-up (1 month later).
Predictors	Bedside SAC Score elements: postprandial symptoms (1pt), RUQ tenderness (1pt), Murphy's sign (2pts), gallbladder thickening (2pts), presence of gallstones (3pts); score range 0-9pts.
Comparison	Medical record review of patient outcomes up to 1mo ED visit (discharge diagnosis, additional abdo imaging, lab tests, surgical pathologies). If no MRR information, patients were emailed/called to ascertain outcomes (3 attempts). If no outcomes information confirmed, patients deemed to be negative for acute cholecystitis.
Outcomes	*Primary:* Performance of the Bedside SAC score; predictive value to diagnose acute cholecystitis. *Secondary:* Score performance at different cutoffs.

Key Results *N* = 153 patients included in the analysis. 24% (56/153) had a confirmed Dx acute cholecystitis. Avg age 43.5yrs, 34% males.

Table 2
Test performance of the Bedside SAC Score at all possible thresholds. Operating characteristics for each threshold include scores below but not including the score

Score	Sensitivity	Specificity	Accuracy	PPV	NPV	LR+	LR-
1	100% (90–100%)	9% (4–15%)	30% (23–38%)	25% (18–33%)	100% (69–100%)	1.09 (1.03–1.16)	0
2	100% (90–100%)	35% (27–44%)	50% (42–59%)	32% (24–42%)	100% (91–100%)	1.54 (1.35–1.76)	0
3	92% (78–98%)	55% (45–64%)	63% (55–71%)	38% (28–50%)	96% (88–99%)	2.02 (1.62–2.53)	0.15 (0.05–0.46)
4	89% (74–97%)	68% (58–76%)	73% (65–79%)	46% (34–58%)	95% (88–99%)	2.74 (2.06–3.64)	0.17 (0.06–0.42)
5	69% (52–84%)	88% (81–93%)	84% (77–89%)	64% (47–79%)	90% (83–95%)	5.8 (3.39–9.93)	0.35 (0.21–0.57)
6	67% (49–81%)	92% (85–96%)	86% (79–91%)	71% (53–85%)	90% (83–95%)	7.8 (4.13–14.7)	0.36 (0.23–0.58)
7	44% (28–62%)	96% (90–99%)	84% (77–89%)	76% (53–92%)	85% (78–91%)	10.4 (4.09–26.4)	0.58 (0.43–0.78)
8	17% (6–33%)	98% (94–100%)	79% (72–85%)	75% (35–97%)	79% (72–86%)	9.75 (2.06–46.2)	0.85 (0.73–0.98)
9	14% (5–30%)	100% (97–100%)	80% (73–86%)	100% (48–100%)	79% (72–86%)	∞	0.86 (0.76–0.98)

PPV/NPV = positive/negative predictive values, LR+/LR− = positive/negative likelihood ratios. Confidence intervals are included in parentheses.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The patients were representative of those with the problem.	✓	X	?
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	?	?✓X	?✓X
3. All patients underwent the same clinical evaluation.	?	?✓X	?✓X
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	✓	?✓X	?✓X
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	?	?✓X	?✓X
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	✓	?✓X	?✓X
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓	?✓X	?✓X
8. All patient-important outcomes were considered.	?	?✓X	?✓X
9. The follow-up was complete.	X	?✓X	?✓X
10. The point estimates and respective precisions are clinically significant.	✓	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	None.
Conflict of interest	3 authors disclosed funding support for unrelated research from GE/EMF (HS, CKH, ASL).

Potential threats to validity

Chance	None?
Selection bias	Convenience sampling used at 2 study sites introduces risk of selection bias. No comments on standardized history/physical exam for clinical assessment.
Measurement bias	Close agreement between ED POCUS and formal radiology diagnoses for gallstones (Kappa 88.4%), wall thickening (K 86.7%), pericholecystic fluid (90.7%), and sonographic Murphys sign (77.6%). AUC for different BedSAC scores was 0.874 (90.3-100%). 9/162 patients lost to follow-up (6%).
Analysis bias	Final ED physician adjudication may/may not have been blinded to initial SAC assessments? Risk of classification bias.
Confounding	POCUS image acquisition/interpretation will be strongly dependent on operator training/experience; no extra training provided for ED staff in this study.

Administrative details

Key words	Acute cholecystitis, clinical decision rules, emergency department POCUS
Appraisers	Upadhye S,
Reference(s)	Graglia S, Shokoohi H, Loesche MA, Dante D, Haney RM, Huang CK, Morone CC, Springer C, Kimberly HH, Liteplo AS. Prospective validation of the bedside sonographic acute cholecystitis score in emergency department patients. Am J Emer Med 2021; 42: 15-19. https://doi.org/10.1016/j.ajem.2020.12.085

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC 2
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the diagnostic accuracy for different clinical and laboratory findings for Giant Cell Arteritis (GCA)?

BEEM Bottom Line

Why is this study important? Giant cell arteritis is a rare but "can't miss" diagnosis in the ED, as a missed diagnosis could lead to vision loss.

Which, if any, threats to validity are most likely to have an impact on the results and how? Patient selection bias was unclear/high with majority of studies. Considerable risk of bias also associated with differential use/reporting of reference standards. Both of these will skew the overall results of the index tests. No analysis done with combining clinical features to improve diagnostic accuracy. There is some overlap in the cutoffs used for lab tests (ie. ESR=60) to confirm/exclude a GCA diagnosis.

How do the key results compare with the current evidence? These results update a prior meta-analysis on diagnostic utility of individual clinical & laboratory features, with increase precision. There is overall confirmation of no single finding to definitively confirm/exclude a GCA diagnosis.

How should this study impact the care of ED patients? No single demographic, clinical nor laboratory test is definitive enough to rule in or out a GCA diagnosis, but it may influence subsequent diagnostic testing (imaging, biopsy) or decisions to initiate glucocorticoid therapy with specialist follow-up. "Classic" features for GCA (eg. Headache, scalp tenderness, constitutional symptoms) have limited utility in raising/lowering risk of GCA. The authors suggest an ESR cutoff of 60mm/hr to differentiate "positive" vs "negative" results (in isolation).

Study Summary

Article	van der Geest KSM, Sandovici M, Brouwer E, Mackie SL. Diagnostic Accuracy of Symptoms, Physical Signs and Laboratory Tests for Giant Cell Arteritis: A Systematic Review and Meta-analysis. JAMA Intern Med 2020; 180(10): 12995-1304. doi:10.1001/jamainternmed.2020.3050
Design	Systematic review and meta-analysis of diagnostic accuracy studies
Population	*Included:* Consecutive patients being evaluated for GCA in the included studies (with at least 5 true positives and negatives), with an appropriate reference standard(s), and raw data available for meta-analysis. *Excluded*: Case-control studies, case reports, conference abstracts. Also excluded cases of previously confirmed GCA or closely related condition (eg. PMR). Excluded reporting of composite findings.
Index Test	Symptoms, physical signs, and laboratory tests for GCA.
Reference Test	Temporal artery biopsy (TAB), imaging, or clinical diagnosis of GCA (based on definite clinical criteria, or agreement of 2+ physicians). Where multiple reference standards available, the clinical Dx was considered for the main study analyses.
Diagnosis of Interest	Giant cell arteritis.

Key Results *N* = 14037 patients in 68 included studies; 4277 (30.5%) confirmed with GCA. 71% observational studies, 82% completed at academic centers. Pre-defined cutoffs for significance: LR+ >2.0 or LR- <0.50 (CI not including 1.00).

Index Test	*Positive Likelihood Ratio (95% CI)*	*Negative Likelihood Ratio (95% CI)*
Symptoms, Demographics	Limb claudication = 6.01 (1.38-26.16) Jaw claudication = 4.90 (3.73-6.41)	Age > 70 = 0.48 (0.27-0.86)
Physical Signs, Lab tests	TA thickening = 4.70 (2.65-8.33) Loss of TA pulsations = 3.25 (2.49-4.23) TA tenderness = 3.14 (1.14-8.65) Abnormal TA = 2.29 (1.61-3.26) Anterior ischemic optic neuropathy = 2.15 (1.53-3.03) ESR > 60 mm/hr = 2.40 (1.71-3.36) ESR > 80 = 2.79 (1.78-4.37) ESR > 100 = 3.11 (1.43-6.78) Platelets > 400x103/ul = 3.75 (2.12-6.64).	ESR > 40 = 0.18 (0.08-0.44) ESR > 50 = 0.42 (0.38-0.62) ESR > 60 = 0.42 (0.28-0.61) CRP > 2.5mg/dl = 0.38 (0.25-0.59) CRP > ref value = 0.40 (0.29-0.56)

CI: Confidence Interval; TA: Temporal Artery; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search included all languages, databases, abstracts, bibliographies, and expert contact.	?	X
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	X
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	?	X
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	?	✓
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = C. Bedard

QUADAS = quality assessment of diagnostic accuracy studies; ROC = receiver operating characteristic curve.

Funding and conflicts of interest

Funding This study was supported by TARGET partnership grant MR/N011775/1 from the Medical Research Council (Dr Mackie) and the Mandema Stipend from the University Medical Center Groningen (Dr van der Geest). Funding bodies had no roles in any part of study planning, conduct, data analyses, nor publication.

Conflict of interest 1. van der Geest: speaker fees from Roche. 2. Brouwer: speaker/consultancy fees from Roche (paid to university). 3. Mackie: Grant meeting support from Roche, consultancy fees from Roche/Sanofi, trial investigator for Sanofi/GSK. No other conflicts disclosures.

Potential threats to validity

Chance There were several features with insufficient data to reliably pool studies; however, the primary meta-analyses appear to have an adequate number of cases resulting in moderately precise confidence intervals.

Selection bias Search terms were comprehensive, but the search was limited to certain electronic databases, reference lists and was restricted to English-language only. However, there was minimal evidence of publication bias on funnel plot testing.

Measurement bias Data extracted singly by one author, then validated independently by another (not parallel independent abstractions). Clinical diagnosis of GCA as a reference standard is subjective and is strongly related to the experience of the individual diagnosing physician. Many symptoms lacked a clear definition in included studies (e.g., Jaw claudication).

Analysis bias Dichotomizing continuous variables (e.g., age, lab results) could artificially skew index test results. Uncertainty of the validity of the reference standard (particularly TAB) may have led to lowered estimates of accuracy of the individual index tests.

Confounding No study was low risk of bias; of particular concern was the frequent use of clinical diagnosis as both the index and reference tests may have inflated accuracy estimates. Concurrent treatment of glucocorticoid during assessment of laboratory features may have lowered the accuracy of these variables.

Administrative details

Key words	Giant cell arteritis, diagnostic test accuracy.
Appraisers	Upadhye S, Bedard C.
Reference(s)	van der Geest KSM, Sandovici M, Brouwer E, Mackie SL. Diagnostic Accuracy of Symptoms, Physical Signs and Laboratory Tests for Giant Cell Arteritis: A Systematic Review and Meta-analysis. JAMA Intern Med 2020; 180(10): 12995-1304. doi:10.1001/jamainternmed.2020.3050

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Chloe Bedard, PhD
Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the utility of low-dose ketamine (compared to IV morphine) for ED acute pain analgesia?

BEEM Bottom Line

Why is this study important? Acute pain in the ED is a very common complaint, and having effective analgesia options are important for patient satisfaction/safety. The quest for non-opioid alternatives is increasingly relevant, in the context of the opioid epidemic in North America.

Which, if any, threats to validity are most likely to have an impact on the results and how? Insert text here. Notes: Top 3 fatal flaws in order of priority. Explain in simple terms for clinician readers. Comment on GRADE. Notes:

How do the key results compare with the current evidence? Results are congruent with those of previous studies/reviews.

How should this study impact the care of ED patients? Low-dose ketamine infusion (0.2-0.5mg/kg) can be an effective alternative to IV morphine for acute ED analgesia, and is opioid sparing, esp with patients who may already be on naltrexone (alcohol withdrawal) or buprenorphine (opioid dependence). LDK may also be a useful non-opioid alternative in those patients with critical hypotension, underlying lung disease, decreased level of consciousness, and impaired renal morphine clearance.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Balzer N, McLeod SL, Walsh C, Grewal K. Low-dose Ketamine for Acute Pain Control in the Emergency Department: A Systematic Review and Meta-analysis. Acad Emerg Med 2021; 0:1-11. doi: 10.1111/acem.14159
Design	Systematic review and meta-analysis of randomized controlled trials.
Population	*Included:* Adults (≥ 18yo) with acute ED/prehospital pain conditions. *Excluded*: Pediatric patients, non-ED/prehospital settings, ketamine use in ED procedural sedation, or as an adjunct to other ED analgesics.
Intervention	Low-dose ketamine (LDK) infusion at different doses (0.2-0.5mg/kg.
Comparison	IV morphine (IVM) at 0.1mg/kg bolus doses (all included studies).
Outcomes	*Primary:* Mean differences in pain scores using standardized pain scales (0-10pt Likert scales) at specific time (15min) intervals. *Secondary:* Need for rescue analgesia, adverse events (nausea, hypoxia).

Key Results *8 included studies (all conducted in ED)* = 1191 patients (598 LDK, 593 IVM).

Sig.	*Outcome*	*N/Studies*	*Outcome Measure (95% CI)*	*Level of Evidence Certainty*
NSS	MD <15min	6 (757 pts)	MD -0.15 (-0.68 to 0.38)	Low LoE for all
	MD 15-30min	6	MD -0.03 (-0.37 to 0.32)	
	MD 30-45min		MD 0.40 (-0.37 to 0.32)	
	MD 45-60min		MD 0.52 (-0.03 to 1.07)	
	Rescue Meds needed	3 (306 pts)	RR 1.26 (0.50-3.16)	Very Low LoE
	Nausea	7 (1065 pts)	RR 0.97 (0.63-1.49)	Low LoE
	Hypoxia	3 (405 pts)	RR 0.38 (0.10-1.41)	Low LoE
SS	MD 60-90min		MD 0.12 (0.03-0.22) favours IVM	
	MD 90-120min		MD 0.08 (0.05-0.11) favours IVM	

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	X	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	✓	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	None reported.
Conflict of interest	None (reported)

Potential threats to validity

Chance	None?
Selection bias	None or enter text here (incomplete search, publication bias, etc.). English only studies included. No reported assessment of publication bias. One included trial was in abstract form, so unable to complete full RoB assessment.
Measurement bias	None or enter text here (e.g., missing details on study selection; missing results of quality assessments). Independent quality assessment of studies using Cochrane Risk of Bias tool; majority of included studies had low/uncertain risk of bias.
Analysis bias	None or enter text here (e.g., fixed vs. random effects, combined results of studies of different design). Random effects analysis for all outcomes (good). Variable heterogeneity (0-91%) across various time interval outcomes.
Confounding	Dosing effects of LDK; there may be different outcomes/adverse events based on LDK doses used. Also most included studies did not specify LDK

Administrative details

Key words	Acute pain, analgesia, emergency department, ketamine
Appraisers	Upadhye S,
Reference(s)	Balzer N, McLeod SL, Walsh C, Grewal K. Low-dose Ketamine for Acute Pain Control in the Emergency Department: A Systematic Review and Meta-analysis. Acad Emerg Med 2021; 0:1-11. doi: 10.1111/acem.14159

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

For drainage of skin abscesses, how does loop drainage compare to traditional I&D?

BEEM Bottom Line

Why is this study important? Treating skin abscess in the ED is common, yet potentially painful with traditional I&D, with unproven repeated packing thereafter (also painful), and associated with 10% treatment failures. Loop drainage technique provides a minimally invasive, less painful single intervention that can improve abscess outcomes.

Which, if any, threats to validity are most likely to have an impact on the results and how? None significant.

How do the key results compare with the current evidence? These findings support prior trials/reviews that loop drainage results in less Tx failures compared to traditional I&D. This augments the benefits of lesser pain for patients, reduced follow-up visits for packing changes, and better cosmetic outcomes.

How should this study impact the care of ED patients? Loop drainage is a superior abscess drainage technique with better outcomes compared to traditional I/D, less pain, less follow-up visits and better cosmetic outcomes. This should be the preferred technique for simple skin abscess drainage in the ED.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emerg Med/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Gottlieb M, Schmitz G, Peksa GD. Comparison of the Loop Technique with Incision and Drainage for Skin and Soft Tissue Abscesses: A Systematic Review and Meta-analysis. Acad Emerg Med 2020; 1-9. doi: 10.1111/acem.14151
Design	Systematic review and meta-analysis of all comparative studies.
Population	*Included:* All articles (retro/prospective) comparing Loop Drainage technique (LDT) with traditional I&D (TID). *Excluded*: Case reports/series, review articles.
Intervention	Loop drainage technique (LDT)
Comparison	Traditional I&D (TID)
Outcomes	*Primary:* Treatment failure (defined as per original studies, but could include repeat I/D, additional antibiotics use, need for hospitalization/operative management) *Secondary:* Pre-defined subgroups analyses = pediatrics vs adults, RCTs only.

Key Results *8 studies, 910 patients included for final meta-analysis*

Sig.	*Outcome*	*N/Studies*	*Measure NNT (95% CI)*	*I^2*
NSS	OR Tx failure in adults only; OR 1.54 (95%CI 0.79-3.00)		N/A	
NSS	OR Tx failure in children only; OR 3.23 (0.92-11.36)		N/A	
SS	OR Tx failure 2.02 (1.29-3.18) against TID		**NEEDS NNT calculation	

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	?	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	✓	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	None.
Conflict of interest	None.

Potential threats to validity

Chance	None.
Selection bias	No evidence of publication bias on funnel plot testing.
Measurement bias	None. No statistical heterogeneity amongst included studies.
Analysis bias	Use of random effects meta-analysis models for assumed clinical heterogeneity (appropriate).
Confounding	Possibly some minimal concerns about variable definitions used in primary trial outcomes (single vs composite). No significant differences noted with analysis of RCTs only.

Administrative details

Key words	Skin abscess, loop technique, incision & drainage.
Appraisers	S Upadhye,
Reference(s)	Gottlieb M, Schmitz G, Peksa GD. Comparison of the Loop Technique with Incision and Drainage for Skin and Soft Tissue Abscesses: A Systematic Review and Meta-analysis. Acad Emerg Med 2020; 1-9. doi: 10.1111/acem.14151

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emerg Med/Health Research
Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

CARDIO-RESP

Research Question

What are the latest recommendations in evaluating acute (ED) chest pain patients?

BEEM Bottom Line

Why is this study important? This guideline updates Recommendations on evaluating patients with acute chest pain, and many Recs are relevant to ED practice.

What, if any, threats to validity are most likely to have an impact on the results and how? The acquisition, evaluation and inclusion of relevant evidence is not explicitly reported, and no summary of Evidence/Findings tables presented. No patient/public stakeholders were included on the panel to establish topic priorities, and outcomes values/preferences. The majority of Recs are based on lower levels of evidence/expert opinion, so they don't lend themselves to use as quality improvement performance metrics. The majority of this guideline focuses on acute coronary syndromes (ACS)

How do the key results compare with the current evidence? These updated CPG Recs help to refine ED risk stratification processes, clinical decision pathways, testing and disposition. There is emphasis on reducing low-value testing and treatments in patients at low risk of 30day MACE (major adverse cardiac events). Recs are congruent and much more comprehensive than those published by SAEM GRACE (Guidelines for Reasonable & Appropriate Care in ED) for Recurrent Low-Risk Chest Pain (July 2021).

How should this study impact the care of ED patients? This guideline helps ED physicians to address chest pain risk stratification for ACS, and offers guidance on management, and disposition. Many Tables and Figures/algorithms are presented that can be adapted/adopted into clinical ED practice.

Study Summary

Article	Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/ SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021 Nov 30;144(22):e368-e454.
Design	Clinical Practice Guideline
Population	***Included:*** Numerous recommendations around the evaluation and management of chest pain. ***Excluded:*** No recommendations re: need/modalities of revascularization.
Scope of Recs	Guidance for the evaluation of acute or stable chest pain (or anginal equivalents), in different clinical settings, with an emphasis on diagnosing ischemic causes.

Key Recommendations (LoE = Level of Evidence)

**Only Class of Recommendation 1 (Strong, benefit >> harm), and 3 Harm (Strong, harm >> benefit). For brevity, CoR2 (Moderate/Weak) Recs are not included. Only those relevant to EM practice are listed here.

Recommendation	*Strength of Rec, Level of Supporting Evidence*
1. For intermediate-risk patients with acute chest pain and no known CAD eligible for diagnostic testing after a negative or inconclusive evaluation for ACS, CCTA is useful for exclusion of atherosclerotic plaque and obstructive CAD.	CoR1, A
2. For intermediate-risk patients with acute chest pain who have known CAD and present with new onset or worsening symptoms, guideline-directed medical therapy (GDMT) should be optimized before additional cardiac testing is performed.	CoR1, A
3. For intermediate-risk patients with acute chest pain who have worsening frequency of symptoms with significant left main, proximal left anterior descending stenosis, or multivessel CAD on prior anatomic testing or history of prior coronary revascularization, ICA is recommended.	CoR1, A
4. For **intermediate-high risk patients with stable chest pain and no known CAD**, CCTA is effective for diagnosis of CAD, for risk stratification, and for guiding treatment decisions.	CoR1, A
5. For patients with **obstructive CAD and stable chest pain**, it is recommended to optimize GDMT.	CoR1, A
6. For patients with obstructive CAD who have stable chest pain despite GDMT and moderate/severe ischemia, ICA is recommended for guiding therapeutic decision-making.	CoR1, A
7. For patients with obstructive CAD who have stable chest pain despite optimal GDMT, those referred for ICA without prior stress testing benefit from FFR or instantaneous wave free ratio.	CoR1, A
1. For patients with acute chest pain and suspected ACS initially evaluated in the office setting, delayed transfer to the ED for ECG, hs-cTn or other diagnostic testing should be avoided.	CoR3, C-LD
2. With availability of hs-cTn, creatine kinase myocardial (CK-MB) isoenzyme and myoglobin are not useful for diagnosis of acute myocardial injury.	CoR3, B-NR

BEEM Critique

Risk of bias assessment (amalgamated from AGREE-II/NEATS instruments)

	A1
1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.	✓
2. Financial conflicts of interest of guideline development group (GDG) members have been disclosed and managed.	✓
3. The CPG development group includes all the relevant multidisciplinary stakeholders, including clinicians, methodologists and patients/caregivers. **No patients/caregivers.**	✓
4. The CPG objectives, health questions, scope of relevant providers and target recipients of care are clearly defined.	✓
5. Values/preferences of patients, caregivers, advocates and/or the public with experience with the clinical disease management has been sought/integrated into CPG development (reported clearly). **No reps on group; obtained from literature review.**	X
6. The search strategy for evidence is thoroughly developed and described.	?
7. The criteria for selecting relevant studies/evidence are clearly described.	✓
8. The quality, strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.). Summaries of evidence tables are provided.	X
9. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓
10. There is an explicit approach linking the evidence to formulate the recommendations.	✓
11. The strength of recommendations is clearly reported, including confidence in underlying evidence.	✓
12. Recommendations are clear and unambiguous, and easily identified in the CPG publication.	✓
13. Different options for management for managing the health questions are clearly presented.	?
14. Experts externally reviewed the guideline prior to its publication.	✓
15. The CPG describes a procedure to update the guideline.	✓
16. The CPG provides advice, tools and/or clinical pathways for easy adoption/adaptation into practice.	✓
17. The CPG describes barriers and facilitators to implement recommendations.	?
18. Performance metrics for monitoring implementation of recommendations for audit/feedback have been defined appropriately.	X
19. Resource implications for implementing CPG recommendations have been discussed.	✓

A1 = S. Upadhye

Funding and conflicts of interest

Funding	(Reported). Funding provided by ACC/AHA. Guideline committee members volunteer their time.
Conflict of interest	(Reported in Supplemental Appendix materials). Many conflicts reported amongst authorship group. Voting recusals by section were reported.

Potential threats to viability

Development	*Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible?* There is an important absence in patient/public stakeholders in the panel, which may ignore important patient-centred priorities, and values/preferences with different interventions and outcomes. The details of the literature review are missing, so the magnitude and quality of the evidence base used to inform Recs is unclear (ie. no Evidence Summary tables presented). **Two academic EM physicians were included on the CPG authorship panel.**
Presentation	*Well organized with easy to find recommendations?* No; CPG Recs are scattered throughout the long document, and ideally should have been summarized at the beginning. A "Top Ten" takeaways infographic is presented, which is helpful. Clinical algorithms for assessing different chest pain presentations are well presented, and readily adaptable/adoptable into ED practice. Useful descriptive tables for chest pain descriptors, useful tests, prior test "warranties," testing cut-offs, etc., are provided.
Comprehensive	*Was the information to inform decision-making complete?* There are no ER-specific Recs provided, but many of these can be adapted into ED practice. Useful info is provided in risk-stratifying chest pain patients for potential ACS.
Clinical Validity	*Are the recommendations clinically sound and appropriate for the intended patients?* Yes

Administrative details

Key words	Chest pain syndromes, angina, coronary artery disease, acute coronary syndrome, myocardial ischemia/infarction/injury, noncardiac chest pain, accelerated diagnostic pathway, clinical decision pathway, sex differences, troponins, biomarkers, shared decision-making, cardiac imaging.
Reference(s)	Musey PI, Bellolio F, Upadhye S, Chang AM, Diercks DB, Gottlieb M, Hess EP, Kontos MC, Mumma BE, Probst MA, Stahl JH, Stopyra JP, Kline JA, Carpenter CR. Guidelines for reasonable and appropriate care in the emergency department (GRACE): Recurrent low-risk chest pain in the emergency department. Acad Emerg Med 2021; 1-27. DOI: 10.1111/acem.14296

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc FRCPC **No conflicts of interest (ICMJE)**
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Research Question

What is the utility of lung point-of-care ultrasonography (LUS) for diagnosing acute decompensated heart failure (ADHF)?

BEEM Bottom Line

Why is this study important? Acute dyspnea is a common ED presentation, and acute decompensated heart failure (ADHF) is the most common cause of ED death in these patients. Rapid and accurate diagnosis of ADHF can facilitate early treatment and, possibly, improved patient-oriented outcomes. This review compares the diagnostic performances of LUS and chest x-ray (CXR) for ADHF.

What, if any, threats to validity are most likely to have an impact on the results and how? The search strategy was very limited and, therefore, might have missed important contributory studies. The LUS diagnostic criteria (i.e., number of B-lines and lung zones) and the varied between studies thereby, impacting on both the validity and heterogeneity. All CXRs were read by a radiologist and the LUS operator was not blind to other clinical information. Incorporation bias occurred in determining the reference standard because of the inclusion of the CXR result.

How do the key results compare with the current evidence? Presence of lung US B lines have been positively correlated with pulmonary capillary wedge pressure (PCWP) measures, right atrial and pulmonary artery systolic pressures. This review expands on prior ones that support use of LUS as a viable & accurate ED bedside diagnostic tool.

How should this study impact the care of ED patients? Lung POCUS for ADHF is a valuable diagnostic modality and might perform better than CXR but both are dependent on the skill of the operator and reader respectively.

Study Summary

Article	Chiu L, Jairam MP, Chow R, Chiu N, Shen M, Alhassan A, Lo CH, Chen A, Kennel PJ, Poterucha TJ, Topkara VK. Meta-Analysis of Point-of-Care Lung Ultrasonography versus Chest Radiography in Adults with Symptoms of Acute Decompensated Heart Failure. Am J Cardiol 2022; 174: 89-95. DOI: 10.1016/j.amjcard.2022.03.022
Design	Systematic Review with Meta-analysis.
Population	***Included:*** Adult patients with ADHF investigated with chest Xray and lung US. ***Excluded:*** Case studies/series, reviews, non-clinical studies.
Index Test	Lung point-of-care ultrasonography (LUS)
Reference Standard	CXR results, medical results final diagnoses.
Diagnoses of Interest	Diagnostic accuracy of lung POCUS, CXR for diagnosis of ADHF.
Key Results	**8 studies included, 2787 patients included**. Mean age 71-81yo, males 46-54%. Studies conducted in Italy, Australia & Netherlands. Mixed scanning personnel: 3 studies with 1 ED physician scanner. Lung zones scanned per hemithorax 3-6; **positive LUS if >2 zones with 3+ B-lines.** **LUS Test Characteristics (pooled):** Sens 91.8% (95%CI 80.5-96.8, Spec 92.3% (86.6-95.7). **LR+ 11.92, LR- 0.09** **CXR Test Characteristics (pooled):** Sens 76.5% (67.2-83.7), Spec 87.0% (79.3-92.1). **LR+ 5.88, LR- 0.27.** Results robust after excluding 1 study with lack of uniform CXR reference standard use.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **5 electronic databases searched; no other lit searches reported.**	X	X
3. The search for studies was unbiased and reproducible. **No comment on duplicate searches?**	?	?
4. The selection of studies was unbiased and reproducible. **Duplicate screening of titles/abstracts.**	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	?	?
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible. **Initial QUADAS ratings by 1 author, then checked by 2 others; not independent.**	?	?
7. The quality of the primary studies is high. **Variable QUADAS domain scores for included studies.**	?	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	?	?
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Not reported.
Conflict of interest	Reported. No conflicts of interest declared.

Potential threats to viability

Chance	High QUADAS Risk of Bias in Patient selection (convenience sampling in 5/8 studies; 3 used consecutive sampling).
Selection bias	5 electronic databases searched.
Measurement bias	High RoB for reference std (CXR results accessible through medical records).
Analysis bias	Different cutoff thresholds used for US lung "zones" and B-line counts. Some risk of incorporation bias of CXR results in confirming final Dx of ADHF. Most studies at Low risk of concern for applicability.
Confounding	ROC curves suggest a better cut point for LUS compared to CXR (Figure 2). Subjective nature of confirmation reference standard (CXR interpretations, medical record) can alter diagnostic outcomes. Lack of blinding of US interpreter to other clinical data may lead to confirmation bias.

Administrative details

Key words	Acute decompensated heart failure, lung ultrasound, point of care
Reference(s)	Maw AM, Hassanin A, Ho PM, *et al.* Diagnostic accuracy of point-of-care lung ultrasonography and chest radiography in adults with symptoms suggestive of acute decompensated heart failure: a systematic review and meta-analysis. JAMA Netw Open 2019;2: e190703.

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc **No conflicts of interest (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Andrew Worster, MD, MSc **No conflicts of interest (ICMJE)** *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*

Research Question

What is the shortest effective duration of antibiotics for acute exacerbations of chronic obstructive pulmonary disease (AECOPD)?

BEEM Bottom Line

Why is this study important? COPD is the 5th leading cause of mortality worldwide and, although bacterial infections account for 50% of acute exacerbations (AECOPD), antibiotics (ABX) are prescribed for up to 90% of cases with resulting adverse reactions and antimicrobial resistance. This review sought to determine if shorter ABX treatment duration might be as effective and yield fewer adverse effects.

What, if any, threats to validity are most likely to have an impact on the results and how? A limited search using electronic databases and hand-searches has the risk of missing potentially important information. Use of different ABX in different duration studies may limit generalizability of comparisons.

How do the key results compare with the current evidence? The latest GOLD and ERS/ATS guidelines support the use of ABX for AECOPD, but the optimal duration is heretofore unclear. This review suggests that 5 days is sufficient.

How should this study impact the care of ED patients? For patients with spirometrically-confirmed COPD and acute exacerbations, a short-course of antibiotics (5d) is as efficacious as longer courses (7-10d).

Study Summary

Article	Llor C, Moragas A, Miravitlles M, Mesquita P, Cordoba G. Are short courses of antibiotic therapy as effective as standard courses for COPD exacerbations? A systematic review and meta-analysis. Pulm Pharmacol Ther. 2022 Feb;72:102111. doi: 10.1016/j.pupt.2022.102111.
Design	Systematic review/meta-analysis. PROSPERO reference number: CRD42019124894.
Population	***Included:*** RCTs of adults 40+yo, smoker or ex-smokers >10pkyrs, with spirometrically confirmed COPD (GOLD criteria) ***Excluded:*** Patients with suspected exacerbations of asthma, acute/chronic bronchitis, CAP or bronchiectasis.
Intervention	Short course of antibiotics (Abx) for 5 days or less.
Comparison	Standard course of Abx (6 days or more).
Outcomes	1) End-of-therapy clinical cure (clinical success within 2wks of Abx completion). 2) Bacterial eradication: negative throat swab culture within 2 wks of Abx completion 3) Adverse events: diarrhea, GI upset, rash
Key Results	**Eight studies included, 3670 patients (1828 short course, 1842 std course)** 1) End-of-Rx clinical cure (7 studies, 2826pts; Fig 3): **No significant differences** OR 1.14 (95%CI 0.91-1.44); I^2=0. Short course amoxicillin or clarithromycin slightly less Rx success compared to fluroquinolones (NSS). 2) Bacterial eradication (6 studies, 1832pts; Fig 4): **No significant differences** OR 1.16 (0.91-1.48); I^2=11%. 3) Adverse events (7 studies, 3610pts; Fig 5): **No significant differences** OR 0.83 (0.61-1.13); I^2=55%.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Medline, Cochrane databases only; reference lists of selected studies.**	X	X
3. The search for studies was unbiased and reproducible. **Independent duplicate searches**	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible. **Cochrane RoB**	✓	✓
7. The quality of the primary studies is high. **Most studies (except 1) were at mostly low RoB (Figure 2)**	✓	✓
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	?

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Reported; not funded.
Conflict of interest	2 authors (CL, MM) have received industry grants and speaking fees.

Potential threats to viability

Chance	Possible type II errors.
Selection bias	Limited electronic search with reference lists from included articles. No gray literature searched. No language restrictions. No reporting on publication bias assessments.
Measurement bias	Missing details on study selection; missing results of quality assessments.
Analysis bias	Use of random effects analysis due to expected heterogeneity. Some variability in heterogeneity based on Abx compared, duration of Rx, etc.
Confounding	Most short-course studies used fluoroquinolones, and long-course studies used beta-lactams.

Administrative details

Key words	COPD, acute exacerbations, antibacterial agents, drug resistance
Reference(s)	Messous et al. Ther Adv Respir Dis 2022, Vol. 16: 1–10 DOI: 10.1177/17534666221099729

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC **No conflicts of interest (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Andrew Worster, MD, MSc **No conflicts of interest (ICMJE)** *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*

Research Question

What is the risk of major adverse cardiac events (MACE) in ED chest pain patients with prior advanced investigations?

BEEM Bottom Line

Why is this study important? Patients with no known coronary artery disease, may present to the Emergency Department repeatedly for chest pain. If they have had negative advanced investigations for chest pain in the last year, do they need admission or repeat advanced testing when are seen again in the ED? This review summarizes the "warranty period" for such investigations to rule out short term major adverse cardiac events (MACE), assuming a negative ED workup and prior outpatient investigations.

What, if any, threats to validity are most likely to have an impact on the results and how? There is only one RCT on this subject, and this meta-analysis relies on additional observational/cohort data to make conclusions.

How do the key results compare with the current evidence? These results reinforce the SAEM GRACE-1 and ACC-AHA Guidelines for Low-Risk ED Chest Pain (2021), that recommend a "warranty period" of up to 1 year for recent negative advanced CAD testing in otherwise low risk of 30-day MACE in ED chest pain patients.

How should this study impact the care of ED patients? Patients with "negative" ED ECG/troponin testing and negative prior advanced investigations in the preceding 1 year can be safely discharged with low risk of 30-day MACE.

Study Summary

Article	Mehta P, McDonald S, Hirani R, Good D, Diercks D. Major adverse cardiac events after emergency department evaluation of chest pain patients with advanced testing: Systematic review and meta-analysis. Acad Emerg Med. 2022 Jun;29(6):748-764. doi: 10.1111/acem.14407.
Design	Systematic review/meta-analysis. PROSPERO Reg#: 266107
Population	***Included:*** Studies recruiting ED chest pain patients with low/intermediate risk chest pain (TIMI <5 or HEART <6), negative ED ECG and troponins, and prior CAD testing within past 12mo (cCTA = coronary CT angiogram, XST = exercise stress test, stress ECHOcardiography/MPS = myocardial perfusion scan) ***Excluded:*** Unable to access full text of selected studies.
Index Test	ED chest pain testing
Reference Standard	Recent cCTA, XST, stress ECHO/MPS
Diagnoses of Interest	MACE Event rates= Death, MI, hospitalization due to heart failure, percutaneous cardiac catheterization with intervention, or coronary artery bypass grafting. Events at 1mo, 6mo and 12mol.
Key Results Mean age: 54 (+/-11) Female: 47%	**33 articles included (7 RCTs, 17 prospective cohorts, 9 retrospective cohorts).** **cCTA (7153 pts), XST (521), stress ECHO (1892), nuclear MPS (1237).** ***MACE 1mo*** (21 studies): MPS – no results pooled (no events) (Figure 1) cCTA = 0.09% (95%CI 0.03-0.26, I^2=9%) XST = 0.23% (0.01-5.8%, I^2=51%) ***MACE 6mo*** (17 studies): XST and ECHO studies not pooled due to considerable heterogeneity. (Figure 2) cCTA = 0.05% (0-3.41%, I^2=56%) MPS = 0.17% (0.04-0.68%, I^2=0%) ***MACE 12mo*** (8 studies): cCTA = 0.16% (0.04-0.65%, I^2=0%) ECHO = 1.68% (1.09-2.59%, I^2=0%) (Figure 3) ***Subgroups: cCTA no stenosis vs. non-obstructive (<50% stenosis)*** MACE 1mo (17 studies): 0.09% (0.03-0.27%, p=1.00, I^2=9%); no CAD 0.17% vs non-Obx CAD 0.06% MACE 12mo (5 studies): 0.50% (0.21-1.2%).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Electronic databases searched (4) with librarian. No mention of gray literature, contacting authors**	X	X
3. The search for studies was unbiased and reproducible. **No mention of duplicated searches**	?	?
4. The selection of studies was unbiased and reproducible. **Dual independent**	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **Not reported**	?	?
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible. **Use of Cochrane RoB2 (RCTs) and RoBIN-I (non-RCTs) tools for included studies**	✓	✓
7. The quality of the primary studies is high. **Most studies low RoB (Table 1), but only 1 RCT**	✓	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	N/A	?
9. The subgroups were stated a priori and appropriate. **Subgroup analyses based on advanced modality; cCTA further sub-analyzed based on "no CAD" vs "non-obstructive CAD" detected**	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = M. Welsford

Funding and conflicts of interest

Funding	None reported.
Conflict of interest	Reported; no conflicts declared.

Potential threats to viability

Chance	
Selection bias	*Specify comprehensive searches; publication bias?* No duplicate search nor assessment of publication bias reported.
Measurement bias	Some variability in MACE definitions within included studies.
Analysis bias	*Fixed/random effects? Heterogeneity mgt?* Heterogeneity assessed by Cochran Q and I^2 statistics (random effects analysis). I^2 = 47%. Only 1 RCT included and the rest are observational.
Confounding	*Enter independent factors affecting the outcome; clinicians to comment.* Patients lost to follow-up in individual studies were not included in this review (even if no MACE was documented in chart).

Administrative details

Key words	Coronary CTA, ECG, emergency department, low-risk chest pain, MACE, major adverse cardiac events, meta-analysis, myocardial perfusion scintigraphy, stress ECHO, stress EKG, stress testing, systematic review, TIMI
Reference(s)	1. Musey Jr PI, Bellolio F, **Upadhye S**, *et al*. Guidelines for reasonable for appropriate care in the emergency department (GRACE): Recurrent low-risk chest pain in the emergency department. Acad Emerg Med 2021; 00:1-27. DOI: 10.1111/acem.14296 2. Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/ SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021 Nov 30;144(22):e368-e454.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC **No conflicts of interest/Identify conflicts (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Michelle Welsford, MD, FRCPC, DRCPSC **No conflicts of interest** *Professor & Division Director, Emergency Medicine, McMaster University*

Research Question

What is the clinical utility of symptoms, signs and imaging modalities for ruptured abdominal aortic aneurysm diagnosis?

BEEM Bottom Line

Why is this study important? Ruptured AAA (rAAA) is a surgical emergency (50-90% mortality) requiring rapid early diagnosis in the emergency department (ED) to expedite surgical intervention. This study reviews the diagnostic accuracy of clinical symptoms, signs, ED point-of -are ultrasound (POCUS) and computed tomography angiography (CTA) for confirming a diagnosis of rAAA.

What, if any, threats to validity are most likely to have an impact on the results and how? Source studies included mostly positive cases, making it difficult to calculate test-treatment thresholds and bivariate ROC curves.

How do the key results compare with the current evidence? Prior Canadian task Force on Preventive Health Care 2017 guidelines identify older males (age 65-80 years), smokers, those with vasculopathy (e.g., CAD, atherosclerosis, hypercholesterolemia, hypertension) and those with family history of AAA at highest risk of rupture.

How should this study impact the care of ED patients? Nonspecific clinical features have insufficient sensitivity to confidently exclude a rAAA diagnosis. ED POCUS is useful to identify AAA, but not rAAA. If the diagnosis is still in doubt, a CTA is required but still might miss some patients.

Study Summary

Article	Fernando SM, Tran A, Cheng W, Rochwerg B, et al. Accuracy of presenting symptoms, physical examination, and imaging for diagnosis of ruptured abdominal aortic aneurysm: Systematic review and meta-analysis. Acad Emerg Med; 2022: DOI: 10.1111/acem.14475.
Design	Systematic Review/meta-analysis. Registered at Open Science Framework
Population	***Included:*** Adults (age>16yo) with suspected rAAA based on symptoms, signs, POCUS or CTA (CT angiography) findings. ***Excluded:*** Case reports, case series, animal studies. Also excluded studies involving routine AAA screening/surveillance in non-urgent settings (e.g. GP office).
Index Test	Clinical symptoms, physical signs, POCUS or CTA findings.
Reference Standard	Intra-operative confirmation or death from rAAA.
Diagnoses of Interest	Ruptured AAA (rAAA). Performance of POCUS vs CTA or reference standards.
Key Results <u>*Symptoms:*</u> <u>*Signs:*</u> <u>*POCUS:*</u> <u>*CTA:*</u>	**20 studies included, 2077 patients.** 14 retrospective (66.6% pts), 17 single centers (72.7%). 10 studies from North America (38.9% pts), 7 from Europe (41.1%), 2 from Australia (19.1%), and 1 from Asia (0.9%). QUADAS Risk of Bias: 7 studies "unclear", remainder low risk of bias (RoB). (Figure S2). 1) Abdo pain (1091pts): Pooled Sens 61.7% (95%CI: 51.3-72.2); GRADE certainty **Low** 2) Back pain (1072pts): Pooled Sens 53.6% (42.8-64.3); GRADE **Low** 3) Syncope (592pts): Pooled Sens 27.8% (11.7-43.9); GRADE **Low** 4) Hypotension (577pts): Pooled Sens 30.9% (19.3-42.6); GRADE **Low** 5) Pulsatile Abdo mass (894pts): Pooled Sens 47.1% (29.3-64.8); GRADE **Low** 6) POCUS accuracy for unruptured AAA (628pts): Pooled Sens 97.8% (95.4-100), Spec 97% (93.9-100); GRADE **Moderate** CTA accuracy for rAAA (360pts): Pooled Sens 91.4% (81.1-96.4), Spec (93.6% (83.4-97.7) **LR+ 14.3 (5.2-39.6) LR- 0.09 (0.04-0.21)**

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Search 6 electronic databases only.**	X	X	X
3. The search for studies was unbiased and reproducible. **No comments on duplicate searches**	?	?	?
4. The selection of studies was unbiased and reproducible. **Duplicate independent screening**	✓	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓	✓
6. The quality assessment of the primary studies used **QUADAS-2**, was unbiased, and reproducible.	✓	✓	✓
7. The quality of the primary studies is high. **Figure S2**	✓	✓	✓
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	?	?	?
9. The subgroups were stated a priori and appropriate. **POCUS vs CTA, Reference standards**	✓	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓	✓

A1 = S. Upadhye A2 = A. Worster A3 = R. Valani

Funding and conflicts of interest

Funding	Reported. Primary author funded with CAEP Junior Investigator Grant.
Conflict of interest	Reported. No conflicts of interest declared.

Potential threats to viability

Chance	Most included studies had patients with confirmed rAAA, and therefore unable to calculate incidence rates, false/true negative rates. Risk of spectrum bias (patients recruited into studies based on different course of illness); possibly mitigated with inclusion of ED studies when patients are in acute phase of illness.
Selection bias	*Specify comprehensive searches; publication bias?* Search included 6 electronic databases with librarian assistance. RCTs and observational studies were included. There is no mention of manual reference searches or reviewing gray literature. There were no language restrictions. No comments on publication bias.
Measurement bias	Insufficient Spec data to calculate hierarchical summary (HSROC) curves in bivariate models. Unable to calculate test-treatment threshold analyses (not enough negative cases). No study evaluated sequential testing (clinical, imaging), so all analyses calculated in isolation.
Analysis bias	High heterogeneity (I^2 84-95%) in univariate forest plots of symptoms/signs; could not be accounted for in risk of bias analyses.
Confounding	Not all studies included outcomes for patients who didn't have surgery, so results will be at risk of partial verification bias (not all patients receive ref std test) or differential verification bias (pts getting different ref std confirmations based on index test results).

Administrative details

Key words	abdominal aortic aneurysm, computed tomography, point-of- care ultrasound
Reference(s)	Canadian Task Force Preventive Health Care. Recommendations on screening for abdominal aortic aneurysm in primary care. CMAJ 2017 September 11;189:E1137-45. doi: 10.1503/cmaj.170118.

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**
Andrew Worster, MD, MSc *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**
Rahim Valani, MD, MBA, FRCPC *Assoc. Professor, University of Toronto*	**No conflicts of interest (ICMJE)**

Research Question

How well does the Canadian Syncope Risk Score (CSRS) predict serious outcomes?

BEEM Bottom Line

Why is this study important? The Canadian Syncope Risk Score (CSRS) was developed to risk stratify patients with ED syncope for serious outcomes and, thereby, minimize low-value resource expenditures and hospital admissions. The CSRS is comprised of 3 items from each of the clinical evaluation, investigations and the clinician classification of syncope at ED discharge. This study externally validated the CSRS and compared it to another validated score, the Osservatorio Epidemiologico della Sincope nel Lazio (OESIL) score.

What, if any, threats to validity are most likely to have an impact on the results and how? High admission rates in certain countries may have influenced some of the components of the composite outcomes, contributing to potential ascertainment and incorporation bias. Also, the results are partly driven by the clinician classification of syncope at ED discharge.

How do the key results compare with the current evidence? This large international study confirms prior smaller validation studies conducted in other countries with younger patient cohorts (Canada, Italy, Australia).

How should this study impact the care of ED patients? Implementation of CSRS can help to identify (very) low risk syncope patients who can be discharged safely from the ED.

Study Summary

Article	Zimmermann T, du Fay de Lavallaz J, Nestelberger T, *et al.* International Validation of the Canadian Syncope Risk Score: A Cohort Study. Ann Intern Med. 2022 Jun; 175(6):783-794. doi: 10.7326/M21-2313. Epub 2022 Apr 26.
Design	Prospective cohort study to validate syncope risk scores. 14 hospitals in 8 countries. ClinicalTrials.gov: NCT01548352
Population	***Included:*** ED adults 40+ yo with syncope within 12hrs. ***Excluded:*** Patients with non-syncopal loss of consciousness (eg. seizure, intoxication, fall, presyncope, stroke).
Predictor Variables	Syncope risk scores (Canadian, OESIL)
Comparison	N/A.
Outcomes	***Primary:*** Composite serious outcome (30day) = death, life-threatening arrhythmia, MI, serious structural heart disease, aortic dissection, pulmonary embolism, severe pulmonary hypertension, severe hemorrhage, or any other serious cause/procedural intervention for syncope. ***Secondary:*** Composite non-procedural outcome = clinical outcomes above without procedural interventions. Both outcomes up to 720days follow-up. ***Subgroups***: (Very) Low Risk = CSRS <0, OESIL 0-1; Med Risk = CSRS 1-3, OESIL 2; (Very) High Risk CSRS 4+, OESIL 3-4
Key Results	**2283 patients analyzed.** Mean age 68yo, 42% women, 19% had coronary artery disease. 54% hospitalized, 46% discharged from ED. ***Primary outcome 7.2% (n=165), secondary outcome 3.1% (n=70).*** **Primary outcome AUC: CSRS 0.85** (95%CI 0.83-0.88), **OESIL 0.74 (**0.71-0.78); p<0.001 Sens CSRS (Very Low Risk): 0.91 (0.85-0.95), (Very High Risk): 0.45 (0.37-0.53) OESIL (Very LR): 0.82 (0.75-0.87), (Very HR): 0.59 (0.37-0.66) Spec CSRS (VLR): 0.65 (0.64-0.67), (VHR) 0.92 (0.91-0.93), OESIL (VLR): 0.51 (0.49-0.53), (VHR) 0.78 (0.76-0.80) CSRS (VLR): LR+ 2.6, LR- 0.14; (VHR) R+ 5.63, LR- 0.60 OESIL (VLR): LR+ 1.67, LR- 0.35; (VHR) LR+ 2.68, VR- 0.53 **Secondary outcome AUC: CSRC 0.80** (0.75-0.84), **OESIL 0.69** (0.64-0.75); p<0.001 CSRS triaged 60.8% (n=1388) towards very low risk; 30d primary outcome 1.1% (15/1388), 30d secondary outcome 1.1% (15/1388).

	OESIL triaged 48.4% (n=1104) towards low risk; 30d primary outcome 2.7% (30/1104), 30d secondary outcome 2.7% (30/1104). Outcomes 720days (95.2% patients): 20.7% had primary comp outcome, 13.9% sec comp outcome. Event rates higher in VHR/HR/Med risk vs LR/VLR groups.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those with the problem.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	✓	✓
3. All patients underwent the same clinical evaluation.	✓	✓
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	✓	✓
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	✓	✓
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	?	?
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓	✓
8. All patient-important outcomes were considered.	✓	✓
9. The follow-up was complete.	✓	✓
10. The point estimates and respective precisions are clinically significant.	✓	✓

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Swiss National Science Foundation & Swiss Heart Foundation (and others). No role in any phase of the study.
Conflict of interest	Online reporting; some authors had public grants, some industry disclosures.

Potential threats to viability

Chance	No sample size calculation *a priori* (no methodology to justify such). ED workups at discretion of ED physician; may not have completed all rule variables assessments?
Selection bias	Unknown if the sampling method representative of the target population.
Measurement bias	N/A
Analysis bias	*Are the results data- or hypothesis-driven? Is the model over fitted and not applicable?*
Confounding	Residual confounding as with all observational studies because of unknown prognostic factors that cannot be controlled for. High variation in admission rates across all countries (54%; Canada 14% to USA 80%) with higher rates of monitoring/investigations/interventions for composite outcomes (risk of ascertainment and incorporation bias).

Administrative details

Key words	Emergency department, risk scores, syncope
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc FRCPC **No conflicts of interest (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Andrew Worster, MD, MSc **No conflicts of interest (ICMJE)** *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*

Research Question

Is a Drug-Shock treatment strategy (compared to Shock-Only) superior for ED acute atrial flutter conversion to sinus rhythm?

BEEM Bottom Line

Why is this study important? ED presentation of acute atrial flutter is less common that atrial fibrillation. Treatment of symptomatic atrial flutter can be achieved via a Drug-Shock vs. Shock-Only strategy.

Which, if any, threats to validity are most likely to have an impact on the results and how? This was a planned sub-study of a larger ED acute AFib trial; may have been under-powered to detect an MCID of 10% between the two strategies.

How do the key results compare with the current evidence? Results are congruent with prior (Canadian) studies that show excellent outcomes for immediate rhythm control strategies can be achieved, with high ED discharge rates and sustained NSR.

How should this study impact the care of ED patients? There is no statistical difference between either treatment strategy, both during the ED visit, and at 14day follow-up. However, procainamide was NOT very effective (27% conversion) and thus is NOT recommended as the Drug choice for acute Aflutter. Shared decision-making with patients is needed to make an appropriate management decision.

Study Summary

Article	Stiell IG, Sivilotti MLA, Taljaard M, *et al*. A randomized, controlled comparison of electrical versus pharmacological cardioversion for emergency department patients with acute atrial flutter. CJEM. 2021 May;23(3):314-324. doi: 10.1007/s43678-020-00067-7.
Design	Randomized, placebo-controlled, blinded study
Population	*Included:* Stable patient with symptomatic acute atrial flutter ≥3hrs duration with onset within last 48hrs, onset within 7days with adequate anticoagulation ≥4 weeks, or onset within 7days with no left atrial thrombus on TEE. *Excluded*: Hemodynamic instability, required immediate emergency cardioversion (sBP <100), rapid ventricular pre-excitation, acute coronary syndrome, pulmonary edema), spontaneous reversion prior to randomization, previously enrolled in study, non-arrhytmia primary presentation (eg. CAP, PE, sepsis). Other patient safety concerns (listed in online Appendix).
Intervention	Attempted pharmacological cardioversion with IV procainamide (15 mg/kg over 30 min, max 1500mg) followed by electrical cardioversion (≥ 200J x3) if necessary. Infusion was stopped if patient converted to NSR, QTc prolongation >35%, QRS interval >120ms, HR <60bpm or sBP <100mmHg not responsive to IV fluid bolus. (Drug-Shock)
Comparison	Placebo infusion followed by electrical cardioversion. (Shock Only)
Outcomes	*Primary:* Conversion to/maintenance of NSR for 30+ minutes post randomization/3 shocks. Verified by blinded adjudication committee (2 ED physicians/1 electrophysiology cardiologist). *Secondary:* ED length of stay, cardiac rhythm at disposition, adverse events during ED visit. 14day ECG rhythm, recurrence of atrial flutter, ED return visits, hospital admissions, stroke, and survival.

Key Results: *N* = 76 patients. Drug-Shock 33 pts, Shock-Only 43 pts.

Sig.	*Outcome*	*Intervention*	*Comparison*	*AD (95% CI)*	*NNT (95% CI)*
NSS	Primary conversion to NSR	33 (100%)	40 (93%)	7% (-6 to 14%) (p=0.25)	N/A
	ED LOS	9.4hrs	7.5hrs	1.9hrs (-1.2 to 5 (p=0.50)	
	NSR at disposition	100%	100%	N/A	N/A
	14day NSR	92%	91%	N/A	
	14d Rec AFib	0	2.9%	NS	
	14d Return ED visits	21.2%	18.6%	NS	
	14d admission	3%	0	NS	
	Stroke or death	0	0	NS	
SS	Transient ED hypotension	24%	2.3%	21.7% (p=0.004)	

ARR = absolute risk reduction (if the CI includes the value 0, there is no difference in risk between the groups and the NNT is not estimable); CI = confidence interval; *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	X	X
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	?	?
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = M. Welsford ITT = intention to treat.

Funding and conflicts of interest

Funding	Grants from CIHR, Heart & Stroke Foundation of Canada.
Conflict of interest	None (reported).

Potential threats to validity

Chance	Planned for 50 pts enrolled (part of a larger AFib study); eventually screened 165 and enrolled 76.
Selection bias	Some differences noted between both groups at baseline. Convenience sampling strategy resulted in missed eligible patients and may have led to bias.
Measurement bias	Under-powered to adequately rule out MCID 10%.
Analysis bias	Primary ITT. Secondary modified ITT excluding rhythm converters prior to study infusion. Eleven patients were excluded for AFib Dx (not Aflutter).
Confounding	Despite block randomization, the two groups were not evenly balanced for baseline demographics.

Administrative details

Key words	Atrial flutter, cardioversion, emergency department, procainamide
Appraisers	Upadhye S, Welsford M
Reference(s)	Stiell IG, Sivilotti MLA, Taljaard M, Birnie D, Vadeboncouer A, Hohl CM, McRae AD, Morris J, Mercier E, Macle L, Brison RJ, Thiruganasambandamoorthy V, Rowe BH, Borgundvaag B, Clement CM, Brinkhurst J, Brown E, Nemnon MJ, Wells GA, Perry JJ. A randomized, controlled comparison of electrical versus pharmacological cardioversion for emergency department patients with acute atrial flutter. CJEM. 2021 May;23(3):314-324. doi: 10.1007/s43678-020-00067-7.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Michelle Welsford, MD, FRCPC
Director & Professor, Emergency Medicine, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Can ED chest pain patients at low-risk of adverse cardiac events be identified without troponin testing?

BEEM Bottom Line

Why is this study important? There is a cohort of ED chest pain patients who are very low risk of adverse cardiac events at 30days, and do not require troponin testing during their initial visit. This study examines the utility of the HEAR score to avoid such testing in low-risk patients.

What, if any, threats to validity are most likely to have an impact on the results and how? As a secondary analysis of a past prospective study, this is a retrospective validation of the HEAR score using the 3rd rather than 4th Universal Definition of MI as the primary outcome. The HEAR score is an abbreviated version of the HEART score and, as such, is subject to all of the methodological weaknesses of the HEART score including but not limited to its subjective variable generation and interpretation, arbitrary cut offs and poor inter-rater reliability. Also, to be of value, the score will have to demonstrate better performance than clinical gestalt. Further prospective validation is required.

How do the key results compare with the current evidence? This study supports prior work suggesting that use of the HEAR score (0 or 1pt) might safely identify low risk ED chest pain patients who don't necessarily need troponin testing.

How should this study impact the care of ED patients? The HEAR score (cutoff 0 or 1pts) might be proven to be a useful tool to stratify low-risk ED chest pain patients to no troponin testing, thereby saving resources and time in ED but, as yet it is not fully validated for contemporary use. Clinical gestalt remains the best tool for now.

Study Summary

Article	O'Reilly CM, Andruchow JE, McRae AD. External validation of a low HEAR score to identify emergency department chest pain patients at very low risk of major adverse cardiac events without troponin testing. Can J Emerg Med 2021; https://doi.org/10.1007/s43678-021-00159-y
Design	CDR validation using a retrospective trial cohort (secondary analysis).
Population	*Included:* Adults ≥25yo with ED chest pain and requiring troponin testing to exclude AMI. *Excluded:* STEMI, clear acute ischemic/new arrhythmia on ECG, hemodynamic instability, advanced renal failure, ACS Dx 30days prior, unable to consent.
Predictor Variables	HEAR score: History, ECG findings, Age, Risk Factors
Comparison	Adjudicated outcomes assessments by two independent board-certified physicians.
Outcomes	*Primary:* AMI (using 3rd Universal definition), 30day major adverse cardiac events (MACE) = composite of MI, cardiac death, urgent revascularization (PCI, CABG).
All	1150 patients included in analysis. Known CAD rate 330pts. Subgroups analyzed: No known CAD vs all patients (including known CAD)

1) ***No known CAD*** (820pts): 57pts (7%) had index MI, 64 (7.8%) had a 30day MACE
HEAR = 0pts (65pts, 7.9%): Sens 100% (93.7-100) for MI, 100% (94.4-100) for 30d MACE. Spec was 8.5% and 8.6% respectively. LR+ 1.1 (1.1-1.1)
HEAR ≤1pt (202pts, 24.6%): Sens 98.3% (90.6-99.9) for MI, 98.4% (91.6-99.9) for 30d MACE. Spec 26.3% (23.3-29.6) for MI, 26.6% (23.5-29.9) for 30d MACE. NPV 99.5% for both endpts. LR+ 1.3 (1.3-1.4), LR- 0.1 (0.0-0.5) for MI and 30d MACE (0.0-0.4).

2) ***All patients*** (1150pts):
HEAR = 0pts: No MI/composite 30d MACE events noted. LR+ 1.1 (1.1-1.1) for MI and 30d MACE
HEAR = 1pt: 1pt had both MI and 30d urgent revascularization. LR+ 1.2/LR- 0.1 for MI, LR+ 1.2/LR0.0 for 30d MACE
Overall Sens 98.9% (95.6-99.9) for MI, 99.2% (95.6-99.9) for 30d MACE. Spec (HEAR≤1pt) 19.1 (16.7-21.6%) for MI 19.6% (17.2-22.1) for 30d MACE. NPV (HEAR≤1pt) 99.5 (96.6-99.9%).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those with the problem.	✓	?✓X
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	?	?✓X
3. All patients underwent the same clinical evaluation.	✓	?✓X
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	✓	?✓X
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	✓	?✓X
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	✓	?✓X
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓	?✓X
8. All patient-important outcomes were considered.	✓	?✓X
9. The follow-up was complete.	✓	?✓X
10. The point estimates and respective precisions are clinically significant.	✓	?✓X

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding Secondary analysis of a prior investigator-initiated study, funded by an unrestricted grant from Roche Diagnostics Canada.

Conflict of interest None (reported).

Potential threats to viability

Chance N/A. This is a secondary analysis of original trial results, using data available.

Selection bias Mixed sampling = consecutive patients recruited, during research assistant hours 0800-2000 (7days/week). Groups were balanced in original parent study.

Measurement bias Not clear how the HEAR score was calculated for each patient in the parent cohort; while the EAR components are somewhat objective, the History component may be subjective based on original assessing physicians assessment/documentation.

Analysis bias N/A.

Confounding Residual confounding as with all observational studies because of unknown prognostic factors that cannot be controlled for; Independent factors affecting the outcome; clinicians to comment.

Administrative details

Key words Chest pain, HEAR score, risk stratification, troponin testing

Appraisers S. Upadhye, A. Worster

Reference(s)

- Mounmeh et al. Identifying Patients with Low Risk of Acute Coronary Syndrome Without Troponin Testing: Validation of the HEAR Score. Am J Med 2021; 134(4):499-506.e2. doi: 10.1016/j.amjmed.2020.09.021.
- Andruchow et al. Prospective comparative evaluation of the European Society of Cardiology (ESC) 1-hour and a 2-hour rapid diagnostic algorithm for myocardial infarction using high-sensitivity troponin-T. CJEM 2020; 22(5): 712-720.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Andrew Worster, MD, MSc
Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the appropriate period of observation (using hs-troponins) for ED chest pains for ruling out ACS/NSTEMI?

BEEM Bottom Line

Why is this study important? Use of the ESC 0/1hr algorithm (with high sensitivity cardiac troponin [hs-cTn]) for ED chest pain (r/o NSTEMI) accurately identifies 70-75% of patients at 0h and 1hr, but this leaves 25-30% patients unclassified. This study aimed to refine criteria to more accurately identify such patients more accurately/safely.

What, if any, threats to validity are most likely to have an impact on the results and how? Use of hs-cTn results in the final adjudication of NSTEMI is a long-standing confounder and continues here. It is not clear how many patients were lost to follow-up (up to 24mo), and how this may have influenced prevalence numbers and diagnostic test performance characteristics (17% did not have a 3hr hsTrop value).

How do the key results compare with the current evidence? This study refines prior 0/1hr ESC rule in criteria, by advancing the discrimination of test cutoffs and delta change values in the 1-3hr observation period.

How should this study impact the care of ED patients? ED physicians in conjunction with their laboratory and cardiology colleagues, should choose their testing algorithms, based on the hs-cTn tests used in their institutions.

Study Summary

Article	Lopez-Ayala P, Nestelberger T, Boeddinghaus J, *et al*. Novel Criteria for the Observe-Zone of the ESC 0/1h-hs-cTnT Algorithm Circulation. 2021 Sep 7;144(10):773-787. doi: 10.1161/CIRCULATIONAHA.120.052982.
Design	Prospective diagnostic algorithm study (Clinicaltrials Reg: NCT00470587)
Population	*Included:* Adult ED patients with symptoms suggestive of AMI (chest pain rest/exertion) *Excluded:* STEMI on presentation, unclear final diagnosis with 1 elevated hs-cTn value, chest pain >12hrs, CKD on dialysis, missing observation zone hs-cTn values (0-1-3hrs).
Index Test	Patients in the observe-zone of the ESC 0/1h-hs-cTnT-algorithm were triaged using a 0/3h-hs-cTnT change of <7 ng/L to rule-out NSTEMI and a 0/3h-hscTnT-change of ≥7 ng/L to rule-in.
Reference Standard	Fourth universal definition of MI (UDMI), adjudicated by two independent cardiologists.
Diagnoses of Interest	Primary diagnostic end point was NSTEMI (types 1 and 2) at presentation to the ED.

Key Results

564pts included in observe-zone; median age 74yo, 25.4% female.
120pts (21.3%) had NSTEMI (74 T1MI, 46T2MI). NSTEMI patients younger (70 vs 75), more typical chest pain symptoms and ischemic ECG changes.

3hr >7ng/L hsTrop cutoff: Spec 98.4% (96.8-99.2), PPV 85.1% (72.3-92.6).
3hr $\leq$14ng/L cutoff: Sens 93.3% (87.4-96.6), NPV 94.7% to rule out, Spec 32.4% (27.8036.5), PPV 27.1% for rule in.

Diagnostic accuracy for single hsTrop measures (ROC AUC): 0hr 0.65, 1hr 0.69, 3hr 0.76.
Dx accuracy absolute hsTrop changes (ROC AUC): 0hr 0.74, 1hr 0.84.
Dx accuracy combined 3hr level (<15ng/L) and 0-3hr delta (<4ng/L) had best statistical superiority: AUC 0.88, Sens 99.2%, NPV 99.3% to rule out NSTEMI. Absolute 3hr change >6ng/L had Spec 98% (PPV 85.7%) to rule in NSTEMI.

Presence of ECG ST changes increased rule-in performance of hsTrop results.

All findings stable upon sensitivity analysis.

Application of new algorithm in an external validation cohort (1010pts) yielded similar results: Rule-out Sens 98.3% (90.9-99.7), NPV 98.3%, and rule in Spec 95.7% (91.7-97.8), PPV 78.4%.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those likely to undergo testing in the ED.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	?	?
3. All patients underwent the same diagnostic evaluation.	✓	✓
4. All tests were conducted within similar time frames to preclude changes in disease status.	✓	✓
5. The reference standard criteria for the candidate diagnoses are explicit and reproducible.	✓	?
6. The reference standard was applied regardless of and blinded to the index test result.	✓	✓
7. The assignment of the candidate diagnoses was explicit and reproducible.	✓	?
8. Most (> 80%) patients received a diagnosis.	✓	✓
9. Undiagnosed patients received adequate clinical follow-up.	?	?
10. The estimates of disease probability are clinically significant.	✓	✓

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Majority of funding from Swiss govt agencies, some university grants. Some industry donated tests, but no role in project design/implementation/analysis.
Conflict of interest	Declared; some authors had industry ties that were not relevant to current study.

Potential threats to viability

Chance	None
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* All patients recruited/analyzed were in the ED.
Measurement bias	Not all patients had a 3hr hs-cTn sample, so could not be properly adjudicated (16.9%); this has an effect on prevalence measures (NPV, PPV).
Analysis bias	Bootstrap validation of performance estimates at various cutoffs (TRIPOD guidelines). Planned subgroup analyses based on: algorithm performance for type 1 NSTEMI alone, ECG stratification, results >6hrs, and final Dx unclear (designated type 1 NSTEMI).
Confounding	Study methods claimed review of medical records and scheduled follow phone calls/mailings, but no final inclusion/LTFU data reported.

Administrative details

Key words	Acute coronary syndrome, NSTEMI, troponin
Appraisers	S. Upadhye, A. Worster
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Andrew Worster, MD, MSc
Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
Research grant and patent holder. No industry ties.

Research Question

How does IV diltiazem compare to metoprolol in controlling rapid atrial fibrillation?

BEEM Bottom Line

Why is this study important? Atrial fibrillation is the most common ED arrhythmia encountered, and symptomatic rapid ventricular rate (AFib-RVR) can require urgent intervention by ED physicians.

What, if any, threats to validity are most likely to have an impact on the results and how? This review combined many small studies with variable heterogeneity, so pooled results may not be robust.

How do the key results compare with the current evidence? These results are congruent with recently updated CAEP Rapid AFib/Flutter Best Practices Checklist (CJEM 2021) that recommend either agent first (eg. if patient already on oral rate modifier, start with same class IV).

How should this study impact the care of ED patients? ED physicians should likely favour IV diltiazem over metoprolol for faster and safer rate control of rapid AFib patients.

Study Summary

Article	Lan A, Wu F, Han B, Ma L, Han J, Yao Y. Intravenous diltiazem versus metoprolol for atrial fibrillation with rapid ventricular rate: A meta-analysis. Am J Emerg Med 2021; 51:248-256. doi: 10.1016/j.ajem.2021.08.082.
Design	Systematic review/meta-analysis.
Population	*Included:* Patients (age ≥18yo) with Afib-RVR on ECG *Excluded:* Review articles, commentaries, case reports; missing/incomplete/incorrect data.
Intervention	IV diltiazem 0.25mg/kg initial bolus dose, followed by further bolus/infusing dosing prn
Comparison	IV metoprolol 2.5-5mg IV; repeat prn
Outcomes	Efficacy of RVR control, average onset time, ventricular rate, blood pressure changes, adverse events.
Key Results	IV Dilt: 643pts IV Metop: 571pts.
10 studies included (10 high quality, 7 low). 1214 pts.	***Efficacy*** (13 studies, 869pts; I^2=0%): Overall IV Dilt superior to IV Metop (RR 1.11, 95%CI 1.06-1.16), p=0.007). IV Dilt superior at 30min (RR 1.13, 1.03-1.24) and 60min (RR 1.11, 1.01-1.23). No significant difference at 5, 10, 90 and 120min. ***Effect onset*** (7 studies, 411pts; I^2=39%): IV Dilt faster than IV Metop: WMD -1.13min (-1.97 to -0.28) ***Decreased Ventricular Rate*** (12 studies, 755pts; I^2>50%, random effects): Overall IV Dilt superior to IV Metop: WMD -9.48bpm (-12.13 to -6.82, p<0.00001), and significantly superior at 5, 10, 15, 30, 60 and 90min. No difference at 120min. ***Blood Pressure Changes*** (3 studies, 160pts; I^2=19% for sBP, 0% for dBP): IV Metop dropped sBP more than IV Dilt: WMD 9.42mmHg (1.53-17.32, p=0.02) No significant differences in dBP at 5, 10, 15 and 30min. ***Adverse Events:*** (15 studies, 411pts; I^2=0): No difference in AE's with either agent (RR 0.80, 0.55-1.14, p-0.22).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	?	?
3. The search for studies was unbiased and reproducible.	?	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	?	?
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	?	?
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	✓

A1 = S. Upadhye A2 = M. Welsford

Funding and conflicts of interest

Funding	None (reported)
Conflict of interest	None (reported)

Potential threats to viability

Chance	Included studies had relatively small sample sizes, and none alone reached statistically significant difference (only when pooled; see Forest plots)
Selection bias	Search included several electronic databases, article reference lists; but no grey literature. No language restrictions.
Measurement bias	Quality assessments using Jadad scale for RCTs (mostly poor; 6 studies with score 2/5), Newcastle-Ottawa scale for non-RCTs (mostly high; 8 studies with scores 5-8/9).
Analysis bias	Fixed effects analyses with low heterogeneity studies, random effects with mod/high.
Confounding	Drug dosing differences between various studies may contribute to different outcomes.

Administrative details

Key words	Atrial fibrillation, diltiazem, metoprolol, rapid ventricular rate
Appraisers	S. Upadhye, M. Welsford
Reference(s)	Stiell IG, de Wit K, Scheuermeyer FX, *et al*. 2021 CAEP Acute Atrial Fibrillation/Flutter Best Practice Checklist. Can J Emerg Med 2021; published online https://doi.org/10.1007/s43678-021-00167-y

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Michelle Welsford, MD, FRCPC
Director & Professor, Emergency Medicine, McMaster University
No conflicts of interest (ICMJE)

Research Question

What are the predictors and frequency of spontaneous conversion (SCV) back to sinus rhythm in ED patients with acute atrial fibrillation?

BEEM Bottom Line

Why is this study important? Many patients with acute atrial fibrillation (AAF) in the ED will spontaneously revert prior to medical/electrical cardioversion. This study aimed to identify predictors of spontaneous reversion.

Which, if any, threats to validity are most likely to have an impact on the results and how? Some variability in determinants of SCV (eg. Time of symptom onset, use of anti-arrhythmic meds) confound accurate classification of AAF patients, and the predictor values associated with SCV.

How do the key results compare with the current evidence? N/A

How should this study impact the care of ED patients? A better understanding of SCV predictors can facilitate ED discharge planning with rate control strategies and subsequent follow-up management.

Suneel Upadhye MD MSc FRCPC
Associate Professor, Emergency Medicine/ Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article Pluymaekers N, Hermans A, Linz DK, *et al*. Frequency and Determinants of Spontaneous Conversion to Sinus Rhythm in Patients Presenting to the Emergency Department with Recent-onset Atrial Fibrillation: A Systematic Review. Arrhtym Electrophys Rev 2020; 9(4): 195-201. DOI: https://doi.org/10.15420/aer.2020.34

Design Systematic review of all studies examining SCV to sinus rhythm in ED.

Population *Included:* Patients in ED with AAF who spontaneously converted (SCV) to sinus rhythm.
Excluded: Patients with AAF seen in outpt clinics.

Intervention N/A

Comparison N/A

Outcomes *Primary:* Rate of SCV in ED patients.
Secondary: Determinants of ED SCV, adverse events.

Key Results *25 studies* = 4885 patients. **Definition:** conversion was defined as spontaneous if the patient converted to sinus rhythm without active cardioversion (meds/electricity), with rate control and/or placebo medication allowed. If patients were treated with placebo, digoxin, beta blockers or non-dihydropyridine calcium channel blockers and converted to sinus rhythm, it was considered SCV for this review.

Outcome	
Primary:	SCV rate varied from 9-83% in included studies. The most important SCV predictors were: shorter duration of AAF (<24hrs, <48hrs or longer), fewer prior AAF episodes, normal atrial dimensions, absence of prior heart failure/other underlying heart disease. There was insufficient data to differentiate "early vs late" SCV predictors.
Secondary:	Bleeding and stroke events were rare.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	?	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	✓	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	N/A	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	Not reported.
Conflict of interest	None (disclosed).

Potential threats to validity

Chance	None?
Selection bias	Broad search for articles, English language only. No comments on publication bias assessment.
Measurement bias	Some variance in outcomes based on inclusion/exclusion of first-time AAF vs all-comers, and whether pts were on anti-arrhythmic meds/digoxin. Studies varied in when they defined the duration of AAF (pt-reported symptom onset vs ED registration time).
Analysis bias	Higher risk of bias with included smaller observational studies.
Confounding	Inclusion of consecutive patient sampling.

Administrative details

Key words	Spontaneous conversion, AF, determinants, emergency care
Appraisers	Upadhye S
Reference(s)	Pluymaekers N, Hermans A, Linz DK, Dudink E, Luermans J, Weijs B, Vernooy K, Crijns H. Frequency and Determinants of Spontaneous Conversion to Sinus Rhythm in Patients Presenting to the Emergency Department with Recent-onset Atrial Fibrillation: A Systematic Review. Arrhtym Electrophys Rev 2020; 9(4): 195-201. DOI: https://doi.org/10.15420/aer.2020.34

Clinical Appraisal faculty

Suneel Upadhye MD MSc FRCPC
Associate Professor, Emergency Medicine/ Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the utility of using ED POCUS in the assessment of acute dyspnea?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? This guideline is very relevant to the increasingly prevalent practice of ED POCUS for various bedside diagnostic tests. This CPG confirms that there is utility in adding ED POCUS for diagnosing acute dyspnea related to CHF/pleural effusion/pneumonia/PE as an additional adjunct to usual Dx testing strategies, but NOT as a substitute for these. Addition of ED POCUS with lower false positives/negatives associated with standard testing. No direct complications noted for using ED POCUS. Access to formal US devices, and training/experience with ED POCUS for dyspnea will be obvious (but surmountable) barriers.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? There were no significant validity threats in how this CPG group constructed this guidance document. All key steps for "trustworthy" CPG production were followed (IOM 2011 Standards). Authors used the GRADE methodology framework appropriately, and reported all steps explicitly. Outcomes were limited to diagnostic accuracy, but did not examine the following: quality of life, ICU admissions, disease-specific outcomes (unnecessary antibiotics use, respiratory support, referral times, use of lung CT). There was insufficient information to analyze the impact of POCUS on mortality, ED time to diagnosis nor time to treatment.

How should this guideline, and specifically which recommendations should impact the care of ED patients? For ED physicians trained/experienced with ED POCUS, this modality can be a valuable **adjunct** to standard testing modalities for acute dyspnea due to CHF/pleural effusion/CAP/PE in the ED.

Study Summary

Article Qaseem A, Etxeandia-Ikobaltzeta I, Mustafa RA, Kansagara D, Fitterman N, Wilt TJ. for Clinical Guidelines Committee of the American College of Physicians. Appropriate Use of Point-of-Care Ultrasonography in Patients with Acute Dyspnea in Emergency Department or Inpatient Settings: A Clinical Guideline from the American College of Physicians. Annals Int Med 2021. doi:10.7326/M20-7844.

Design Clinical Practice Guideline.

Population Adult ED patients with acute dyspnea, later confirmed with 1 of the following: acute CHF +/- pulmonary edema, pulmonary embolism (PE), pleural effusion, pneumonia, or pneumothorax (PTX).

Scope This guideline is intended for ED clinicians who take care of adult dyspnea patients.

Key Results Overall, the addition of ED POCUS (to standard Dx pathway) increased the proportion of correct ED dyspnea diagnoses from 59-91% (ARD 31.9%, 95%CI 22.4-53.8%); moderate certainty evidence.

Recommendation	*Strength*	*Quality of Evidence*
Clinicians may use point-of-care ultrasonography **in addition to the standard diagnostic pathway** when there is diagnostic uncertainty in patients with acute dyspnea in the ED.	Conditional	Low
There was insufficient evidence to make a recommendation for use of ED POCUS to **replace** standard Dx pathway (no direct results for health outcomes of interest).	None	No direct Evidence

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	✓
2. Systematic methods were used to search for evidence.	✓	✓
3. The criteria for selecting the evidence are clearly described.	✓	✓
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	✓	✓
8. The content of the guideline is free of influence by the views of the funding body.	✓	✓
9. Competing interests of guideline development group members have been recorded and managed.	✓	✓
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = S. Sharif

Funding and conflicts of interest

Funding	Provided exclusively by American College of Physicians (ACP).
Conflict of interest	Full disclosure/management of CoI. No significant concerns noted.

Potential threats to validity

Development	Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible? **YES; 2 patient stakeholders included among various clinical participants.**
Presentation	Well organized with easy to find recommendations? **YES**
Comprehensive	Was the information to inform decision-making complete? **YES**
Clinical Validity	Are the recommendations clinically sound and appropriate for the intended patients? **YES. NOT applicable to handheld devices.**

Administrative details

Key words	Acute dyspnea; CHF; ED POCUS; pleural effusion; pneumonia; pulmonary embolism.
Appraisers	Upadhye S; Sharif S.
Reference(s)	1. See Article above. 2. Supporting Systematic Review (see BEEM manual). Ann Intern Med. doi:10.7326/M20-5504. PMID: 33900798.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Sameer Sharif MD FRCPC DRCPSC
Assisstant Professor, Department of Medicine, Division of Emergency Medicine
Emergency & Critical Care Physician, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the optimal use of high-sensitivity troponins to rule out myocardial infarction in ED chest pain?

BEEM Bottom Line

Why is this study important? This study confirms the diagnostic utility of using hs-troponins in ED chest pain pathways to rapidly rule-out NSTEMI and facilitate earlier safe discharge.

Which, if any, threats to validity are most likely to have an impact on the results and how? Minimal. The study authors used test cutoff thresholds that are congruent with most clinically acceptable miss rates.

How do the key results compare with the current evidence? These results mirror 2 recent "real-world" RCTs suggesting that hs-troponin assays (many platforms), either singly or serially, can be useful to safely rule-out NSTEMI and facilitate rapid ED discharge.

How should this study impact the care of ED patients? ED physicians should know what hs-troponin test is used in their hospital, and how to interpret single vs. serial results for individual patients, ideally in a structured pathway (that may or may not include an incorporated risk score).

Suneel Upadhye MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Westwood ME, Armstrong N, Worthy G, *et al*. Optimizing the Use of High-Sensitivity Troponin Assays for the Early Rule-out of Myocardial Infarction in Patients Presenting with Chest Pain: A Systematic Review. Clin Chem 2021; 67 (1): 237-244. DOI: 10.1093/clinchem/hvaa280
Design	Systematic review; meta-analysis if 4+ studies available for the same assay index test.
Population	*Included:* Adults (_18 years) presenting with acute 'pain, discomfort or pressure in the chest, epigastrium, neck, jaw, or upper limb without an apparent non-cardiac source' (10) due to a suspected, but not proven, AMI *Excluded*: Patients with STEMI
Index Test	Hs-troponin (multiple assays)
Reference Test	Case adjudication using the 3rd Universal AMI Definition (including measurement of troponin T or I (using any method) on presentation and 3-6 hours later or occurrence of MACE (any definition used in identified studies) during 30-day follow-up.
Diagnosis of Interest	Myocardial infarction (NSTEMI)

Key Results *N* = 37 studies included.

N/Studies	*Measure (95% CI)*	I^2
Single Test	***Assay (cutoff): Sens/Spec***	
6 studies	Roche Elecsys (5ng/ml): 0.99 (0.98-100)/0.35 (0.25-0.46)	
3 studies	Abbott ARCHITECT (5ng/ml): 0.97 (0.95-0.98)/0.58 (0.57-0.59)	
1 study	Seimens (5ng/ml): 0.99 (0.97-1.00)/0.52 (0.50-0.55); two combined assays	
	Abbott ARCHITECT (2ng/ml): 1.00 (0.99-1.00)/0.21 (0.16-0.26)	
	Seimens (2ng/ml): 1.00 (0.99-1.00)/ 0.23-0.26 (0.21-0.28); two combined assays	
Multiple Tests	***Strategy (Assay): Sens/Spec (RoR = rule out rate)***	
1 study	ESC 0/1hr rule out pathway (Roche Elecsys): 0.99 (0.98-1.00)/0.68 (0.67-0.70); NSTEMI miss rate 0.67%	
2 studies	ESC 0/1hr rule out pathway (Abbott ARCHITECT): 0.99 (0.98-1.00)/0.57 (0.56-.059); overall RoR = 71%	
	ESC 0/1hr rule out pathway (Beckman Coulter): 0.99 (0.98-1.00)/0.70 (0.66-.74); overall RoR = 60%, miss rate 1.04%	
	ESC 0/1hr rule out pathway (Quidel TriageTrue): 1.00 (0.97-1.00)/0.66 (0.62-0.70); overall RoR = 55%	
	ESC 0/1hr rule out pathway (Siemens assays): 0.99 (0.95-1.00)/0.56 (0.52-0.60); overall RoR = 16%, miss rate 0.88%	
	High-STEACS (Abbott ARCHITECT): 0.99 (0.97-1.00)/0.76 (0.73-0.79); overall RoR = 65%, miss rate 0.73%	
	High-STEACS (Siemens Atellica): 0.98 (0.95-0.99)/0.74 (0.72-0.76); overall RoR = 65%, miss rate 1.45%	

AUC = area under the curve; CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); *N* = number of patients; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; Sig. = significance; SS = statistically significant.
P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	?	?✓X	?✓X
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	?	?✓X	?✓X
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	✓	?✓X	?✓X
9. The subgroups were stated a priori and appropriate.	✓	?✓X	?✓X
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	Multiple research grants/fellowships. No industry. Sponsor had no role in any research planning/conduct/reporting.
Conflict of interest	One author disclosed industry consultant/advisory fees, and speaking honoraria (R. Body)

Potential threats to validity

Chance	None?
Selection bias	Unable to access online search strategy/selection details. No comment on publication bias assessments.
Measurement bias	Unable to access online study quality assessment details.
Analysis bias	All articles were data abstracted by one author, then double-checked by 2nd author.
Confounding	Incomplete literature on the utility of hs-troponins incorporated into clinical risk scores.

Administrative details

Key words	Chest pain, high-sensitivity troponins, myocardial infarction
Appraisers	Upadhye S,
Reference(s)	Westwood ME, Armstrong N, Worthy G, Fayter D, Ramaekers BLT, Grimm S, Buksnys T, Ross J, Mills NL, Body R, Collinson PO, Timmis A, Kleijnen. Optimizing the Use of High-Sensitivity Troponin Assays for the Early Rule-out of Myocardial Infarction in Patients Presenting with Chest Pain: A Systematic Review. Clin Chem 2021; 67 (1): 237-244. DOI: 10.1093/clinchem/hvaa280

Clinical Appraisal faculty

Suneel Upadhye MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Can a diagnostic strategy with YEARS criteria in PERC(+) and age-adjusted D-Dimer thresholds safely predict suspected PE events?

BEEM Bottom Line

Why is this study important? There is a balance for risk-stratifying/investigating patients with suspected ED PE without missing cases and not over-investigating/treating patients. This study aimed to evaluate the non-inferiority of a YEARS + adjusted D-Dimer vs. a standard D-Dimer protocol to assess safety and ED resource utilization.

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal; in a large multicentre pragmatic RCT like this, there are inevitable small issues (eg. selection bias, crossover contamination, patients lost to follow-up, etc.) that can't be avoided. These are addressed in the Limitations discussions.

How do the key results compare with the current evidence? This study builds on prior studies that look at YEARS or PERC rules separately (with/without DDimers), and combines them in a serial risk-stratification process to safely reduce low-likelihood imaging studies. Prevalence of PE in this study is similar to others, although YEARS scores are lower.

How should this study impact the care of ED patients? A combined PERC+/YEARS/Age-adjusted D-Dimer strategy may be safe to avoid missed PE's, and reduce chest imaging studies.

Study Summary

Article	Freund Y, Chauvin A, Jiminez S, et al. Effect of a Diagnostic Strategy Using an Elevated and Age-Adjusted D-Dimer Threshold on Thromboembolic Events in Emergency Department Patients with Suspected Pulmonary Embolism: A Randomized Trial. JAMA 2021; 326(21):2141-2149. doi: 10.1001/jama.2021.20750.
Design	Cluster-randomized, multicentre, cross-over non-inferiority RCT with 18 ED's in France (n=16) and Spain (n=2); ClinicalTrials Reg: NCT04032769
Population	*Included:* Patients with clinical suspicion of PE (acute onset chst pain, worsening dyspnea, syncope and low pre-test probability (PTP <15%) of PE (subjective?) with PERC ≥1pt OR intermediate PTP (16-50%). *Excluded:* Patients with high PTP of PE (>50%), or low PTP with PERC = 0pts. Clinically unwell/ unstable (resp distress, hypotension, dec O_2Sat), current OAC Rx, current VTE dx, pregnancy, correctional facility inmate, or symptoms obviously related to a non-PE Dx.
Intervention	YEARS criteria and D-Dimer testing; PE ruled out if 1) YEARS=0 and neg D-Dimer <1000ng/ml, or 2) YEARS=1+ and D-Dimer < age-adjusted threshold. D-Dimer > threshold = chest imaging.
Comparison	All patients received D-Dimer testing with age-adjusted thresholds; if above threshold, pt received chest imaging.
Outcomes	*Primary:* VTE events at 3mo. (analyzed at patient level); new DVT or PE on appropriate imaging. Patients called for telephone interview, or RTER same hospital if worsening/recurrent symptoms. *Secondary:* ED chest imaging, length of stay, hospital admission, OAC administration, all-cause readmissions 3mo, all-cause death. Outcomes adjudicated by 3 VTE experts, blinded to study period/patients. Unexplained deaths attributed to PE if no other cause identified. Planned sensitivity analysis: isolated subsegmental PE (small emboli that may not need Rx), and for imputed missing primary outcomes data.

Key Results

Mean age 55yo.
Female 58%

1414 pts included; 726 Int, 688 control. Missing primary endpoint in 37pts (2.6%).
1271 pts analyzed per-protocol (648 int, 623 control). Required sample size = 1234pts.
PE Dx in 100pts: 54 Int (7.4%) and 46 control (6.7%).

Primary: Int 1 event, Cont 5 events. Dx failure rate Int 0.15% (0.0-0.86) and Cont 0.80% (0.26-1.86%). **Failure difference = -0.64% (1sided 95%CI -∞ to 0.21%) < 1.35% NI margin.** Results similar in ITT analysis, and with/without imputations for missing data.
No PE missed in YEARS=0 pts and neg DDimer. Insufficient power to confirm safety of Int pts with YEARS=0 with D-dimer above age threshold but below 1000ng/ml. No PE's detected in this group, but upper 95%CI 5.36% was >NI safety margin of 1.35%.

Secondary:
Chest imaging: Int 221pts (30.4%) vs Cont 275pts (40%); Adj Diff -8.7% (-13.8 to -3.5%)
Median ED LOS: Int 6hrs (IQR 4-8) vs Cont 6hrs (5-9); Adj Diff -1.6hrs (-2.4 to -0.9)
No other outcomes significantly different.

No other significant differences with sensitivity analyses.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?✓X
2. The patients were adequately randomized (allocation sequence adequately generated).	N/A	?✓X
3. The allocation sequence was adequately concealed.	N/A	?✓X
4. The patients in all groups were similar with respect to prognostic factors.	✓	?✓X
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	X	?✓X
6. All groups were treated equally except for the intervention.	✓	?✓X
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	?✓X
8. The patients were analyzed in the groups to which they were randomized (ITT).	?	?✓X
9. All patient-important outcomes were considered.	✓	?✓X
10. The effect size of the primary outcome is clinically significant.	✓	?✓X

A1 = S. Upadhye A2 =

Funding and conflicts of interest

Funding	French Health Ministry grant. No role in research design/implementation/analysis.
Conflict of interest	3 authors disclosed industry relationships unrelated to the study work.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Unit of randomization = ED (not patients). Each ED randomized to either intervention or control for 4mo, then 2mo washout period, then started the other arm. ED's stratified by country and volume (< or >50K visits/year). As individual patients were selected by treating physicians in different ED's, some selection bias may be present?
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Interruption of recruiting during COVID March 2020 for 4-6 weeks. Groups balanced at recruitment (Table 1).
Measurement bias	Non-inferiority design using per-protocol analysis for primary outcome. Secondary outcomes analysed as ITT, with imputation for missing data.
Analysis bias	ITT, Per Protocol, As Treated. Analysis at patient level. Noninferiority design with NI margin set at 1.35% (previously validated). 37 pts lost to follow-up; no impact on NI per-protocol analysis, and no difference detected on ITT imputation analysis.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* No biases related to crossover or sequence effects detected. Rare protocol deviations did not change analysis outcomes.

Administrative details

Key words	PERC criteria, YEARS criteria. D-Dimer, suspected pulmonary embolism
Appraisers	S. Upadhye
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the risks of outpatient treatment of pulmonary embolism with direct anticoagulants?

BEEM Bottom Line

Why is this study important? Outpatient treatment of low-risk pulmonary embolism (PE) patients is an important stewardship effort, provided that the discharge direct oral anticoagulants (DOACs) prescribed are safe in the short-term future.

Which, if any, threats to validity are most likely to have an impact on the results and how? Paucity of direct evidence comparing outpatient management strategies between different anticoagulant classes limit generalizability of findings.

How do the key results compare with the current evidence? There are ongoing prospective trials examining the efficacy/safety of DOACs in treating low-risk PE patients in outpatient settings.

How should this study impact the care of ED patients? There are rare major/minor adverse outcomes with treating low-risk PE patients with OACs over 30-90days.

Study Summary

Article	Maughan BC, Frueh L, McDonagh MS, Casciere B, Kline JA. Outpatient Treatment of Low-risk Pulmonary Embolism in the Era of Direct Oral Anticoagulants: A Systematic Review. Acad Emerg Med 2021; 28: 226-239. doi: 10.1111/acem.14108
Design	Systematic review of prospective trials (randomized/non-randomized).
Population	*Included:* Adult patients with acute symptomatic PE discharged from ED/within 48hrs. Randomized and prospective non-randomized studies included. "Low-risk" PE patients defined using Hestia, PESI or sPESI criteria. *Excluded*: Retrospective studies, case reports, editorials, other publication types. Studies re: VTE prophylaxis, no clearly defined outpt cohort, populations with higher risk comorbidities (eg. cancer), or unusual outpt scenarios (eg. patient hotels, hospital-in-the-home).
Intervention	Direct oral anticoagulants (DOACs), any medication/dosage. 863 patients; 97% received rivaroxaban in trials that reported specific drug choices (remainder received apixaban).
Comparison	LMWH or VKA's (1018)
Outcomes	*Major:* All-cause mortality, PE-related mortality, recurrent VTE, major bleeding (ISTH definition). *Minor:* ED return visit, hospital readmission, clinically relevant nonmajor bleeding (CRNMB) All outcomes to be reported at 30 and 90days.

Key Results

12 studies, 3191 patients included. 4 RCTs, 8 non-randomized studies. Avg age 41-62yo.

Outcome	*Median rates (range)*	
All-Cause Mortality	30days 0% (range 0-1.7%, 11 studies)	90days: 0.4% (0-3.3%, 10 studies)
PE Mortality	30days: 0% (range 0-0.6%, 12 studies)	90days: 0% (0-0.4%, 10 studies)
Recurrent VTE	30days: 0% (0-1.4%, 10 studies)	90days: 0.3% (0-2.2%, 10 studies)
Major Rebleeds	30days: 0% (0-1.2%, 11 studies)	90days: 0% (0-1.8%, 9 studies)
	**No statistically significant difference with high-quality studies comparing VKAs vs DOACs for individual major outcomes, nor 90day composite of all 4 major outcomes.	
Minor CRNMB	Median 2% (0.2-5.1%)	
Return ED visits	Median 15.5% (range 14.9-16.0%; 2 studies at 30days); 21.1% (1 study, 90days)	
Hospital Readmissions	30days: 2.4% (1.5-3.0%, 3 studies)	90days: 9.4% (8.2-10.5%, 2 studies)

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	X
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	?	X
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	X	X
8. The methods used to combine the included primary studies were reported and valid.	✓	X
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	?

A1 = S. Upadhye A2 = F. Germini

Funding and conflicts of interest

Funding	None reported.
Conflict of interest	BCM has received national grant funding. JAK has received public grant and institutional industry grant funding (not personal). No other conflicts reported.

Potential threats to validity

Chance	None?
Selection bias	Broad search (electronic, contacted authors, screened reference lists). English-language articles only. No reported assessment of publication bias.
Measurement bias	Overall quality of studies: 4 RCT's low risk of bias, NonRCTs = moderate quality (6 Mod, 2 Serious RoB)
Analysis bias	None. No reporting of heterogeneity, nor attempted meta-analysis.
Confounding	Low variation in patient comorbidity of CHF (0-3.6%), prior VTE (15.1-26.5%), and chronic lung disease (0-12.5%). Varied rates of malignancy in included studies (0-45.5%), and DOACs are not recommended in cancer patients d/t higher risk of bleeding.

Administrative details

Key words	Direct oral anticoagulants, outpatient, pulmonary embolism
Appraisers	Upadhye S,
Reference(s)	Maughan BC, Frueh L, McDonagh MS, Casciere B, Kline JA. Outpatient Treatment of Low-risk Pulmonary Embolism in the Era of Direct Oral Anticoagulants: A Systematic Review. Acad Emerg Med 2021; 28: 226-239. doi: 10.1111/acem.14108 PMID: 32779290

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Federico Germini, MD MSc
Doctoral student, Health Research Methods, Evidence & Impact (HEI), McMaster University
The authors' institution received research funding from Pfizer and Bayer.

Research Question

What is the diagnostic accuracy of ED POCUS in assessing acute adult dyspnea?

BEEM Bottom Line

Why is this study important? Dyspnea is a very common presentation to the emergency department (ED). Overall, this review supports the use of adjunctive point of care ultrasound (POCUS) in assessing ED dyspnea to improve diagnostic accuracy, but not as a substitute for standard testing. None of the studies addressed potential harms of false negatives/positives of ED POCUS and unnecessary follow-up testing.

Which, if any, threats to validity are most likely to have an impact on the results and how? Different prevalences of target diseases could cause spectrum bias, and influence the diagnostic performance of index POCUS testing. Heterogeneity due to differential reference standards, variable "indeterminate" results reporting/analyses and overall high risk of bias in included studies (55%) precluded the ability to pool results for meta-analyses (except for CHF).

How do the key results compare with the current evidence? Overall these results support the growing role of ED POCUS as a diagnostic adjunct in assessing ED patients with acute dyspnea, but not as a replacement for current standardized testing.

How should this study impact the care of ED patients? For ED physicians who are trained and experienced, adding POCUS to the bedside testing of acute dyspnea patients can improve diagnostic accuracy.

Study Summary

Article	Gartlehner G, Wagner G, Affengruber L, Chapman A, Dobrescu A, Klerings I, Kaminski-Hartenthaler A, Speil AO. Point-of-Care Ultrasonography in Patients with Acute Dyspnea: An Evidence Report for a Clinical Practice Guideline by the American College of Physicians. Annals Int Med 2021; doi:10.7326/M20-5504
Design	Systematic narrative review and meta-analysis
Population	Adult patients with acute dyspnea attributable to: congestive heart failure (CHF), pleural effusion, pneumonia, pneumothorax, pulmonary embolism (PE)
Index Test	Point of care ultrasound (POCUS)
Reference Test	Standard diagnostic testing for each clinical condition.
Diagnosis of Interest	CHF, pleural effusion, pneumonia, pneumothorax, PE.

Key Results

N/Studies	*Measure (95% CI)*	*I^2*
572/3 (Low/unclear risk of bias)	POCUS ADDED to Standard Dx Pathways: Sensitivity (Range): 0.70-1.00 (0.52-1.00) for all target conditions Specificity (Range): 0.63-1.00 (0.52-1.00) for all target conditions	N/A
8626/49 (unclear/high risk of bias	POCUS to REPLACE Std Dx Pathways: Sensitivity (CHF; 5 studies) = 0.76 (0.48–0.91) Specificity (CHF; 5 studies) = 0.96 (0.90–0.98)	

AUC = area under the curve; CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); *N* = number of patients; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	?	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	?	?
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	X	X

A1 = S Upadhye A2 = D Kim

QUADAS = quality assessment of diagnostic accuracy studies; ROC = receiver operating characteristic curve.

Funding and conflicts of interest

Funding	Internal funding from American College of Physicians (ACP).
Conflict of interest	None reported (available online).

Potential threats to validity

Chance	None.
Selection bias	Insufficient number of studies to assess for publication bias. Studies selected were all conducted in countries with High Development Index scores. Included studies enrolled patients on a convenience basis.
Measurement bias	High heterogeneity between studies precluded formal meta-analyses for most clinical outcomes (except CHF). Lack of reporting of POCUS "indeterminate" results; introduces bias in subsequent calculations of index test performance.
Analysis bias	Many of the included studies (55%) were deemed to have high risk of bias.
Confounding	Different prevalences of confirmed cases for different conditions may have led to spectrum bias in assessing diagnostic test accuracy. Based on POCUS provider experience and patterns of use, there was minimal impact on sensitivity, but variable changes in specificity. Different studies used different reference standards beyond chart reviews, discharge diagnoses, CXR results, chest CT results, or mixed standards; this can have an influence on the index test performance metrics.

Administrative details

Key words	Point of care ultrasound (POCUS), CHF, pleural effusion, pneumonia, pneumothorax, pulmonary embolism.
Appraisers	Upadhye S; Kim D.
Reference(s)	Gartlehner G, Wagner G, Affengruber L, Chapman A, Dobrescu A, Klerings I, Kaminski-Hartenthaler A, Speil AO. Point-of-Care Ultrasonography in Patients with Acute Dyspnea: An Evidence Report for a Clinical Practice Guideline by the American College of Physicians. Annals Int Med 2021; doi:10.7326/M20-5504.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Daniel Kim, MD FRCPC
Clinical Associate Professor, Department of Emergency Medicine, University of British Columbia
Medical Advisory Board, Clarius Mobile Health

Research Question

What is the diagnostic accuracy of the EDACS score for ED chest pain assessment?

BEEM Bottom Line

Why is this study important? Rapid yet accurate risk stratification of ED chest pain patients can be useful in appropriately determining patients who can be safely discharged for outpatient follow-up vs. those needing admission.

Which, if any, threats to validity are most likely to have an impact on the results and how? It is unclear how modification of the QUADAS-2 tool may have impacted study quality scores, and subsequent inclusion/exclusion for SR/MA. The lower sensitivity of EDACS in North American studies (96%) may lead to unacceptable high false negative rates (tolerance limit 1% for missed cases).

How do the key results compare with the current evidence? Multiple ED chest pain tools have been tested/validated to different degrees for ED use (eg. EDACS, HEART, Vancouver, etc.), so clinicians should choose that which makes most clinical sense/validated in their local practice.

How should this study impact the care of ED patients? Use of the EDACS risk tool may improve decision making in ED chest pain patients.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article:	Boyle RSJ, Body R. The Diagnostic Accuracy of the Emergency Department Assessment of Chest Pain (EDACS) Score: A Systematic Review and Meta-analysis. Annals Emerg Med 2021 Apr;77(4):433-441. doi: 10.1016/j.annemergmed.2020.10.020. Epub 2021 Jan 16.
Design:	Systematic review and meta-analysis of the EDACS risk tool for ED chest pain.
Population:	*Included:* Studies including ED adult patients with minimum 5min chest pain or other ACS-like symptoms. *Excluded*: Tests using a single troponin test or tests >3hrs after ED arrival.
Index Test:	Use of EDACS score and hs-troponin levels.
Reference Test:	Cardiac events adjudicated by 2 independent clinicians, using 3rd Universal AMI definitions.
Diagnosis of Interest:	Major adverse cardiac events (MACE = STEMI, NSTEMI, CV death, cardiac arrest, ventricular arrhythmia, cardiogenic shock, high-grade AV block, emergency revascularization) at 30days.

Key Results

N = 11578 patients in 8 included studies. MACE rate 10.5% overall.
Missed MACE rate with EDACS score: 0.5%.

Measure (95% CI)	I^2
Sensitivity = 0.96 (0.90-0.99) Specificity = 0.61 (0.56-0.66) LR+ 2.47 (2.21-2.76), LR- = 0.06 (0.03-0.16); Diagnostic OR 38 (16-91) AUC = 0.77 (0.73-0.80)	**97%**

AUC = area under the curve; CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); *N* = number of patients; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; Sig. = significance; SS = statistically significant.
P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	?	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	?	?✓X	?✓X
7. The quality of the primary studies is high.	✓	?✓X	?✓X
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	X	?✓X	?✓X
9. The subgroups were stated a priori and appropriate.	✓	?✓X	?✓X
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

QUADAS = quality assessment of diagnostic accuracy studies; ROC = receiver operating characteristic curve.

Funding and conflicts of interest

Funding	None reported.
Conflict of interest	Both authors have disclosed industry funding for research and other commercial activities.

Potential threats to validity

Chance	None?
Selection bias	Low risk of publication bias (reported Deek's funnel plot).
Measurement bias	Significant heterogeneity in different diagnostic assays used and threshold cutoffs between various studies.
Analysis bias	Both authors worked together to assess study quality using a "modified" versions of QUADAS-2 tool?
Confounding	None or enter independent factors affecting the outcome; clinicians to comment.

Administrative details

Key words	EDACS score, chest pain, emergency department
Appraisers	Upadhye S,
Reference(s)	Boyle RSJ, Body R. The Diagnostic Accuracy of the Emergency Department Assessment of Chest Pain (EDACS) Score: A Systematic Review and Meta-analysis. Annals Emerg Med 2021 Apr;77(4):433-441. doi: 10.1016/j.annemergmed.2020.10.020. Epub 2021 Jan 16.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What risk score most accurately identifies high-risk ED syncope patients?

BEEM Bottom Line

Why is this study important? Syncope is a common reason for ED visit (1%), that may lead to over-hospitalization and low-value advanced testing (30-50%; 33% non-diagnostic) for potential serious causes (7-23% event rate of arrhythmia, MI, bleeding or death at 30 days). Accurate risk-stratification of such patients is necessary to determine those high-risk patients needing admission vs. lower-risk patients who can be discharged with outpatient follow-up.

Which, if any, threats to validity are most likely to have an impact on the results and how? Limited search/language restrictions could have missed important studies/results. Not all patients received the same workup, so those "sicker" patients with higher risk scores would be more thoroughly investigated, leading to a "workup" bias that would over-inflate score performance accuracy.

How do the key results compare with the current evidence? The results here support prior reviews suggesting that the CSRS is the most methodologically sound and validated risk stratification tool for ED syncope patients.

How should this study impact the care of ED patients? The CSRS is the most accurate rule for differentiating high- vs. low-risk ED syncope patients who may warrant admission for more intensive workups in hospital.

Study Summary

Article	Sweanor RAL, Redelmeier RJ, Simel DL, *et al*. Multivariable risk scores for predicting short-term outcomes for emergency department patients with unexplained syncope: A systematic review. Acad Emerg Med; 2021, 0-9. DOI: 10.1111/acem.14203.
Design	ED studies examining syncope risk scores in published literature.
Population	*Included:* Patients evaluated for ED syncope age 12+ (not studies with all patients <18yo). *Excluded*: Studies with risk score results that could not be blinded from study outcomes.
Index Test	Multivariate risk scores for syncope.
Reference Test	Clinical outcomes at 30d post-ED visit.
Diagnosis of Interest	Predicting the above 30d serious outcomes.

Key Results

N = 24234 patients in 17 studies. 7.5% of ED syncope patients had 30d adverse event rate.

Rule	*Diagnostic Measures*	I^2
San Francisco Syncope Rule (9 studies, 6311 pt visits). 1.4-11% event rate	LR+ = 1.1-2.2, LR- = 0.03-0.63 (Positive score $\geq$ 1/5)	
OESIL Rule (1 study, 187 pts), 6.4% event rate at 7days (AMI)	LR+ = 1.0 (0.68-1.6) LR- = 0.94 (0.41-2.1) (Positive score $\geq$ 2/4)	
Boston Syncope Rule (3 studies, 757 pts.), 6.4-25% event rate	LR+ = 1.3-2.6 LR- = 0.01-0.48 (Positive score $\geq$ 1/8)	
ROSE Rule (2 studies, 1254 pts), 6.4-7.6% event rate	LR+ = 1.2-3.5 LR- = 0.1-0.2 (Positive score $\geq$ 1/8)	
Cdn Syncope Risk Score (CSRS; 2 studies, 7849 pts), 3.6-3.7% event rate at 30d	LR+ (score>4) = 11 (8.9-14) LR- (score$\leq$0) = 0.10 (0.06-0.20)	

AUC = area under the curve; CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); *N* = number of patients; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	ü	X
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	X	X
3. The search for studies was unbiased and reproducible.	?	✓
4. The selection of studies was unbiased and reproducible.	ü	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	X	✓
7. The quality of the primary studies is high.	?	?
8. The methods used to combine the included primary studies were reported and valid.	N/A	X
9. The outcomes are clinically relevant.	ü	X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	X

A1 = S. Upadhye A2 = V. Thiruganasambandamoorthy

Funding and conflicts of interest

Funding	Not reported.
Conflict of interest	Not reported.
Disclosure	VT led the team that created the CSRS

Potential threats to validity

Chance	None or enter text here.
Selection bias	None or specify comprehensive searches; publication bias. Reasonable electronic search, screening of reference lists. Limited to English language. No gray literature used. No comment on publication bias.
Measurement bias	No distinct quality assessment tool used to assess included studies; authors used an amalgam of QUADAS, QIPS and TRIPOD criteria. No included reporting of final quality assessments.
Analysis bias	No meta-analysis due to likely heterogeneity of outcomes measures (between scores, and within same-score studies).
Confounding	Inclusion of pre-syncope patients who are less well defined, and whose outcomes may confuse the rule accuracy calculations of true syncope patients.

Administrative details

Key words	syncope predictors, risk scores, outcomes
Appraisers	Upadhye, S; Thiruganasambandamoorthy, V.
Reference(s)	Sweanor RAL, Redelmeier RJ, Simel DL, Albassam OT, Shadowitz S, Etchells EE. Multivariable risk scores for predicting short-term outcomes for emergency department patients with unexplained syncope: A systematic review. Acad Emerg Med; 2021, 0-9. DOI: 10.1111/acem.14203.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Venkatesh Thiruganasambandamoorthy MBBS MSc
Professor, Emergency Medicine/Epidemiology & Public Health, University of Ottawa
No conflicts of interest/Identify conflicts (ICMJE)
Disclosures: Led the team that created the CSRS

INFECTIONS

Research Question

What is the benefit of treating fever in febrile adults?

BEEM Bottom Line

Why is this study important? Treating fever in adults is a common cornerstone of care (i.e., fix an abnormal vital sign). However, objective, patient-relevant benefits (e.g., mortality, adverse events) of fever treatment are unclear. This review aimed to answer such questions.

What, if any, threats to validity are most likely to have an impact on the results and how? The majority of included studies had a high or "concerning" Risk of Bias, although the overall GRADE primary outcomes were considered "high" certainty of evidence.

How do the key results compare with the current evidence? Prior studies show mixed results in different patient populations (e.g., infectious vs non-infectious, critically vs non-critically ill, etc.). These results suggest that fever treatment in various subgroups and disease states may not actually matter.

How should this study impact the care of ED patients? Treating an abnormal vital sign (i.e., fever/hyperthermia) may not lead to clinically important outcomes (e.g., all-cause mortality, serious and non-serious adverse effects).

Study Summary

Article	Holgersson J, Ceric A, Sethi N, Nielsen N, Jakobsen JC. Fever therapy in febrile adults: systematic review with meta-analyses and trial sequential analyses. BMJ 2022 Jul 12;378:e069620. doi: 10.1136/bmj-2021-069620.
Design	Systematic review with meta-analysis, trial sequential analysis. PROSPERO CRD42019134006.
Population	***Included:*** Adults with fever of any origin. Randomized trials only. ***Excluded:*** None listed.
Intervention	Any fever therapy.
Comparison	No fever therapy.
Outcomes	***Primary:*** All-cause mortality, serious adverse outcomes ***Secondary:*** Quality of life, non-serious adverse outcomes
Key Results	**42 trials, 5140 patients included.** 3007 were critically ill, 1892 were non-critically ill, 3277 had infectious fever, and 1139 had non-infectious fever. 3062 participants were admitted to hospital, and 2078 were outpatients. ***Primary:*** 1) All-cause mortality (16 trials, 2415 pts all admitted to hospital; 2050 critically ill, 251 not critically ill). Infectious fever 1658, non-infectious fever 477. 9/16 used fever meds, 5/16 used physical cooling, 2/16 used combined Rx. **Fever treatment deaths 23% vs no treatment 22.6%, NO DIFFERENCE = RR 1.04 (95%CI 0.90-1.19, I^2=0; high certainty of evidence).** 2) Serious AE's (16 trials, 2415 pts all admitted to hospital as above. **NO DIFFERENCE** fever Rx (24%) vs no fever Rx (24.2%). **RR 1.02 (0.89-1.17, I^2=0, high certainty of evidence).** No differences in subgroup analyses detected. ***Secondary:*** 3) Quality of life (EQ-5D-5L at 24, 48, 72hrs; 1 trial, 37pts): No Difference. 4) Non-serious AE's (4 trials): No Difference RR 0.92 (0.67-1.25; I^2=66.5%, very low certainty of evidence. 5) Exploratory subgroups: No difference in resolution of fever (1 trial), variable reductions in fevers.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Electronic databases only. No mention of gray literature, language restrictions, etc.**	X	X
3. The search for studies was unbiased and reproducible. **Not reported**	?	?
4. The selection of studies was unbiased and reproducible. **Not reported**	?	?
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible. **Use of Cochrane Risk of Bias2 tool.**	✓	✓
7. The quality of the primary studies is high. **21 trials high Risk of Bias, 21 trials "concerning" RoB**	X	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	✓	✓

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Reported; funding from Swedish Research Council grant. No role in study design, conduct, data analysis or manuscript preparation.
Conflict of interest	Reported; no conflicts of interest declared.

Potential threats to viability

Chance	Use of trial sequential analysis to reduce type I & II errors but overall small sample size.
Selection bias	*Limited/incomplete search, publication bias, etc.* Limited electronic databases search.
Measurement bias	*Missing details on study selection; missing results of quality assessments.* Use of GRADE methods to analyze/rate the certainty of evidence.
Analysis bias	Most trials small so tests of heterogeneity may be under-powered; use of random effects analysis still very conservative despite low heterogeneity of primary outcomes.
Confounding	*List as reported.*

Administrative details

Key words	Antipyretics, fever
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC **No conflicts of interest/Identify conflicts (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Andrew Worster, MD, MSc **No conflicts of interest (ICMJE)** *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*

Research Question

Are antibiotics + steroids superior to either agent alone in treating acute otitis externa (AOE)?

BEEM Bottom Line

Why is this study important? Acute otitis externa (AOE) is a relatively common condition affecting up to 1% of the general population incidence and often seen in the emergency department (ED). Pseudomonas aeruginosa and Staphylococcus aureus are typically the pathogens causing the otalgia, tenderness, edema and otorrhea. This trial examines the comparative effectiveness of combined topical antibiotics and steroids to each alone.

What, if any, threats to validity are most likely to have an impact on the results and how? Although the primary outcome, a combination of microbiological clinical and cure, shows non-superiority of combination treatments, some secondary outcomes may show superiority.

How do the key results compare with the current evidence? Prior work demonstrates benefit of combined antibiotics and steroids in diffuse AOE in children with tympanostomy tubes, and for analgesia outcomes.

How should this study impact the care of ED patients? ED physicians should have a shared decision-making discussion with patients and caregivers to ascertain preferred values/preferences of outcomes (therapeutic/clinical/microbial cure, symptoms, etc.), and proceed with a mutually agreed-upon treatment plan accordingly.

Study Summary

Article	Chu L, Acosta AM, Aazami H, Dennis P, De Valle O, Ehmer D Jr, Hedrick JA, Ansley JF. Efficacy and Safety of Ciprofloxacin Plust Fluocinolone Acetonide Among Patients with Acute Otitis Externa: A Randomized Clinical Trial. JAMA Netw Open. 2022 Jul 1;5(7):e2221699.
Design	Superiority randomized controlled trial (36 US centers); ClinicalTrials.gov Identifier: NCT03196973
Population	***Included:*** Patients >6mo with AOE <21days in at least 1 ear, otalgia (mod/severe), otorrhea, and Brighton scale grade II/III AOE. ***Excluded:*** Recent AOE within past 4wks, or any AOE past 6mo., existing TM perforation, concurrent diabetes/AOM/malignant AOE/suspected viral or fungal infection, suspected sensitivities to study meds, recent use of any antimicrobials/steroids within 1wk (any route), or concurrent anti-inflammatory use (e.g., NSAIDs).
Intervention	CIP-FLU = ciprofloxacin 0.3% + fluocinolone 0.025% ear drops.
Comparison	CIP = ciprofloxacin 0.3% alone, FLU = fluocinolone 0.025% drops alone.
Outcomes	***Primary:*** Therapeutic cure at end of treatment period (clinical, microbiological); 4 visits up to 15-17days. ***Secondary:*** Time to end of painful ear; measured using Wong FACES pain scale. Other outcomes = sustained microbiological cure, clinical/micro cure at visit 3 & 4, therapeutic cure at visit 4, ear physical changes visit 3 & 4, adverse events (AEs).
Key Results	**493 patients recruited; 51.5% female, mean age 38.2yo.** 197 pts received CIP+FLU, 196 CIP only, and 100 FLU only. 48.5% had positive baseline microbiological culture (MITT); 27% had *P. Aerginosa* or *S. Aureus* (MITT-PA/SA), 28.6% other pathogens. Discontinuations: CIP+FLU 4.6%, CIP 6.1%, FLU 5%. CITT Compliance: CIP+FLU 96.4%, CIP 95.9%, FLU 97%. ***Primary:*** No overall therapeutic cure superiority of CIP+FLU over either CIP or FLU alone. Similar results noted with CITT and MITT-PA/SA subgroups. ***Secondary:*** Some CIP+FLU superiority for therapeutic cure over CIP (but not FLU) at visit 4, but neither at visit 3. Superiority of CIP+FLU over either alone for sustained microbiological cure at Visit 4. Superiority of CIP+FLU over CIP or FLU alone demonstrated for otalgia, but not for otorrhea nor edema.

	No significant differences in AE's amongst groups; 15 AEs total, all mild/moderate, self-limited. 1 serious AE (seizure) was noted, not attributed to study drug use. Less rescue meds used in CIP+FLU (1.5%) group compared to CIP (8.2%) or FLU (4%) groups.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively. **No reporting of consecutive sampling.**	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Double blinded**	✓	✓
6. All groups were treated equally except for the intervention. **Not reported in manuscript, appendix.**	?	?
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Reported; Laboratorias Salvat SA had a role in study design and manuscript preparation/review. No role in study conduct, data acquisition/measurement/analysis/ interpretation, and manuscript submission decisions.
Conflict of interest	Reported; no conflicts declared.

Potential threats to viability

Chance	Sample size 500 need total, 493 recruited. Relative low numbers of positive culture patients in MITT group attenuate certainty of findings in this subgroup.
Selection bias	Patients randomized 2:2:1 to CIP-FLU, CIP & FLU groups respectively; stratified by age to <18yo or 18yo to ensure group balancing.
Measurement bias	Pain scores measured at intake, and twice daily in pain diary. Clinical and microbiological cures, and pain time resolution defined in Methods (reasonable). Missing data treated as efficacy failures.
Analysis bias	CITT = clinical ITT analysis, MITT = microbiological ITT, MITT-PA/SA for *P. Aeriginosa* & *S. Aureus* specifically.
Confounding	All study medications dispensed at study sites with identical packaging. There is no reporting of cointerventions in the manuscript or appendices, so it's uncertain if all groups treated identically except for study meds.

Administrative details

Key words	Acute otitis externa, antibiotics, steroids
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**
Andrew Worster, MD, MSc *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**

Research Question

What are the latest guidelines for the management of sepsis and septic shock (SSC 2021)?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? This guideline updates SSC 2016 sepsis/septic shock recommendations, a number of which are relevant to EM practice.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? There is no clear involvement of patient/public stakeholders (focus on patient values/preferences?), nor any review by external organizations for revisions/endorsement. There are numerous conflicts of interest listed with many authors, but evidently only panelists without CoI were allowed to vote on recommendations (reducing bias of CPG Recs).

How should this guideline, and specifically which recommendations should impact the care of ED patients? This guideline reinforces prior EM-relevant care strategies, with minor modifications to use of screening tools, balanced crystalloids for initial fluid resuscitation, and transfusion strategies.

Why is this guideline and at least some of its recommendations important? This guideline updates SSC 2016 sepsis/septic shock recommendations, a number of which are relevant to EM practice.

Study Summary

Article	Evans L, Rhodes A, Alhazzani W, Coopersmith CM, French C et al. Executive Summary: Surving Sepsis Campaign International Guidelines for the Management of Sepsis and Septic Shock 2021. Crit Care Med 2021; 49(11): e1063-e1143. doi: 10.1097/CCM.0000000000005337.
Design	Clinical Practice Guideline.
Population	Adults with sepsis/septic shock.
Scope	This guideline is intended for clinicians who manage sepsis/septic shock in adult patients.

Key Results

Recommendation	*Strength*	*Quality of Evidence*
For adults with sepsis or septic shock, we recommend **against** using starches for resuscitation.	Strong	High
For adults with septic shock, we recommend using norepinephrine as the first-line agent over other vasopressors.	Strong	
For adults with sepsis-induced ARDS, we recommend using a low tidal volume ventilation strategy (6 mL/kg), over a high tidal volume strategy (> 10 mL/kg).	Strong	
For hospitals and health systems, we recommend using a performance improvement program for sepsis, including sepsis screening for acutely ill, high-risk patients and standard operating procedures for treatment.	Strong	Moderate
We recommend **against** using qSOFA compared with SIRS, NEWS, or MEWS as a single screening tool for sepsis or septic shock.	Strong	
For adults with septic shock on vasopressors, we recommend an initial target mean arterial pressure (MAP) of 65 mm Hg over higher MAP targets.	Strong	
For adults with sepsis or septic shock, we recommend using crystalloids as first-line fluid for resuscitation.	Strong	
For adults with septic shock on norepinephrine with inadequate mean arterial pressure levels, we suggest adding vasopressin instead of escalating the dose of norepinephrine.	Weak	
For adults with sepsis-induced severe ARDS, we recommend using an upper limit goal for plateau pressures of 30 cm H2O, over higher plateau pressures.	Strong	
For adults with sepsis-induced moderate/severe ARDS, we recommend using prone ventilation for greater than 12 hr daily.	Strong	
For adults with septic shock and an ongoing requirement for vasopressor therapy we suggest using IV corticosteroids.	Weak	
For adults with sepsis or septic shock we recommend using a restrictive (over liberal) transfusion strategy.	Strong	
For adults with sepsis or septic shock, we recommend initiating insulin therapy at a glucose level of ≥ 180mg/dL (10 mmol/L).	Strong	
For adults suspected of having sepsis, we suggest measuring blood lactate.	Weak	Low
For patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30 mL/ kg of IV crystalloid fluid should be given within the first 3 hr of resuscitation.	Weak	
For adults with sepsis or septic shock, we suggest guiding resuscitation to decrease serum lactate in patients with elevated lactate level, over not using serum lactate.	Weak	
For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within 1 hr of recognition.	Strong	
For adults with sepsis or septic shock, we suggest using dynamic measures to guide fluid resuscitation, over physical examination, or static parameters alone.	Weak	Very Low
For adults with septic shock, we suggest using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion.	Weak	

For adults with possible sepsis without shock, we suggest a time-limited course of rapid investigation and if concern for infection persists, the administration of antimicrobials within 3 hr from the time when sepsis was first recognized.	Weak
For adults with suspected sepsis or septic shock, we suggest **against** using procalcitonin plus clinical evaluation to decide when to start antimicrobials, as compared to clinical evaluation alone.	Weak
For adults with septic shock and cardiac dysfunction with persistent hypoperfusion despite adequate volume status and arterial blood pressure, we suggest either adding dobutamine to norepinephrine or using epinephrine alone.	Weak
For adults with sepsis-induced hypoxemic respiratory failure, we suggest the use of high flow nasal oxygen over noninvasive ventilation.	Weak

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	X
2. Systematic methods were used to search for evidence.	✓	✓
3. The criteria for selecting the evidence are clearly described.	✓	✓
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	?	?
8. The content of the guideline is free of influence by the views of the funding body.	✓	✓
9. Competing interests of guideline development group members have been recorded and managed.	?	?
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = E. Lang

Funding and conflicts of interest

Funding	None (e.g.,industry support?).
Conflict of interest	Multiple authors disclosed various sources of funding, including some from industry sources. Only panelists with no CoI were allowed to vote on recommendations.

Potential threats to validity

Development	Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible? **Appropriate use of GRADE methods. All medical professionals listed in authorship panels; no patient/public stakeholders reported. No reporting of external review/revisions, helpful to see recs presented as changes to previous edition of guideline.**
Presentation	Well organized with easy to find recommendations? **Yes.**
Comprehensive	Was the information to inform decision-making complete? **Yes; ideally would include clinical pathways/algorithms for immediate ED adaptation/adoption.**
Clinical Validity	Are the recommendations clinically sound and appropriate for the intended patients? **Yes.**

Administrative details

Key words	Adults; evidence-based medicine; guidelines; sepsis; septic shock
Appraisers	Upadhye S; Lang E.
Reference(s)	1. Evans L, Rhodes A, Alhazzani W, Coopersmith CM, French C et al. 1Surving Sepsis Campaign International Guidelines for the Management of Sepsis and Septic Shock 2021. Crit Care Med. 2021 49(11): e1063-e1143. doi: 10.1097/CCM.0000000000005337. 2. Evans L, Rhodes A, Alhazzani W, Coopersmith CM, French C et al. Executive Summary: Surving Sepsis Campaign International Guidelines for the Management of Sepsis and Septic Shock 2021. Crit Care Med 2021; 49(11): 1974-1982. DOI: 10.1097/CCM.0000000000005357

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Eddy Lang MD CCFP(EM)
Guideline Methodologist (WHO/ILCOR/NASEMSO)
No conflicts of interest (ICMJE)

Research Question

What is the most effective method of HIV screening in the Emergency Department?

BEEM Bottom Line

Why is this study important? Early detection of HIV in the ED setting can fast-track connecting previously undiagnosed patients with proper continuity of care and improve patient outcomes.

Which, if any, threats to validity are most likely to have an impact on the results and how? A large proportion of patients offered testing in all 3 arms declined, raising the risk of type II error.

How do the key results compare with the current evidence? These results do support some screening, as the reported case detection in all 3 arms exceeded historic 0.1% test prevalence thresholds that make such screening cost-effective.

How should this study impact the care of ED patients? While all strategies did yield comparable rates of new HIV Dx and linkage to subsequent care, there was no benefit for targeted/enhanced screening vs routine strategies.

Study Summary

Article	Haukoos JS, Lyons MS, Rothman RE, White DAE, Hopkins E, et al. Comparison of HIV Screening Strategies in the Emergency Department: A Randomized Clinical Trial. DOI: DOI: 10.1001/jamanetworkopen.2021.17763
Design	Randomized controlled trial (RCT). Conducted at 4 US high-volume ED's in Baltimore MD, Cinicinnati OH, Denver CO, and Oakland CA. Recruiting from Aprii 2014 to January 2016.
Population	*Included:* Adults (≥ 16yo), not critically ill/mentally altered, no prior HIV Dx, anticipated ED LOS ≥30min. *Excluded*: Age <16yo, unable to consent for HIV testing/other care, known HIV positive, sexual assault victim, occupational HIV exposure, or anticipated ED LOS <30min.
Intervention	Enhanced targeted screening (ETS) using quantitative HIV risk assessment tool (Denver HIV Risk Score), or traditional targeted screening (TTS) using CDC guidelines.
Comparison	Nontargeted HIV screening (NTS).
Outcomes	*Primary:* New HIV diagnoses. *Secondary:* Composite HIV Dx (new + unanticipated repeat), behavioural risk in ETS and TTS arms, CD4 counts & viral loads at Dx, and successful linkage to follow up care. Follow up for 1yr to assess initiation of antiretroviral Rx, unscheduled medical care visits, hospitalizations and mortality.

Key Results

N = 76561 patients. Median age 40yo, 51.2% women. Black 39.4%, white 32.6%, Hispanic 21.4%. NTS: 25469 pts (6744 completed testing, 10 new positive cases), ETS 25453 pts (4488 tests, 7 positives), TTS: 25639 pts (3173 tests, 7 positives). Overall 55 positives (0.38%), 24 new positives (0.17%).

91% new cases linked to follow-up care (22/24), 63% started antiretroviral Rx (15/22). 4 patients (17%) died during 1yr follow-up period.

Sig.	*Outcome*	*RR (95% CI)*	*NNT (95% CI)*
NSS	<u>New HIV Dx (ITT)</u>		
	TTS vs NTS	0.70 (0.30-1.56)	N/E
	ETS vs NTS	0.70 (0.27-1.84)	
	ETS vs TTS	1.01 (0.35-2.87)	
	No difference New HIV Dx for those at higher risk using TTS or ETS		

ARR = absolute risk reduction (if the CI includes the value 0, there is no difference in risk between the groups and the NNT is not estimable); CI = confidence interval; *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	✓	✓
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. (**Table 1**)	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	X	X
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	?	X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = K. Yadav ITT = intention to treat.

Funding and conflicts of interest

Funding This study was funded by an investigator-initiated grant from the National Institute of Allergy and Infectious Diseases (NIAID) (No. R01AI106057). Sponsor had no role in any aspect of study design, execution, data analysis or reporting.

Conflict of interest Reported. Most authors had govt grant supports, and few had industry funding (outside of the study submitted work).

Potential threats to validity

Chance **High rates of declined tests** in those offered one (NTS 55-72%, ETS 39-66%, TTS 32-46%); see Supplement eFigures 1-4. This could result in a Type II error (ie. false confirmation of null hypothesis of no difference between the 3 testing strategies).

Selection bias Groups well balanced for baseline demographic features (Table 1).

Measurement bias None.

Analysis bias None; ITT analysis as stated. 2 of 24 new cases (8%) were lost to follow-up at 12mo.

Confounding None.

Administrative details

Key words HIV screening, emergency department.

Appraisers Upadhye S; Yadav K.

Reference(s)

1. Haukoos JS, Lyons MS, Rothman RE, White DAE, Hopkins E, et al. Comparison of HIV Screening Strategies in the Emergency Department: A Randomized Clinical Trial. DOI: DOI: 10.1001/jamanetworkopen.2021.17763
2. Spagnolello O, Gallagher B, Lone N, Ceccarelli G, D'Ettorre G, Reed MJ. The Role of Targeted HIV Screening in the Emergency Department: A Scoping Review. Curr HIV Res. 2021;19(2):106-120. doi: 10.2174/1570162X18666201123113905.
3. Mwachofi A, Fadul NA, Dortche C, Collins C. Cost-effectiveness of HIV screening in emergency departments: a systematic review. AIDS Care. 2021 Oct;33(10):1243-1254. doi: 10.1080/09540121.2020.1817299. Epub 2020 Sep 15.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Krishan Yadav MD, MSc, FRCPC
Assistant Professor, Emergency Medicine, University of Ottawa
Associate Scientist, Ottawa Hospital Research Institute
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the latest guidelines for the early management of community-acquired pneumonia (CAP)?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? This Policy updates the prior 2009 ACEP Policy (addressed low-value routine blood cultures for low-risk CAP patients). CAP is still a leading cause of death and hospital admission worldwide, so it is important for ED physicians to hone their clinical decision-making in risk-stratifying CAP patients for certain ED tests, admission and treatment.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? Lack of patient/public stakeholders to ensure patient-relevant outcomes for CPG questions. This is a common flaw with ACEP Policy processes. Limited English-electronic electronic database searches for evidence risk missing important information from other sources (eg. Grey literature).

How should this guideline, and specifically which recommendations should impact the care of ED patients? Enter text here. Notes:

Study Summary

Article	Smith MD, Fee C, Mace SE, Maughan B, Perkins JC, Kaji A, Wolf SJ. Clinical Policy: Critical Issues in the Management of Adult Patients Presenting to the Emergency Department with Community-Acquired Pneumonia (CAP). Annals Emerg Med 2021; 77: e1-e57. https://doi.org/10.1016/j.annemergmed.2020.10.024.
Design	Clinical Practice Guideline.
Population	Adult ED patients with a Dx of CAP. CAP defined is as an acute pulmonary parenchymal infection (new infection), usually bacterial that are treatable with anitbiotics (Abx). Causes may be community-, hospital- or ventilator-acquired. Exclusion = Pregnant, pediatric patients
Scope	This guideline is intended for physicians working in the ED who evaluate/treat CAP.

Key Results

Key Questions:

Q1. In the adult ED patient diagnosed with community-acquired pneumonia, what clinical decision aids can inform the determination of patient disposition?

Q2. In the adult ED patient with community-acquired pneumonia, what biomarkers can be used to direct initial antimicrobial therapy?

Q3. In the adult ED patient diagnosed with community-acquired pneumonia, does a single dose of parenteral antibiotics in the ED followed by oral treatment versus oral treatment alone improve outcomes?

Recommendation	*Strength*
Q1. The Pneumonia Severity Index (PSI) and CURB-65 decision aids can support clinical judgement by identifying patients at low risk of mortality who may be appropriate for outpatient treatment. PSI is supported by a larger body of evidence and is preferred by other society guidelines (ATS/IDSA 2019 guidelines).	Level B
Q3. Given the lack of evidence, the decision to administer a single dose of parenteral antibiotics prior to oral therapy should be guided by patient risk profile and preferences.	Level C
Q2. Do not rely upon any current laboratory test(s), such as procalcitonin and/or C-reactive protein (CRP), to distinguish a viral pathogen from a bacterial pathogen when deciding on administration of antimicrobials in ED patients who have CAP.	Level C
Q1. Do not routinely use biomarkers to augment the performance of clinical decision aids to guide the disposition of ED patients with CAP.	Consensus

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	?	?
2. Systematic methods were used to search for evidence.	X	X
3. The criteria for selecting the evidence are clearly described.	✓	✓
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	✓	✓
8. The content of the guideline is free of influence by the views of the funding body.	✓	?
9. Competing interests of guideline development group members have been recorded and managed.	✓	✓
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = E. Lang

Funding and conflicts of interest

Funding	ACEP. No role in collecting/analyzing literature, nor crafting recommendations.
Conflict of interest	None reported.

Potential threats to validity

Development	Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible? **As with long-standing ACEP Policy processes, the working group rarely includes patient/public stakeholders (which is problematic). The evidence search was limited to English language articles from electronic databases.**
Presentation	Well organized with easy to find recommendations? **Yes**
Comprehensive	Was the information to inform decision-making complete? **Variable; CURB-65 and PSI tools provided (available with online apps also). No shared decision-making tools provided.**
Clinical Validity	Are the recommendations clinically sound and appropriate for the intended patients? **Yes? Mostly low-strength recommendations with low certainty/absent supporting evidence.**

Administrative details

Key words	Community-acquired pneumonia; decision aids; biomarkers; intravenous antibiotics
Appraisers	Upadhye S, ; Lang E.
Reference(s)	Free Policy download: Downloadable at: https://www.acep.org/patient-care/clinical-policies/community-acquired-pneumonia/ (free PDF version) The ATS/IDSA 2019 CPG updates CAP recommendations (available free at https://www.atsjournals.org/doi/full/10.1164/rccm.201908-1581ST). The NICE (UK) 2019 CPG update is available at: https://www.nice.org.uk/guidance/ng138. CADTH Rapid Review (2020) is freely accessible at: https://cadth.ca/management-patients-presenting-pneumonia-emergency-department-guidelines. https://www.mdcalc.com/psi-port-score-pneumonia-severity-index-cap https://www.mdcalc.com/curb-65-score-pneumonia-severity

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Eddy Lang MD CCFP(EM)
Guideline Methodologist (WHO/ILCOR/NASEMSO)
No conflicts of interest (ICMJE)

Research Question

Are self-obtained vaginal swabs sufficiently accurate for diagnosing sexually transmitted diseases in the ED?

BEEM Bottom Line

Why is this study important? Neisseria gonorrhoeae (NG) and Chlamydia trachomatis (CT) testing is often performed in ED, and can be challenging in busy/overcrowded situations, or where patient privacy/preference is compromised. Self-obtained vaginal swab (SOVS) could improve patient and ED management since they are non-inferior to physician-performed endocervical sampling (PPES). In this study, 75% of patients preferred SOVS to PPES.

Which, if any, threats to validity are most likely to have an impact on the results and how? The study was conducted in ED with a convenience sample of specific US population (English and Spanish speaking) leading to its application in a similar setting.

How do the key results compare with the current evidence? SOVS performed as well as PPES in this ED setting. The results are congruent with previous reports in family medicine/gynecologic clinics where SOVS was validated for NG/CT screening.

How should this study impact the care of ED patients? SOVS can be used alternatively to obtain NG/CT testing in the ED when a pelvic clinical examination may not be warranted or nor useful to patient care. Sensitivities of the SOVS are non-inferior to the PPES ones, and the diagnostic likelihood ratios are outstanding for ruling in/out disease.

Study Summary

Article	Chinnock B, Yore M, Mason J, et al. Self-obtained vaginal swabs are not inferior to provider-performed endocervical sampling for emergency department diagnosis of Neisseria gonorrhoeae and Chlamydia trachomatis. Acad Emerg Med. 2021 Jun;28(6):612-620. doi: 10.1111/acem.14213. Epub 2021 Mar 24. PMID: 33460481.
Design	Prospective observational cohort study. Non-inferiority design.
Population	*Included:* Female (English and Spanish speaking) patients ≥ 18 years old needing NG/CT testing as per the ED physician. 2018 to 2020 *Excluded*: Inmates, acute psychiatric conditions, non-English/Spanish language, and use of NG/CT treatment in the preceding 4 weeks.
Index Test(s)	Self-obtained vaginal swab (SOVS) following a brief one-page instruction form (no additional assistance by ED staff). NG/CT tests by rapid nucleic acid amplification test (NAAT).
Reference Test(s)	Provider-performed endocervical sampling (PPES). NG/CT tests by NAAT assay.
Outcomes	*Primary:* Sensitivity of no less than 90% for the composite NG/CT diagnosis by SOVS compared to PPES. *Secondary:* Sensitivity for NG and CT specifically. Patients' acceptability of SOVS.

Key Results *N* = 515 out of 533 enrolled (86 (17%) positive to NG, CT or both).

Sig.	*Outcome*	*Result Report LR, Sens & Spec*
SS	Composite NG/CT	Sensitivity = 95 (95% CI: 88 to 99)
SS	Composite NG/CT	Specificity = 99 (95% CI: 97 to 100)
		***LR+ 83 (34-198), LR- 0.05 (0.02-0.13)**
SS	NG only	Sensitivity = 97 (95% CI: 87 to 100)
SS	NG only	Specificity = 100 (95% CI: 99 to 100)
SS	CT only	Sensitivity = 94 (95% CI: 84 to 99)
SS	CT only	Specificity = 99 (95% CI: 98 to 100)
	AUC: not available	
SS	Patients' preference SOVS vs PPES	P = 75%

AUC = Area Under the Curve; CI = Confidence Interval; LR = Likelihood Ratio; *N* = number of patients; NA = not applicable; Statistically Significant; *p* = probability; Sig. = Significance; SS = Statistically Significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those likely to undergo testing in the ED.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	X	?
3. All patients underwent the same diagnostic evaluation.	✓	✓
4. All tests were conducted within similar time frames to preclude changes in disease status.	✓	✓
5. The reference standard criteria for the candidate diagnoses are explicit and reproducible.	?	?
6. The reference standard was applied regardless of and blinded to the index test result.	✓	✓
7. The assignment of the candidate diagnoses was explicit and reproducible.	✓	✓
8. Most (> 80%) patients received a diagnosis.	✓	✓
9. Undiagnosed patients received adequate clinical follow-up.	?	?
10. The estimates of disease probability are clinically significant.	✓	✓

A1 = M. Émond A2 = S. Upadhye

Funding and conflicts of interest

Funding	Local funding – University of California San Francisco-Fresno research fund
Conflict of interest	None.

Potential threats to validity

Chance	None.
Selection bias	Convenient sample; may lead to sampling bias (missing different patients/demographics during night hours?). Patient were eligible by MD need to test. Refusals were more prone to have PPES.
Measurement bias	Low: 15/533 patients were removed for incomplete samples. 3 for indeterminate results. Overall enrollment goal was not met (due to COVID19 pandemic cessation of study), but required sample size of 80+ positive cases was met.
Analysis bias	Low: To be a true positive at the composite outcome NG/CT, concordance needed to be 100%
Confounding	Patients who declined enrollment: Too unwell/painful (36%), 26% procedural uncertainty (uncomfortable with SOVS, concerned about procedural error, prefer PPES = 17%).

Administrative details

Key words	Sexually transmitted disease (STD); vaginal swab.
Appraisers	Emond M, Upadhye S.
Reference(s)	Lunny C, Taylor D, Hoang L, et al. Self-Collected versus Clinician-Collected Sampling for Chlamydia and Gonorrhea Screening: A Systemic Review and Meta-Analysis. PLoS One. 2015 Jul 13;10(7):e0132776. doi: 10.1371/journal.pone.0132776. PMID: 26168051; PMCID: PMC4500554.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Marcel Émond, MD, MSc, CCFP(EM), FRCP(C)
Associate professor, Université Laval
No conflicts of interest

Research Question

What is the accuracy of various signs & symptoms in the diagnosis of adult community-acquired pneumonia (CAP)?

BEEM Bottom Line

Why is this study important? A clinical assessment of CAP is important in determining who needs a CXR to confirm the diagnosis, and who may need antibiotics (in order to rationalize CXR ordering and Abx stewardship).

Which, if any, threats to validity are most likely to have an impact on the results and how? Most included studies had low risk of bias (some moderate). Some heterogeneity between study definitions, settings & inclusion criteria acknowledged (not a serious threat to results). All studies used CXR as a reference standard (not always confirmed on CT scan?).

How do the key results compare with the current evidence? Various clinical signs/symptoms for CAP have some moderate pre-CXR diagnostic accuracy, but no single item is definitive enough to obviate a CXR and proceed directly to Abx treatment (LR+ values ranging from 0.5-2.0). Various S/S, when present, increased the likelihood of CAP Dx, but the absence of such did not reduce the risk as much. Presence of acute cough was useless for Dx accuracy, and should not prompt CXR ordering. The absence of abnormal VS was helpful to exclude CAP Dx. Based on Dx OR values, the most useful findings were overall clinical impression, egophony, any abnormal VS, any abnormal lung finding, tachypnea, and objective fever.

How should this study impact the care of ED patients? This updated review reinforces that the overall clinical impression of an experienced ED physician is the best "test" for clinically diagnosing CAP, ordering confirmatory CXR, and treating with Abx.

Study Summary

Article	Ebell MH, Chupp H, Cai X, Bentivegna M, Kearney M. Accuracy of Signs and Symptoms for the Diagnosis of Community-acquired Pneumonia: A Meta-analysis. Acad Emerg Med 2020; 27: 542-553. doi: 10.1111/acem.13965
Design	Systematic review and meta-analysis of diagnostic accuracy of CAP signs & symptoms.
Population	*Included:* Adults/adolescents with signs/symptoms of CAP being managed in outpatient settings (including ED). *Excluded*: Patients with dyspnea NYD or sepsis, patients in specialized nursing facilities, immunocompromised patients, known chronic lung diseases, hospital/ventilator-acquired pneumonia, or pathogen-specific diagnostic studies. Case control studies also excluded.
Index Test	Clinical assessment of signs/symptoms of CAP.
Reference Test	Imaging confirmation of CAP (CXR used in all included studies)
Diagnosis of Interest	CAP

Key Results

N = 8,544 patients in 16 studies. Prevalence of CAP: 10% in primary care studies, 20% in ED studies

N/Studies	*Clinical Characteristic: Sens/Spec/LR+/LR-/Dx test OR/AUROC*	I^2
7/5081	Overall Clinical impression: 0.50/0.92/6.32/0.54/11.5/0.741	
3/748	Hx of COPD: 0.19/0.91/ 2.37/0.88/2.74/Not calc	
8/4097	Subjective Fever: 0.63/0.55/1.47/0.68/2.10/0.623	
7/2453	Chills: 0.55/0.62/1.44/0.73/2.00/0.610	
10/5626	Dyspnea: 0.63/0.51/1.30/0.75/1.75/0.598	
8/5031	Chest Pain: 0.51/0.58/1.21/0.86/1.41/0.549	
3/1116	Egophony: 0.05/0.99/6.17/0.96/6.46/NC	
7/1932	Percussion dullness: 0.14/0.94/2.62/0.94/2.29/NC	
4/1596	Confusion: 0.11/0.95/2.15/0.94/2.29/NC	
12/5898	Crackles: 0.42/0.79/ 2.00/ 0.74/2.70/0.611	
6/4322	Dec breath sounds: 0.25/0.87/1.96/0.87/2.29/NC	
8/2875	Any abnormal lung exam: 0.60/0.67/1.90/0.61/3.18/0.669	
5/2375	Rhonchi: 0.23/0/87/1.76/0.89.1.99/NC	
5/4162	Toxic appearance: 0.42/0.70/1.46/0.83/1.77/NC	
3/604	Any abnormal VS: 0.93/0.30/1.37/0.25/6.01/NC	

AUC = area under the curve; CI = confidence interval; I2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); N = number of patients; N/A = not applicable;

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	?	✓
4. The selection of studies was unbiased and reproducible.	?	?
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	✓	✓
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	X	X
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = A. Worster

QUADAS = quality assessment of diagnostic accuracy studies; ROC = receiver operating characteristic curve.

Funding and conflicts of interest

Funding	No commercial support reported.
Conflict of interest	Declared (as per publisher guidelines) but not reported.

Potential threats to validity

Chance	None.
Selection bias	No reporting of publication bias evaluation.
Measurement bias	None.
Analysis bias	None.
Confounding	Most included studies examined individual clinical CAP S/S, but not necessarily combinations.

Administrative details

Key words	Community-acquired pneumonia, signs, symptoms, diagnosis
Appraisers	Upadhye S, ; Worster A.
Reference(s)	Ebell MH, Chupp H, Cai X, Bentivegna M, Kearney M. Accuracy of Signs and Symptoms for the Diagnosis of Community-acquired Pneumonia: A Meta-analysis. Acad Emerg Med 2020; 27: 542-553.

Clinical Appraisal faculty

S. Upadhye, MD, MSc, FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

A. Worster, MD, MSc
Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the determinants of ED physician prescribing of antibiotics for respiratory tract infections?

BEEM Bottom Line

Why is this study important? This review explores those factors associated with ED antibiotic prescribing for adult respiratory tract infections.

Which, if any, threats to validity are most likely to have an impact on the results and how? There is a somewhat limited search of articles, which could have led to selection bias. There is no quality assessment of included articles reported, nor is there an attempt to quantify the magnitude of different predictors of Abx prescribing determinants.

How do the key results compare with the current evidence? The results support a proactive strategy of multimodal education strategies for providers/patients in order to improve RTI Abx prescribing practices.

How should this study impact the care of ED patients? There is a need to recognize personal biases in prescribing Abx for adult RTI's where they may not be warranted. Structured education for both providers and patients can optimize Abx stewardship.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article Lim DW, Htun HL, Ong LS*, et al*. Systematic review of determinants influencing antibiotic prescribing for uncomplicated acute respiratory tract infections in adult patients in the emergency department. Inf Cont Hosp Epid 2020; 1-10. doi:10.1017/ice.2020.1245

Design Systematic review of ED-based trials for antibiotic prescribing determinants. No meta-analysis.

Population *Included:* Adult ED patients with uncomplicated respiratory tract infections (RTIs).
Excluded: Studies including mixed populations, non-ED settings, complicated RTIs (eg. Abscess, other)

Intervention Factors associated with ED Abx prescribing

Comparison Appropriate versus inappropriate antibiotic prescribing behaviours (if intervention is available)

Outcomes *Primary:* antibiotic prescribing rates and antibiotic use

Key Results *12 studies* = 150 to >37million visits analyzed in various studies. Most predictors addressed only in 1-2 studies.

Abx Rx Determinants
NEGATIVE Predictors: 1) Provider factors: comanagement with house staff 2) Patient factors (Symptoms, Comorbidities): Prior URTI in last 6 weeks 3) Investigations: Normal CRP value, positive rapid influenza test
POSITIVE Predictors: 1) Provider: Older age, non-physician (NP, PA), non-EM/IM, patient expectations. Clinical Dx bronchitis, AECOPD, sinusitis, pharyngitis, CAP. 2) Patient: Older male, CHF comorbidity, patient satisfaction score, ED LOS. Symptoms = Purulent sputum, dyspnea, symptoms >2days. Signs = Abnormal resp exam, fever? 3) Investigations: Blood culture ordered

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	X	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	?	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	X	?✓X	?✓X
7. The quality of the primary studies is high.	?	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	N/A	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	None (reported).
Conflict of interest	None (reported).

Potential threats to validity

Chance	None or enter text here (e.g., sample size, Type I & II errors?
Selection bias	None or enter text here (incomplete search, publication bias, etc.). Search: English articles only. Electronic databases; no gray literature mentioned. No assessment of publication bias.
Measurement bias	None or enter text here (e.g., missing details on study selection; missing results of quality assessments). No quality assessment for included studies reported.
Analysis bias	None or enter text here (e.g., fixed vs. random effects, combined results of studies of different design). No attempt to quantify magnitude of predictor determinants of Abx prescribing (qualitative descriptions only).
Confounding	None?

Administrative details

Key words	Antibiotic prescribing, emergency department, respiratory infections
Appraisers	Upadhye S; Yeung C; Zeraatka D; Worster A; Kanters D.
Reference(s)	Lim DW, Htun HL, Ong LS, Guo H, Chow A. Systematic review of determinants influencing antibiotic prescribing for uncomplicated acute respiratory tract infections in adult patients in the emergency department. Inf Cont Hosp Epid 2020; 1-10. doi:10.1017/ice.2020.1245

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the latest guidelines for the management of acute rheumatic fever/heart disease?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? Acute rheumatic fever/heart disease (ARF/AHD) is more prevalent in women and native populations, and these particular vulnerable populations merit special attention to avoid catastrophic cardiac complications. This guideline updates prior 2012 guidance on diagnosing/managing ARF/AHD in general and specific populations.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? Lack of an explicit literature search, detailed quality assessment of included studies limits reproducibility of evidence reviews.

How should this guideline, and specifically which recommendations should impact the care of ED patients? This updated CPG has a strong culturally competent focus to address ARF/AHD in high-risk populations, and makes clear recommendations with support tables on acute and ongoing management of ARF/AHD for ED clinicians.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Ralph AP, Noonan S, Wade V, Currie BJ. The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease. Med J Aust. 2021 Mar;214(5):220-227. doi: 10.5694/mja2.50851. Epub 2020 Nov 15.
Design	Clinical Practice Guideline.
Population	Patients (adult, pediatric) diagnosed with acute rheumatic fever (ARF) or rheumatic heart disease (RHD).
Scope	This guideline is intended for physicians who diagnose/manage ARF or AHD.

Key Results

Recommendation	*Strength*	*Quality of Evidence*
GAS skin infections should be treated with Cotrimoxazole or IM PenG.	Strong.	High
Population-based screening for RHD using auscultation is NOT recommended.	Strong.	
ECHO screening of patients at risk of undiagnosed RHD is recommended.	Strong.	
Patients diagnosed with RHD should be referred to specialist cardiology services for possible anticoagulant Rx.	Weak.	
Pregnant women with high risk of ARF/AHD with worsening dyspnea, orthopnea, wheeze or worsening fatigue should be investigated with ECHO.	Strong.	
Patients at high-risk of ARF with sore throat should be treated with 1st line PenV. (Box 3)	Weak.	Moderate
Identification/treatment of GAS skin infections may decrease the burden of ARF.	Weak.	
All patients with ARF should be hospitalized for cardiac investigations (ECG, ECHO) and other diagnoses excluded.	Strong.	
There may be a role for corticosteroids for severe rheumatic carditis or Syndenhams chorea.	Weak.	

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	X	?
2. Systematic methods were used to search for evidence.	?	?✓X	?✓X
3. The criteria for selecting the evidence are clearly described.	X	?✓X	?✓X
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	X	?✓X	?✓X
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	X	?✓X	?✓X
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	?✓X	?✓X
7. Experts externally reviewed the guideline prior to its publication.	✓	?✓X	?✓X
8. The content of the guideline is free of influence by the views of the funding body.	✓	?✓X	?✓X
9. Competing interests of guideline development group members have been recorded and managed.	✓	?✓X	?✓X
10. The strength and certainty of the key recommendations are clearly identified.	✓	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding National Heart Foundation of Australia. No comments in role of sponsor in evaluating evidence or generating recommendations.

Conflict of interest Various authors employed by RHDAustralia (nationally funded organization).

Potential threats to validity

Development Explicit and broad representation of various stakeholders, including Aboriginal/native stakeholders, was included elicit lived experiences, and to ensure culturally competent recommendations. Literature review is minimally described, and no specific details provided re: quality assessment of evidence or risk of bias assessments. Use of GRADE methods to write recommendations (no explicit info on GRADE methods used, or Summary of Evidence/Findings Tables provided). Quality of evidence rated as A-D scale (A = high, D = very low), and recommendations were Strong (1) or Weak (2).

Presentation Well organized with easy to find recommendations? **Yes**

Comprehensive Was the information to inform decision-making complete? **Yes; useful tables provided.**

Clincal Validity Are the recommendations clinically sound and appropriate for the intended patients? **Yes**

Administrative details

Key words Acute rheumatic fever, rheumatic heart disease.

Appraisers Upadhye S,

Reference(s) Ralph AP, Noonan S, Wade V, Currie BJ. The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease. Med J Aust. 2021 Mar;214(5):220-227. doi: 10.5694/mja2.50851. Epub 2020 Nov 15.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the overall effects of delaying antibiotics for respiratory tract infections (RTI)?

BEEM Bottom Line

Why is this study important? Antibiotic stewardship is critical in the growing challenge of increased antibiotic resistance. Antibiotic over-use is most common in primary care for respiratory infections, representing the single largest opportunity for stewardship interventions.

Which, if any, threats to validity are most likely to have an impact on the results and how? No validity threats. No study included use of POC testing, decision aids nor specific HCP training to de-implement Abx use. This group also used a 10-member patient/public stakeholder panel to help with study design, implementation and data interpretation. This group also advised on how to use these results in knowledge translation strategies. Three stakeholders included as authors.

How do the key results compare with the current evidence? This IPDMA reinforces prior Cochrane study-level SR/MA's that support a delayed vs immediate/no Abx strategy for common RTIs.

How should this study impact the care of ED patients?

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Stuart B, Hounkpatin H, Becque T, *et al*. Delayed antibiotic prescribing for respiratory tract infections: individual patient data meta-analysis. BMJ 2021;372:n808. http://dx.doi.org/10.1136/bmj.n808
Design	Individual patient data meta-analysis. Only RCTs/observational cohort studies included.
Population	*Included:* Patients treated for RTI in a community setting. *Excluded*: Patients treated in hospital. Non-RCTs/observational studies.
Intervention	Delayed antibiotics for RTI.
Comparison	Immediate or no Abx.
Outcomes	*Primary:* Average symptom severity 2-4 days after initial consultation. *Secondary:* Duration of illness after initial consultation, illness complications resulting in hospitalization/death, reconsultation for same/worsening symptoms, patient satisfaction (4 pt Likert scale).

Key Results

IPD available from 13 studies (n=55682 patients)

Sig.	*Outcome*	*N/Studies*	*Outcome Measure (95% CI)*	*I^2*
NSS	Avg duration of symptoms with delayed vs. no Abx	7/3907 pts	Mean Diff 7pt scale: 0.003 (-0.12 to 0.11)	N/A
NSS	Avg duration of symptoms with delayed vs. immediate Abx	8/3752 pts	0.02 (-0.11 to 0.15)	N/A
NSS	Reconsultation rates: delayed vs immediate Abx		OR 0.95 (0.74-1.22)	N/A
NSS	Complications (hospitalization/ death) with delayed vs no Abx, nor delayed vs immediate Abx		OR 0.62 (0.30-1.27) OR 0.78 (0.53-1.13)	N/A
NSS	Patient satisfaction delayed vs no Abx		Mean Diff 0.09 (0.06-0.11)	
SS	Children <5yo with higher symptom severity at 2-4d follow up		Mean Diff 7pt scale: 0.10 (0.03-0.18)	N/A
SS	Longer time to symptom resolution with delayed vs immediate Abx		HR 1.04 (1.01-1.08)	N/A
SS	Lower reconsultation rates with delayed vs no Abx		OR 0.72 (0.60-0.87)	N/A

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

No other pre-specified subgroups had any effectiveness differences between Abx groups.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	✓	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	N/A	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding This work was funded by the NIHR Research for Patient Benefit (RfPB) Programme (grant No PB-PG-0416-20005). The funder had no role in interpretation/publication of study results.

Conflict of interest None (explicit disclosure).

Potential threats to validity

Chance None.

Selection bias None. The included studies for IPD included 93% of all potential eligible study populations.

Measurement bias None.

Analysis bias None. Use of one- and two-stage random effects analyses for pre-defined sensitivity analyses.

Confounding Unclear impact of findings from LMIC countries (higher probability of serious illness/complications), or different pathogens or access to reconsultation care/secondary care if clinical deterioration. Authors did use propensity scores to mitigate potential confounding of observational data sets (much larger than RCT IPD sets).

Administrative details

Key words Delayed antibiotics, lower respiratory infections

Appraisers Upadhye S,

Reference(s) Stuart B, Hounkpatin H, Becque T, Yao G, Zhu S, Alonso-Coello P, Altiner A, Arroll B, Bohning D, Bostock J, Bucher HC, Chao J, de la Poza M, Francis N, Gillespie D, Hay AD, Kenealy T, Loffler C, McCormick DP, Mas-Dalmau G, Munoz L, Samuel K, Moore M, Little P. Delayed antibiotic prescribing for respiratory tract infections: individual patient data meta-analysis. BMJ 2021;372:n808
http://dx.doi.org/10.1136/bmj.n808

PubMed ID: 33910882

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

NEURO/STROKE

Research Question

What is the optimal diagnostic strategy for non-traumatic ED sudden onset headache?

BEEM Bottom Line

Why is this study important? Ruling out dangerous pathologies in ED sudden onset headache (eg. SAH) is critically important to avoid significant morbidity/mortality. Having a diagnostic strategy to detect these cases without exposing patients to low-value/harmful interventions is critical to optimize diagnosis, reduce harms and use resources wisely.

What, if any, threats to validity are most likely to have an impact on the results and how? Heterogeneity of various diagnostic definitions, outcomes measured/reported, and low outcome event rates in various subgroups erode certainty in pooled results.

How do the key results compare with the current evidence? Findings align with recent CPG Recs that a CT-only (read by neuroradiologists) for headache <6hrs is a safe strategy to identify potential SAH patients without further testing.

How should this study impact the care of ED patients? Strong evidence supports a CT-only strategy for sudden ED headaches <6hrs, read by neuroradiologists (or experienced rad readers), to rule out SAH.

Study Summary

Article	Walton M, Hodgson R, Eastwood A, Harden M, Storey J, Hassan T, Randall MS, Hassan A, Williams J, Wade R. Management of patients presenting to the emergency department with sudden onset severe headache: systematic review of diagnostic studies. Emerg Med J 2022, emermed-2021-211900.
Design	Systematic review. PROSPERO reg: CRD42020173265
Population	***Included:*** Studies with any care pathway for ruling out clinically suspicious SAH (including Dx tests +/- CDRs) in neurologically intact adults with sudden severe headache (max intensity within 1hr). ***Excluded:*** Patients with a head injury, case studies.
Index Test	Diagnostic strategies (imaging, CDRs, etc.)
Reference Standard	Varied
Diagnoses of Interest	Diagnostic strategy accuracy, quality of life, adverse events.
Key Results	37 studies included. 1) Clinical Decision Rules (including Ottawa SAH rule): 13 studies total, 8 OSAHR = 8114pts Mean SAH prevalence: 5% OSAHR Pooled Sens: 99.5% (95%CI 90.8-100), Spec: 23.7% (15.5-34.4); LR+ 1.3, **LR- 0.02** 2) CT Scan <6hrs, neurorad read (alone): 4 studies, 2377 pts. Mean SAH prevalence 10.8% (9.2-12.7%) Pooled Sens: 98.7% (96.5-100), Spec 100% (99.7-100); LR+ infinity, **LR- 0.01** 3) CT any time: 3 studies, 3889pts. Prevalence SAH 2.7-7.7% Pooled Sens CT >6hrs: 85.7% (78.3-90.9), Spec 90.0% (76.3-97.2); LR+ 8.57, **LR- 0.16** 4) CT read by ER physicians (1 study, high RoB): N=269 Prevalence SAH 8% Results: Sens 84% (63.9-95.5), Spec 95% (90.9-97.2); LR+ 16.8. LR- 0.17 5) Spectrophotometric LP CSF after neg CT (3 studies, 1235pts). SAH Prev 0.65%. Pooled Sens: 100% (100-100), Spec: 95.2 (86-98.5); LR+ 20.83, **LR- 0.00** 6) Visual LP CSF inspection after neg CT (3 studies, 1043 pts). SAH Prev 2%. Pooled Sens: 84.9% (60-95.5), Spec 97.6 (95.3-98.8); LR+ 35.37, **LR- 0.15** 7) LP RBC thresholds (2 studies, not pooled): Sens 81.6-100%, Spec 91.2-97.3 for RBC <2000 $x10^6$/L and neg xanthochromia.

	8) CTA after normal CT/LP: 2 small studies, no SAH cases found. 9) Clinical features of SAH: 3 studies, not pooled. Clinical suspicion SAH 49%. No individual feature was strongly predictive of SAH (age>65yo, temp>38C, SBP>160mmHg, neck stiffness, vomiting, transient loss of consciousness).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Electronic databases++, conference abstracts, no other gray literature. All languages.**	?	?
3. The search for studies was unbiased and reproducible. **No mention of duplicated searches, detailed search strategy and terms summarized in Supplement 1**	?	✓
4. The selection of studies was unbiased and reproducible. **Dual independent screening of titles/ abstracts.**	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **Extracted by 1 researcher, checked by another (not dual independent with 3rd party adjudications).**	X	X
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible. **Most QUADAS2-rated studies had low Risk of Bias, other non-QUADAS studies "Unclear" RoB**	?	?
7. The quality of the primary studies is high. **As above 6.**	?	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies. **High degree of heterogeneity for outcomes measured.**	X	X
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = K. Lin

Funding and conflicts of interest

Funding	None reported
Conflict of interest	Reported; no significant conflicts noted

Potential threats to viability

Chance	Certain pooled outcomes had small numbers of patients/outcome events, leading to potential type I or II errors. Prospective trials do a better job of evaluating eligibility criteria (compared to retrospective designs).
Selection bias	*Specify comprehensive searches; publication bias?*
Measurement bias	QUADAS2 tool used for most included studies for quality assessment (n=28); for studies without a reference standard, researchers used a previously created/validated tool (n=9); Supp file 3.
Analysis bias	*Fixed/random effects? Heterogeneity mgt?* Random effects analysis for pooled meta-analysis. High degree of heterogeneity in reporting outcomes for included studies; X^2 values not reported.
Confounding	*Enter independent factors affecting the outcome; clinicians to comment.* Patient collaborator with lived sudden headache experience involved with all aspects of the project, and 3 other patients added into study advisory group.

Administrative details

Key words	Emergency department, sudden onset headache
Reference(s)	National Institute for Health and Care Excellence. Subarachnoid haemorrhage caused by a ruptured aneurysm: diagnosis and management. Draft for consultation, 2021. Available: https://www.nice.org.uk/guidance/GID-NG10097/documents/draft-guideline [Accessed 15 Mar 2021].

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**
Katie Lin, MD MPH FRCPC *Assistant Professor, Emergency Medicine/Clinical Neurosciences, University of Calgary*	**No conflicts of interest (ICMJE)**

Research Question

Is IV tenecteplase non-inferior to alteplase for acute stroke reperfusion?

BEEM Bottom Line

Why is this study important? Tenecteplase (TNK) can be delivered via single bolus administration and has a longer plasma half-life than alteplase (ALT), making it a potentially attractive alternative to alteplase infusions for acute ischemic stroke (AIS).

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. Lack of consecutive recruiting/other factors during COVID19 pandemic are a research reality, but required sample size (with built-in LTFU buffers) was still met.

How do the key results compare with the current evidence? Prior phase 2 trials show a benefit of TNK over alteplase for AIS at varied doses. This is the first phase 3 trial to demonstrate benefit with larger sample sizes.

How should this study impact the care of ED patients? Eligible AIS patients presenting within the reperfusion window (<4.5 hours) would do just as well with IV bolus TNK compared to infusion ALT. ED AIS reperfusion protocols could be adapted for such.

Study Summary

Article	Menon BK, Buck BH, Singh N, *et* al; AcT Trial Investigators. Intravenous tenecteplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial. Lancet. 2022 Jul 16;400(10347):161-169. doi: 10.1016/S0140-6736(22)01054-6. Epub 2022 Jun 29. PMID: 35779553
Design	Pragmatic multi-centre open-label non-inferiority RCT (22 primary stroke centres in Canada); ClinicalTrials.gov, NCT03889249
Population (as per Cdn Best Stroke Practices Recs)	***Included:*** Adults >18yo with AIS with disabling neurologic deficits with symptom onset 4-5hrs. ***Excluded:*** Absolute = Active bleeding, high risk of bleeding, pregnant women. Many other relative exclusions in Supplemental Appendix.
Intervention	TNK at 0.25mg/kg single bolus dose, max dose 25mg
Comparison	Alteplase 0.9mg/kg IV, delivered as loading bolus (10% of dose) + infusion (remaining 90% of dose), max dose 90mg
Outcomes	***Primary:*** Modified Rankin Scale (mRS; 7pt Likert scale) score of 0-1 at 90 and 120 days post-treatment. ***Secondary:*** 90-120 day mRS scores (0-2, any), return to baseline function 90d, 90-120d EQ-VAS and EQ-5D-5L scores, door-to-needle time, recanalization status at first endovascular angiography test, baseline CT to arterial puncture time for patients undergoing endovascular Rx, cognitive assessment tool scores (telephone interview), hospital length of stay (LOS), and discharge destination. ***Adverse events:*** Symptomatic ICH <24hrs, orolingual angioedema <24hrs, or any extracranial bleeding requiring blood transfusion <24hrs. 90day all-cause mortality. **Pre-specified subgroups analyzed (for both ITT and Per Protocol analyses):** Age < and >80yo, gender, baseline NIHSS stroke severity, large vessel occlusion on baseline CT angiography, type of enrolling centre, and source registry (OPTIMISE vs QuICR).
Key Results Median age: 74yo (IQR 63-83) Female 47.9% vs male 52.1% Median symptom onset to Rx: 2hrs (IQR 1.5-3hrs) Loss to follow-up at 90-days: 0.6% (N=10)	806 TNK pts in ITT group (800 treated, 6 lost to follow-up, 790 analyzed per protocol) 771 alteplase pts in ITT group (762 treated, 4 LTFU, 760 analyzed PP) ***Primary:*** TNK 36.95% vs. ALT 34.8%; Unadj Risk Diff 2.1% (95%CI -2.6% to 6.9%); **lower bound 95%CI >-5%, so TNK is non-inferior to ALT.** TNK **not superior** to ALT in secondary analysis (p=0.19). Efficacy results similar in ITT vs PP analyses. ***Secondary:*** **No significant differences** in all outcomes (Table 2). **No heterogeneity of treatment effects in pre-specified subgroups, nor in sensitivity analyses with imputation for missing data.** **No significant differences in any safety outcomes (rare in both groups, both ITT and PP analyses).**

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	X	X
2. The patients were adequately randomized (allocation sequence adequately generated). **Central randomization, allocation balance per site.**	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Treatment was open label, but outcomes assessments blinded.**	?	?
6. All groups were treated equally except for the intervention. **As per Cdn Best Stroke Practices**	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up). **Minimal LTFU**	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = K. Lin

Funding and conflicts of interest

Funding	CIHR (Alberta SPOR Unit); no role in study design, conduct nor data analysis.
Conflict of interest	Various authors declared financial interests (stock ownership, consulting fees, industry grants, advisory boards, speaking honoraria) and some public grant supports.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* NI margin of -5%, sample size recruiting target met.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Unable to guarantee consecutive recruiting during COVID19 pandemic (and other potential institutional restrictions). Groups otherwise balanced at initiation.
Measurement bias	Unable to practically blind patients and treating clinicians, but were able to blind outcomes assessors.
Analysis bias	*ITT, Per Protocol, As Treated.* Both ITT and PP analyses used for all outcomes assessed.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Impractical to blind patients and treating clinicians, although outcomes assessors were blinded.

Administrative details

Key words	Acute ischemic stroke, alteplase, tenecteplase, thrombolysis
Reference(s)	Menon BK, Buck BH, Singh N, et al. Intravenous tenectaplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised controlled, non-inferiority trial. Lancet. 2022;400(10347):161-169.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Katie Lin, MD MPH FRCPC *Assistant Professor, Emergency Medicine/Clinical Neurosciences, University of Calgary*	**Associated with AcT Trial Investigator Group (ICMJE)**

Research Question

Are peripheral nerve blocks effective for primary headaches?

BEEM Bottom Line

Why is this study important? Primary headaches are the most common neurological ED presentation, and can be time- and resource-consuming depending on therapeutic agents selected. Peripheral nerve blocks (and trigger point injections) may offer a rapid, safer and resource-saving alternative to traditional headache therapies in the ED.

What, if any, threats to validity are most likely to have an impact on the results and how? There is limited data to confirm early benefits (<15min). Blinding is difficult in these types of studies, as medication delivery and local responses may be very different for analgesics delivered. **Significant heterogeneity in control agents used with few using metoclopramide IV. Very little longer-range data.**

How do the key results compare with the current evidence? There is a growing body of evidence in support of interventional anesthetics for acute pain control in the ED, primarily for musculoskeletal pain syndromes. This work expands the indications for PNB in the ED setting. Current analgesics for ED headache are slower in onset, less favourable administration routes, and unpleasant side effects. PNBs are less invasive and more rapid-acting, and may overcome HA-related nausea & vomiting problems that limit the utility of oral analgesics.

How should this study impact the care of ED patients? Peripheral nerve blocks and trigger point injections may be useful alternatives for rapid and effective treatment of primary headaches in the ED.

Study Summary

Article	Patel D, Yadav K, Taljaard M, Shorr R, Perry JJ. Effectiveness of Peripheral Nerve Blocks for the Treatment of Primary Headache Disorders: A Systematic Review and Meta-Analysis. Annals Emerg Med 2021; 1-11. DOI: 10.1016/j.annemergmed.2021.08.007
Design	Systematic Review of human RCTs (PROSPERO ID: CRD42020212187)
Population	*Included:* Patients with primary headaches (any age). Primary headache = acute/chronic migraines, tension or cluster headaches. *Excluded:* Nonrandomized trials, review articles, and studies that assessed patients with secondary headache disorders.
Intervention	Peripheral Nerve Block (PNB) = Greater occipital nerve (GON), sphenopalatine ganglion block (SGB) and trigger point injections (TPI)
Comparison	Placebo (10 trials) or other treatments (NS 1 trial, DA agonists 2 trials)
Outcomes	*Primary:* Effectiveness of PNBs for treating ED primary headaches on reducing pain intensity within 120min (reported on VAS, NRS or similar pain scale). *Secondary:* Pain intensity between 2-72hrs, adverse events, headache relapse resulting in ED revisit or clinic within 72hrs.

Key Results

11 studies, 860 patients (67% women). Eight studies conducted in ED setting. Lidocaine 10-80mg used in 5 studies, bupivacaine 3-80mg in 3 studies. SGB delivered by intranasal drops (5 studies) or Tx360 device (2 studies)

All time intervals favoured PNB vs control:
1 min (2 studies): SMD -1.33 (-2.56 to -0.09); I^2= 41%
2 min (2 studies): SMD -0.51 (-1.86 to 0.85); I^2=78%
5 min (5 studies): SMD -1.07 (-1.79 to -0.35); I^2=46%
15min* (7 studies): SMD -1.17 (-1.82 to 0.51); I^2=49%, p=0.0005
30min* (5 studies): SMD -0.99 (-1.66 to -0.32); I^2=36%, p=0.04
*****Most clinically important time points (survey 10 academic EM physicians)***

No change in outcomes after sensitivity analyses after excluding highly biased & out-patient clinic studies.

Most adverse events (6 studies) were minor (burning/numbness sensation, dizziness, injection site pain).

Need for rescue meds – see Appendix

ED Revisits (2 studies): See Appendix

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	?	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	X

A1 = S. Upadhye A2 = E. Lang

Funding and conflicts of interest

Funding	None (reported)
Conflict of interest	None (reported)

Potential threats to viability

Chance	A small number of studies (and included patients) may have resulted in a Type II error (failure to detect a real treatment difference), as suggested by the 95%CI crossing the MCID threshold.
Selection bias	Thorough validated independent searches/retrievals. No comment on publication bias analysis.
Measurement bias	*Missing details on study selection; missing results of quality assessments.* Majority of studies were of low (4)/to moderate certainty and at low (4) risk of bias (using Cochrane Risk of Bias tool). GRADE certainty of evidence = Moderate. Blinding is a challenge based on different delivery modalities, or local responses to injected solutions.
Analysis bias	*Fixed vs. random effects, combined results of studies of different design.* Varying levels of heterogeneity in outcomes analyzed by random effects models. Most individual pain scale pooled estimates were <1.5 point change on 10pt scale (MCID), the CI's did surpass this threshold of possible clinically significant improvements.
Confounding	Heterogeneity in time points measured in included studies, dosing of lidocaine vs. bupivacaine, and pooling of GON and SGB blocks. Minimal reporting of TPI outcomes. Difficult to blind patients in individual studies.

Administrative details

Key words	Emergency department, primary headache, peripheral nerve block
Appraisers	S. Upadhye; E. Lang.
Reference(s)	https://www.youtube.com/watch?v=6Dj5zYbvLxo

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Eddy Lang, MD CCFP(EM)
Professor and Department Head
Cumming School of Medicine, University of Calgary
Alberta Health Services
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the utility of IM ketamine in rapid control of acutely agitated ED patients?

BEEM Bottom Line

Why is this study important? The need for rapid-acting and safe agents for acutely agitated ED patients is important, and benzodiazepines (Bzds) and antipsychotics (APs) have concerning side-effects. Ketamine is a potentially fast-acting and safe alternative for agitated/violent patients.

What, if any, threats to validity are most likely to have an impact on the results and how? This trial was prematurely terminated due to the COVID pandemic, and missed target sample size enrollment by 57%, which introduces significant uncertainty in the results presented due to uncertainty (risk of Type I error?).

How do the key results compare with the current evidence? The results are congruent with prior small studies supporting the use of IM ketamine for rapid agitation control.

How should this study impact the care of ED patients? This study supports growing evidence on the utility and safety of IM ketamine as an ED agitation control agent. Larger trials are needed to confirm benefits and safety profiles.

Study Summary

Article	Barbic D, Andolfatto G, Grunau B, Scheuermeyer FX, Macewan B, Qian H, Wong H, Barbic SP, Honer WG. Rapid Agitation Control With Ketamine in the Emergency Department: A Blinded, Randomized Controlled Trial. Annals Emerg Med 2021; 78(6):788-795. doi: 10.1016/j.annemergmed.2021.05.023.
Design	Prospective RCT (ClinicalTrials.gov: NCT03375671); protocol previously published
Population	*Included:* Adults (19-60yo) with severe psychomotor agitation (Richmond Agitation Score RASS $\geq$ +3). *Excluded:* Previously enrolled, police custody, pregnant/breast-feeding, known allergy, intolerance or hyper-sensitivity, other specific comorbidities (Appendix E1 Box 1)
Intervention	Ketamine (Ket) IM 5mg/kg, max 4ml of 50mg/kg at a single site)
Comparison	Midazolam 5mg + Haloperidol 5mg IM (MidHal) at a single site
Outcomes	*Primary:* Time to adequate sedation, defined as RASS $\leq$ -1 (assessed by blinded research staff q5min up to 30min) *Secondary:* Need for rescue meds (Bzds, APs, other sedatives) at ED MD discretion (every 5min up to 30min), adverse effects (predefined), occurrence of neuroleptic malignant syndrome (NMS) within 72hrs (via chart review & telephone f/u).
Key Results	Total 80 patients enrolled: 68% men, median age 35yo, 73% arrived via EMS. More men in Ket arm (M 85% vs F 50%), and higher RASS scores +4. Primary (Sedation time): Ket 5.8min vs MidHal 14.7min (Diff 8.8min, 95% CI 3-14.5); greater sedation with Ket at each 5min time interval (Fig 2). Secondary: Similar rescue meds needed (Ket 13%, MidHal 15%). Adverse events not significantly different (Ket 12.5% vs MinHal 5%, Diff 7.5% [95%CI -4.8% to 19.8%]). One Ket pt had temporary laryngospasm requiring airway positioning/supp oxygen; no intubations/ICU admissions needed. No data on ED LOS provided.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	X	X
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	✓	?
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	?	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	X
10. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = E. Lang

Funding and conflicts of interest

Funding	Peer-reviewed funding from Vancouver Coastal Health & Providence Health Care Research Institute, and Cdn Assoc Emerg Phys (CAEP). Sponsor had no roles in study design, conduct, analysis, nor results interpretation.
Conflict of interest	None (reported)

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Single site Cdn academic ED (Vancouver BC). Sample size needed total 184pts (92 each arm); enrolled total 80 (stopped early due to COVID pandemic spring 2020) and 2 were LTFU in Ket arm.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Convenience based on availability of research staff (0800-midnight daily). Block randomization (2, 4,6,8 pts/block). Groups were imbalanced by gender, RASS score before early termination; bias (risk of Type I error?).
Measurement bias	Opaque sealed envelopes to mask group allocation; only unblinded ED nurse opened the envelope and administered study meds (not involved with outcomes assessments nor results interpretation).
Analysis bias	ITT analysis planned.
Confounding	As above.

Administrative details

Key words	Ketamine, haloperidol, midazolam, rapid agitation
Appraisers	S. Upadhye; E Lang.
Reference(s)	https://pubmed.ncbi.nlm.nih.gov/34823192/

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Eddy Lang
Professor and Department Head
Cumming School of Medicine, University of Calgary
Alberta Health Services
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Do people who wake up with new acute stroke symptoms benefit from treatments to reopen the blocked blood vessels (recanalization therapies)?

BEEM Bottom Line

Why is this study important? Approximately 1 in 5 patients wake up with stroke symptoms, and are historically excluded from time-dependent reperfusion trials. Providing reperfusion Rx to "wake-up" stroke patients may be useful for subsequent morbidity/mortality.

What, if any, threats to validity are most likely to have an impact on the results and how? Nearly all of the included trials (6/7) were prematurely terminated for a variety of reasons, which is a threat to final conclusions of treatment efficacy/safety.

How do the key results compare with the current evidence? There is congruence of this review with recent studies/ reviews on this under-studied topic, but those reviews also include studies analyzed here.

How should this study impact the care of ED patients? For patients presenting to ED with wake-up stroke and relevant imaging findings, it may be appropriate to initiate "acute stroke" protocols to facilitate reperfusion therapies (especially those using mechanical endovascular thrombectomy).

Study Summary

Article	Roaldsen MB, Lindekleiv H, Mathiesen EB. Intravenous thrombolytic treatment and endovascular thrombectomy for ischaemic wake-up stroke. Cochrane Database of Systematic Reviews 2021, Issue 12. Art. No.: CD010995. DOI: 10.1002/14651858.CD010995.pub3.
Design	Systematic review of randomized controlled trials.
Population	*Included:* Patients with acute wake-up stroke symptoms and appropriate imaging changes, within 6-24hrs of last seen/known well. *Excluded:* Not specified in review Methods; some included trials described exclusions.
Intervention	IV thrombolytics or mechanical endovascular recanalization
Comparison	Standard medical management
Outcomes	*Primary:* Functional outcome at the end of the follow-up period. Favourable functional outcome was defined as a modified Rankin scale (mRS) score of 0 to 2. *Secondary:* All-cause death and neurologic status (7-14d), symptomatic ICH, quality of life at end of follow-up.
Key Results Seven studies included (5 IV thrombolytics, 2 mechanical thrombectomy), 980 patients.	***Primary*: Benefit for IV lytics** (66%) vs control (50%); RR 1.13 (1.01-1.26; 5 studies, 763pts), p=0.03, high certainty of evidence **Benefit for mech thromb** (46%) vs control (9%); RR 5.12 (2.57-10.17; 2 studies, 205pts), p<0.001, high certainty of evidence No difference noted on planned subgroup analyses: age, gender, stroke severity, large vessel occlusion on imaging, time from first observed symptoms to treatment; no difference on use of random effects analysis. ***Secondary*:** All-cause death (end of 90d follow-up) – **Benefit for IV lytics** (7%) vs control (10%); RR 0.68 (0.43-1.07); 763 pts, p=0.09, high certainty of evidence. **Benefit for mech thromb** (22%) vs control (33%); RR 0.68 (0.43-1.07); 205pts, p=0.10, high certainty of evidence Symptomatic ICH (745pts) – IV lytics (3%) vs control (1%): RR 3.47 (0.98-12.26); p=0.05, high certainty of evidence All-cause death 7-14d, neuro status 7-14d or end of follow-up, quality of life – no data available

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	✓	✓
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	✓	✓

A1 = S. Upadhye A2 = K. Lin

Funding and conflicts of interest

Funding	None (reported)
Conflict of interest	Two authors are currently involved in the TWIST (Tenecteplase in Wake-Up Ischemic Stroke Trial) study.

Potential threats to viability

Chance	Study participants may not represent all those with wake-up stroke; included patients had to meet specific imaging criteria involving advanced neuroimaging (CTP/MRI).
Selection bias	Thorough search and assessments. No funnel plot for publication bias (too few included studies).
Measurement bias	Independent quality assessments using GRADE (summary tables presented). All included studies measured primary outcome to 90days.
Analysis bias	All outcomes calculated using fixed effects analyses; no difference noted with random effects analysis. Heterogeneity low (0%) for most outcomes analyzed.
Confounding	Majority of trials (6/7) were terminated early for various reasons. Two trials terminated for showing efficacy at interim analysis.

Administrative details

Key words	Intravenous thrombolysis, endovascular thrombectomy, wake-up stroke
Appraisers	S. Upadhye, K. Lin
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Katie Lin, MD MPH FRCPC
Asst. Professor, Emergency Medicine/Stroke Medicine
University of Calgary
No conflicts of interest

Research Question

What is the utility of the Canadian TIA Score (compared to ABCD2 or ABCD2i) to predict subsequent stroke?

BEEM Bottom Line

Why is this study important? Accurate risk-stratification of ED TIA patients as Low vs. High risk allows for appropriate disposition decisions. This study compares the discriminative abilitiy of the Canadian TIA Score with the ABCD2/ABCD2i scores.

Which, if any, threats to validity are most likely to have an impact on the results and how? None.

How do the key results compare with the current evidence? These results build on prior work that assesses ED physician stroke risk tolerances, and the accuracy of prior risk stratification tools to guide ED disposition decisions.

How should this study impact the care of ED patients? The Canadian TIA Score is more discriminating than prior tools to risk-stratify ED TIA patients for short-term stroke risk, and can be used to make appropriate resource-optimizing decisions.

Study Summary

Article	Perry JJ, Sivilotti MLA, Emond M, *et al*. Prospective validation of Canadian TIA Score and comparison with ABCD2 and ABCD2i for subsequent stroke risk after transient ischemic attack: a multicentre prospective cohort study. BMJ 2021; 372:n49. http://dx.doi.org/10.1136/bmj.n49
Design	Prospective cohort study to implement/validate the Canadian TIA Score.
Population	*Included:* Adults ≥ 18yrs with an ED discharge Dx of TIA or minor stroke. *Excluded*: Neuro deficits >24hrs, decreased LOC (GCS <15 in previously normal patients), alternative neuro Dx (eg. migraines, seizure, hypoglycemia, electrolyte imbalance), ED presentation >7 days after onset of symptoms, or reperfusion (tPA, embolectomy) for acute ED stroke.
Predictors	Canadian TIA Score.
Comparison	ABCD2 and ABCD2i score variables.
Outcomes	*Primary:* Stroke or carotid endarterectomy/stenting with 7days of ED TIA visit. Total 182 outcome events (1.4% strokes, 1.1% carotid intervention). *Secondary:* Stroke with 7days of ED TIA visit (with/without carotid endarterectomy or stenting).

Key Results

N = 7607 pts consecutively enrolled via ED over 5yrs. Mean age 68.5yrs, 52.3% female; 75% first reported TIA. 96.5% had CT head and 91% ECG during ED visit. Majority of discharged patients continued/started on ASA, clopidogrel, or both in ED. Predefined risk thresholds for primary outcome: Low = <1%, Med = 1-5%, High>5%.

Cdn Risk Score	Low Risk (-3 to 3) Med Risk (4-8) High Risk (≥9)	Interval LR 0.20 (0.09-0.44) 0.94 (0.85-1.04) 2.56 (2.02-3.25)	Est. Risk 0.7% 2.1% 6.3%	Observed Risk 0.5% 2.3% 6.3%
ABCD2 /ABCD 2i	Low risk = 0 Med Risk = 3-97% High Risk = 3-7%	Neither score correctly correctly classified any patients as Low risk.		
	Cdn TIA Score ABCD2 ABCD2i	AUC 0.70 (0.66-0.73) AUC 0.60 (0.56-0.64) AUC 0.64 (0.59-0.68)	Cdn TIA Score able to correctly risk-stratify TIA patients for stroke risk compared to ABCD2/I scores.	Absolute net reclassification index between Cdn TIA Score and ABCD2i = 8.5%.

CI = confidence interval; *N* = number of patients; N/A = not applicable; NSS = not statistically significant; *p* = probability; OR = odds ratio (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those with the problem.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	✓	✓
3. All patients underwent the same clinical evaluation.	✓	✓
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	✓	✓
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	✓	✓
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	✓	✓
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓	✓
8. All patient-important outcomes were considered.	✓	✓
9. The follow-up was complete.	✓	✓
10. The point estimates and respective precisions are clinically significant.	✓	✓

A1 = S. Upadhye A2 = K. Lin

Funding and conflicts of interest

Funding CIHR grant.

Conflict of interest Two authors supported by public grants (JJ, JL); otherwise no coi declared.

Potential threats to validity

Chance Study nurses reviewed all ED visits to identify potential/missed patients.

Selection bias Consecutive sampling over 5yrs at 13 Cdn Eds (10 university hospitals, 3 community); no time limitations. 80.6% of all screened patients were enrolled; patients not enrolled were demographically similar to enrollees, but more frequently admitted [18.4% vs 5.8%]). Only 34 patients (0.4%) were lost to 7d follow-up.

Measurement bias All ED physicians formally trained and applied the data collection forms for all 3 scores compared. Telephone follow-up of patients at 7 and 90days, using validated Questionnaire for Verifying Stroke Free Status tool. May have missed patients who received vascular intervention at greater than 7 days from index visit (many guidelines recommend intervention within the first 14 days following index event).

Analysis bias All outcomes adjudicated by site committees (neurologists, ED physician) blinded to index ED visit management.

Confounding None

Administrative details

Key words Canadian TIA Score, carotid endarterectomy/stenting, stroke

Appraisers Upadhye S; Lin K.

Reference(s) Perry JJ, Sivilotti MLA, Emond M, Stiell IG, Stotts G, Lee J, Worster A, Morris J, Cheung KW, Jin AY, Oczkowski WJ, Sahlas DJ, Murray HE, Mackey A, Verreault S, Camden MC, Yip S, Teal P, Gladstone DJ, Boulos MI, Chagnon N, Shouldice E, Atzema C, Slaoui T, Teitlebaum J, Abduzlaziz K, Nemnom MJ, Wells GA, Sharma M. Prospective validation of Canadian TIA Score and comparison with ABCD2 and ABCD2i for subsequent stroke risk after transient ischemic attack: a multicentre prospective cohort study. BMJ 2021; 372:n49. http://dx.doi.org/10.1136/bmj.n49

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Katie Lin, MD MPH FRCPC
Assistant Professor, Emergency Medicine/Stroke Medicine
University of Calgary
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the most effective/safe agent for use in acutely agitated ED patients?

BEEM Bottom Line

Why is this study important? It is important to achieve reduction of agitation without risk of deep sedation/respiratory depression/hypoxemia in ED agitated patients. This study compares 3 common medications used (at 4 different doses).

Which, if any, threats to validity are most likely to have an impact on the results and how? This trial was originally conducted in 2005, but is only being published now. Majority of agitated patients were intoxicated with alcohol, so it may be difficult to generalize these results to other contemporary "agitators" (eg. Bath salts, methamphetamines, etc.).

How do the key results compare with the current evidence? The results are congruent with recent trials examining similar comparisons (listed in Table 5).

How should this study impact the care of ED patients? Use of droperidol is effective and safe in reducing acute agitation in the ED, with less risk of deep sedation/respiratory depression/hypoxemic events.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article:	Martel ML, Driver BE, Miner JR, *et al*. Randomized Double-Blind Trial of Intramuscular Droperidol, Ziprasidone and Lorazepam for Acute Undifferentiated Agitation in the Emergency Department. Acad Emerg Med 2021; 28: 421-434. doi: 10.1111/acem.14124 PMID: 32888340
Design:	4 arm parallel RCT.
Population:	*Included:* Adult patients with acute undifferentiated agitation in ED. Consent exemption approved under REB review. *Excluded*: Police custody, pregnant/breast-feeding, previously enrolled in study, or documented allergy to any of the study medications.
Intervention:	4 different arms: Droperidol 5mg, Ziprasidone 10 & 20mg, and lorazepam 2mg. All doses given intra-muscularly.
Comparison:	Inter-arm comparisons above
Outcomes:	*Primary:* proportion of patients adequately sedated at 15min (defined as Altered Mental Status Scale [AMSS] score of ≤ 0 [range -4 to +4]). Cross-correlated with BARS scores (Behavioural Activity Rating Scale). *Secondary:* Need for additional rescue sedation, ED LOS, respiratory depressions events (SpO_2 <90, requiring supplemental oxygen, or ETCO2>15mm).

Key Results

N = 115 patients. **Chloe/Dena to help with ARR/NNT calculations for comparisons?

Sig.	*Outcome*	*Intervention*	*Control*	*ARR (95% CI)*	*NNT (95% CI)*
NSS		Events/n	Events/n		State "Not estimable" if CI includes harm
SS					Always round up so whole numbers only.

ARR = absolute risk reduction (if the CI includes the value 0, there is no difference in risk between the groups and the NNT is not estimable); CI = confidence interval; *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The patients were recruited consecutively.	✓	X	?
2. The patients were adequately randomized (allocation sequence adequately generated).	?	?✓X	?✓X
3. The allocation sequence was adequately concealed.	?	?✓X	?✓X
4. The patients in all groups were similar with respect to prognostic factors.	✓	?✓X	?✓X
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	?	?✓X	?✓X
6. All groups were treated equally except for the intervention.	✓	?✓X	?✓X
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	?✓X	?✓X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	?✓X	?✓X
9. All patient-important outcomes were considered.	✓	?✓X	?✓X
10. The effect size of the primary outcome is clinically significant.	✓	?✓X	?✓X

A = appraiser ITT = intention to treat.

Funding and conflicts of interest

Funding	Unknown?
Conflict of interest	None (reported).

Potential threats to validity

Chance	None or enter text here. Type I & II errors?
Selection bias	None or enter text here. Is the sampling method representative of the target population; are the groups balanced? Convenience sampling used (risk of bias from missing other eligible patients during non-sampling times). No details on randomization process, nor allocation concealment. 149 patients, 34 rejected for unknown reasons (selection bias?). Patients balanced on baseline demographic factors (Table 2).
Measurement bias	None? What is the MCID for the AMSS scale? Respiratory depression differences driven by change in ETCO2 measurements; no differences in hypoxia rates in 4 arms.
Analysis bias	None or enter text here. ITT, Per Protocol, As Treated. All patients analyzed in their assigned groups. Paired comparisons reported.
Confounding	None or enter text here. Independent factors affecting the outcome; clinicians to comment. Majority of patients in each arm equally agitated with alcohol intoxication (approx. 80%).

Administrative details

Key words	Acute ED agitation, droperidol, lorazepam, ziprasidone
Appraisers	Upadhye S,
Reference(s)	Martel ML, Driver BE, Miner JR, Biros MH, Cole JB. Randomized Double-Blind Trial of Intramuscular Droperidol, Ziprasidone and Lorazepam for Acute Undifferentiated Agitation in the Emergency Department. Acad Emerg Med 2021; 28: 421-434. doi: 10.1111/acem.14124

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the effectiveness of dimenhydrinate vs metoclopramide in treating ED vertigo/nausea?

BEEM Bottom Line

Why is this study important? Vertigo (ED incidence 3.3%) can be associated with intense nausea, and needs effective treatment in the ED. Both dimenhydrinate (DMH) and metoclopramide (MCP) are common anti-nauseants in ED care.

Which, if any, threats to validity are most likely to have an impact on the results and how? This study was designed based on superiority of DMH vs MCP, yet reported equivalence based on failed superiority; one cannot claim equivalence/non-inferiority based on failed superiority. The patient sampling strategy is not reported, which may have introduced an element of selection bias. Finally, the minimal clinical important difference (MCID) on a the VAS measurements is inconsistently reported.

How do the key results compare with the current evidence? Both agents are helpful for reducing vertigo/nausea intensity as monotherapy, consistent with prior trials cited.

How should this study impact the care of ED patients? Either DMH or MCP can be effective IV monotherapy for treating ED acute vertigo/nausea within 30min.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article Ercin D, Erdur B, Turkcuer I, *et al*. Comparison of efficacy dimenhydrinate and metoclopramide in the treatment of nausea due to vertigo: a randomized study. Am J Emerg Med 2021; 40: 77-82. https://doi.org/10.1016/j.ajem.2020.12.010

Design Single center prospective DB-RCT

Population *Included:* Adults (≥ 18 and ≤ 65 years) with an ED Dx of vertigo/motion sickness.
Excluded: Consent refused, hypersensitivity/other CI for either agent, pregnant/breast-feeding, suspected/proven GI bleed, bowel obstruction/perforation, prior Hx psychiatric/neurologic disorder, renal failure, or mild nausea from vertigo (<4cm on VAS).

Intervention Dimenhydrinate (DMH) 50mg in 150ml NS solution, infused over 15min.

Comparison Metoclopramide (MCP) 10mg in 150ml NS solution, infused over 15min.

Outcomes *Primary:* Reduction of vertigo intensity at 30min (on VAS 1-10 scale).
Secondary: Reduction in nausea intensity on VAS, and change in 30min VAS scores for vertigo & nausea.

Key Results *N* = 200 patients (100 per group, needed 88/group as per sample size calculation). 72% female, mean age 31yo.

Sig.	*Outcome*
NSS	Vertigo intensity at 30min: No SS difference (both dropped approx. 5pts on 10pt VAS) Nausea intensity at 30min: No SS difference (both dropped approx. 5pts on 10pt VAS) Adverse effects at 30min: No SS difference
SS	Drop in systolic BP with both meds over 30min; not symptomatic, no Rx needed

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The patients were recruited consecutively.	?	X	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	?✓X	?✓X
3. The allocation sequence was adequately concealed.	✓	?✓X	?✓X
4. The patients in all groups were similar with respect to prognostic factors.	✓	?✓X	?✓X
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	?✓X	?✓X
6. All groups were treated equally except for the intervention.	✓	?✓X	?✓X
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	?✓X	?✓X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	?✓X	?✓X
9. All patient-important outcomes were considered.	✓	?✓X	?✓X
10. The effect size of the primary outcome is clinically significant.	X	?✓X	?✓X

A1 = S. Upadhye A2 = A3 = ITT = intention to treat.

Funding and conflicts of interest

Funding	Research supported by Pamukkale University Faculty of Medicine Research Fund, grant number (2012TPF034).
Conflict of interest	None (declared).

Potential threats to validity

Chance	None? Sample size calculation for superiority design met/exceeded.
Selection bias	The patient sampling/recruiting strategy (eg. Convenience, consecutive, etc.) is not reported.
Measurement bias	Use of 1-10 VAS scales; MCID (meaningful clinically important difference) had been previously defined in an another vertigo study (not same authors?), but later contradicted in limitations discussion?
Analysis bias	ITT.
Confounding	In addition to study meds, patients were treated with Epley maneuver, betahistine or piracetam tabs (co-interventions not reported). Patients also received a rescue dose of diazepam 5m for insufficient vertigo relief, or 5mg granisetron for insufficient nausea relief.

Administrative details

Key words	Dimenhydrinate, emergency department, metoclopramide, nausea, vertigo.
Appraisers	Upadhye S,
Reference(s)	Ercin D, Erdur B, Turkcuer I, Seyit M, Ozen M, Yilmaz A, Ercins DOZ. Comparison of efficacy dimenhydrinate and metoclopramide in the treatment of nausea due to vertigo: a randomized study. Am J Emerg Med 2021; 40: 77-82. https://doi.org/10.1016/j.ajem.2020.12.010

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the effectiveness of dimenhydrinate (DMH) + metoclopramide (MCP) in the treatment of ED acute posttraumatic headache?

BEEM Bottom Line

Why is this study important? Acute posttraumatic headaches can be common and debilitating after traumatic head injury. Effective treatment of such in the ED can have immediate and sustained benefits.

Which, if any, threats to validity are most likely to have an impact on the results and how? Comparing active treatments to placebos (as opposed to standard therapies) generally with favour the active therapy (over-inflated benefit?).

How do the key results compare with the current evidence? The results are congruent with prior cited trial evidence for similar headache syndromes.

How should this study impact the care of ED patients? Combination DMH+MCP may be useful for short-term relief of acute posttraumatic headache intensity, but less so for other sustained post-concussive symptoms.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Friedman BW, Irizarry E, Cain D, Caradonna A, Minen MT, Solorzano C, Zias E, Zybert D, McGregor M, Bijur PE, Gallagher EJ. Randomized Study of Metoclopramide Plus Diphenhydramine for Acute Posttraumatic Headache. Neurol 2021; 96; e2323-22331. doi:10.1212/WNL.0000000000011822
Design	Multi-site DB-RCT.
Population	*Included:* Adults (≥ 18) meeting Int Classification of Headache Disorders criteria for acute posttraumatic headache. Moderate/severe intensity. *Excluded*: Headache >10days elapsed since initial injury, already treated with antidopaminergic meds, study meds allergies/other Cis, or pregnancy. Pre-trauma headache syndrome with similar headache features.
Intervention	DMH 25mg + MCP 20mg IV over 15min.
Comparison	Placebo (normal saline IV over 15min).
Outcomes	*Primary:* Headache intensity on VAS 0-10 scale at baseline and 1hr. *Secondary:* Headache intensity on IHS ordinal scale (4pts) at 0, 1, 2 & 48hrs. Patient satisfaction with ED care, willingness to repeat same Tx, and headache symptoms up to 7d post-ED visit. Patients also asked to rate Post Concussion Symptom Scale (PCSS) scores with RA coaching (22 items, 0-6 Likert scales) at 48hrs & 7days.

Key Results

N = 160 patients. Needed 144 based on sample size calculations. 81pts in Rx arm, 79 in placebo.

****Chloe/Dena to help with specific calculations**

Sig.	*Outcome*	*Intervention*	*Control*	*ARR (95% CI)*	*NNT (95% CI)*
NSS	Secondary (No Difference in post-ED outcomes)	Events/n	Events/n		State "Not estimable" if CI includes harm
SS	Primary (Mean Diff 1.4 [95%CI 0.7-2.2])				Always round up so whole numbers only.

No significant differences in non-study analgesics used pre/intra/post ED visit (Table 3)

Mean PCSS score different in ED at 1hr (Mean Diff 9 [95%CI 3-15], p<0.01) but not different at 1 week (Mean Diff 7, [0-15], p=0.06)

Adverse effects higher in Int arm (43%) vs placebo (28%); Diff 15% (1-30), p=0.04. None were serious or unexpected, or required extra Rx.

Most patients did not know what arm they were allocated to (approx. 50% each).

No difference in willingness to repeat same medication treatment.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The patients were recruited consecutively.	?	X	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	?✓X	?✓X
3. The allocation sequence was adequately concealed.	✓	?✓X	?✓X
4. The patients in all groups were similar with respect to prognostic factors.	✓	?✓X	?✓X
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	?✓X	?✓X
6. All groups were treated equally except for the intervention.	✓	?✓X	?✓X
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	?✓X	?✓X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	?✓X	?✓X
9. All patient-important outcomes were considered.	✓	?✓X	?✓X
10. The effect size of the primary outcome is clinically significant.	?	?✓X	?✓X

A1 = S. Upadhye A2 = A3 = ITT = intention to treat.

Funding and conflicts of interest

Funding	Publication was supported in part by the Harold and Muriel Block Institute for Clinical and Translational Research at Einstein and Montefiore grant support (UL1TR001073).
Conflict of interest	None (declared).

Potential threats to validity

Chance	None?
Selection bias	None. Sampling strategy (consecutive, convenience, etc.) not clearly reported. Study conducted in a urban socioeconomically depressed area, which could influence post-ED headache outcomes/limit generalizability.
Measurement bias	None. Use of mixed VAS, ordinal and other Likert scales. Unclear of MCID determinations for different scales used. Unknown if various previously published scales have been validated for ED use/reliability.
Analysis bias	ITT.
Confounding	DMH may have some anticholinergic effects that can be confused with postconcussive symptoms. IV placebo effects likely higher than oral.

Administrative details

Key words	Acute posttraumatic headache, dimenhydrinate, metoclopramide, post-concussive.
Appraisers	Upadhye S,
Reference(s)	Friedman BW, Irizarry E, Cain D, Caradonna A, Minen MT, Solorzano C, Zias E, Zybert D, McGregor M, Bijur PE, Gallagher EJ. Randomized Study of Metoclopramide Plus Diphenhydramine for Acute Posttraumatic Headache. Neurol 2021; 96; e2323-22331. doi:10.1212/WNL.0000000000011822

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

How useful is the HINTS exam to rule out stroke in ED patients with acute vestibular syndrome (AVS)?

BEEM Bottom Line

Why is this study important? Determining which ED patients with acute vertigo/vestibular syndromes may have central causes (ie. stroke) is very important to avoid critical misses. The HINTS exam has been proposed as a test with good discriminative value for central vs. peripheral vertigo.

Which, if any, threats to validity are most likely to have an impact on the results and how? Overall, the review and meta-analysis was conducted without bias, however it is likely that the spectrum and detection bias in the included studies has lead to an inflated estimate of diagnostic accuracy. Only one included study incorporated the HINTS exam performance by ED physicians (with neurology/vascular fellowship training), and even with such advanced credentialling, the HINTS exam did not perform with sufficient accuracy to include/exclude central stroke.

How do the key results compare with the current evidence? There is a lack of evidence supporting the use of HINTS exam by ED physicians.

How should this study impact the care of ED patients? The HINTS exam is insufficient to rule in/out central stroke in ED AVS patients.

Study Summary

Article	Ohle R, Montpellier RA, Marchadier V, *et al*. Can Emergency Physicians Accurately Rule Out a Central Cause of Vertigo Using the HINTS Examination? A Systematic Review and Meta-analysis. Acad Emerg Med 2020; 27: 887-896. doi: 10.1111/acem.13960
Design	State true design not what the investigators call it. Systematic review and meta-analysis of
Population	*Included:* Adult patients with acute vestibular syndrome/vertigo. *Excluded*: Not reported.
Index Test	HINTS exam.
Reference Test	CT or MRI imaging.
Diagnosis of Interest	Central cause of vertigo (ie. stroke).

Key Results

N = 617 patients in 5 studies. Prevalence of stroke in ED AVS patients: 9.3-44%

N/Studies	*Measure (95% CI)*	I^2
	Neurologists/Neuro-ophthalmologists only (4 studies)	0
	LR+ = 16-63.9	
	LR– = 0.01-0.38	
	Sensitivity = 96.7 (93.1-98.5)	
	Specificity = 94.8 (91-97.1)	
	ED physicians with vascular/neurology fellowship training (1 study)	N/A
	Sensitivity = 83.3 (63.1-93.6)	
	Specificity = 43.8 (36.7-51.2)	
	LR+ = 1.48, LR- = 0.007	

AUC = area under the curve; CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); *N* = number of patients; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	X	X
8. The methods used to combine the included primary studies were reported and valid.	?	✓
9. The outcomes are clinically relevant.	?	n/a
10. The statistical heterogeneity of the primary outcome is low (< 25%).	✓	✓

A1 = S. Upadhye A2 = C. Bedard

QUADAS = quality assessment of diagnostic accuracy studies; ROC = receiver operating characteristic curve.

Funding and conflicts of interest

Funding None (not reported).

Conflict of interest None (reported).

Potential threats to validity

Chance The meta-analysis overall appears to have narrow confidence intervals but there is insufficient data to address their objective to compare the diagnostic accuracy between emergency physicians and neurologists/neurootologists. The individual studies included in the review did not report study sampling strategies and many were suspected at risk of spectrum bias.

Selection bias Comprehensive unlimited searches limit the risk of missing relevant studies, though there are too few studies found to statistically determine the probability of publication bias.

Measurement bias Risk of bias assessment was reliable. However, the overall risk of bias for included studies was high.

Analysis bias The meta-analysis had low risk of bias; however, possible detection bias was present in many included studies, in addition to suspected spectrum bias, this likely lead to inflated sensitivity and specificity.

Confounding It is likely that the above stated spectrum and detection bias lead to an inflated estimate of diagnostic accuracy.

Administrative details

Key words Acute vestibular syndrome, HINTS exam, stroke

Appraisers Upadhye S, Bedard C.

Reference(s) Ohle R, Montpellier RA, Marchadier V, Wharton A, McIsaac S, Anderson M, Savage D. Can Emergency Physicians Accurately Rule Out a Central Cause of Vertigo Using the HINTS Examination? A Systematic Review and Meta-analysis. Acad Emerg Med 2020; 27: 887-896. doi: 10.1111/acem.13960

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Chloe Bedard, PhD
Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

PEDIATRICS

Research Question

What is the optimal fluid resuscitation strategy for pediatric diabetic ketoacidosis?

BEEM Bottom Line

Why is this study important? DKA is a common manifestation of pediatric diabetes mellitus (15-67%), and cerebral edema is a rare (<1%) leading cause of DKA mortality (21-24%). Historically, fluid resuscitation was limited as it was thought to precipitate cerebral edema. However, this is now being challenged.

What, if any, threats to validity are most likely to have an impact on the results and how? Small numbers of included studies (and DKA events) with no demonstrated differences may present a potential type II error (false confirmation of null hypothesis).

How do the key results compare with the current evidence? There is a paucity of recent trial evidence showing no difference in fluid resuscitation strategies based on fluid composition and rates. This SRMA includes such evidence.

How should this study impact the care of ED patients? Local practice patterns are changing to include more liberal fluid resuscitation. ED physicians should collaborate with their pediatric partners to develop care pathways to optimize DKA IV fluid resuscitation practices.

Study Summary

Article	Hamud AA, Mudawi K, Shamekh A, Kadri A, Powell C, Abdelgadir I. Diabetic ketoacidosis fluid management in children: systematic review and meta-analyses. Arch Dis Child. 2022 Jun 23:archdischild-2022-324042. doi: 10.1136/archdischild-2022-324042.
Design	Systematic review with meta-analysis
Population	***Included:*** Patients <18yo with DKA (RCTs only). ***Excluded:*** Non-randomized studies.
Intervention	Liberal fluid resuscitation with intravenous fluids (IVF); 20-500cc/kg boluses to rapidly replace assumed fluid deficits (10% body weight) within 12-24hrs
Comparison	Conservative fluid resuscitation; 10-500cc/kg replaced over 48hrs, based on 5% body weight fluid deficits
Outcomes	***Primary:*** Time to recovery from DKA. ***Secondary:*** Frequency of PICU admissions, incidence of cerebral edema/AKI, all-cause mortality. Subgroups: Risk of bias in included studies, concentrations of NaCl used in fluid resuscitation.
Key Results	**3 RCTs included, 1457 DKA events analyzed.** ***Time to DKA recovery*** *(2 studies, n=1439pts)*; Fig 4: Mean Difference 1.42hrs longer in conservative IVF group (95%CI 0.28-2.56, I^2=98%) ***Cerebral edema incidence*** *(2 studies, 1439pts)*; Fig 3: No difference RR 0.50 (0.15-1.68, I^2=0); no difference with IV fluids (<0.9% saline vs normal saline) ***Reduction in GCS*** *(1 study, n=1361 events)*: No significant difference between fluid strategies RR 0.47 (0.44-1.36, I^2=0); no difference with IV fluids (<0.9% saline vs normal saline) No clinically significant differences in hospital length of stay (regardless of fluid strategy and concentration). No reporting of PICU admissions, AKI incidence or all-cause mortality in included studies. Serious adverse events <3% in both groups: Higher rates of hyperchloremic acidosis & hypocalcemia in liberalized IVF group, similar rates of hypoglycemia & hypokalemia in both groups.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Limited electronic search (5), reference lists. All languages included.**	?	X
3. The search for studies was unbiased and reproducible. **No comments of duplicated searches**	X	X
4. The selection of studies was unbiased and reproducible. **Duplicate independent screening of titles**	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible. **Independent assessments using Cochrane Risk of Bias tool. Use of GRADE to rate overall evidence.**	✓	✓
7. The quality of the primary studies is high. **High risk of bias for blinding of participants, personnel and outcomes assessors. Otherwise all other risk of bias elements low. (Fig 2)**	?	?
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	X

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Reported; no funding.
Conflict of interest	Reported; no conflicts of interest declared.

Potential threats to viability

Chance	There are few included studies, with relatively small total sample size; risk of type II error.
Selection bias	*Limited/incomplete search, publication bias, etc.* Incomplete search of grey literature, abstracts, etc. Planned analysis for publication not done (too few studies included).
Measurement bias	Low GRADE quality of evidence for brain edema outcomes, Very Low for DKA recovery.
Analysis bias	*Fixed vs. random effects, combined results of studies of different design.* Planned random effects for high heterogeneity outcomes. Mixed heterogeneity I^2 values for different outcomes (0-98%).
Confounding	*List as reported.*

Administrative details

Key words	Children, cerebral edema, diabetic ketoacidosis, glasgow coma scale, intravenous fluids, normal saline
Reference(s)	Kuppermann N, Ghetti S, Schunk JE, et al. Clinical trial of fluid infusion rates for pediatric diabetic ketoacidosis. N Engl J Med 2018;378:2275–87.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Rahim Valani, MD, MBA, M Med Ed, LLM *Associate Professor of Medicine, University of Toronto*	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

What is the diagnostic accuracy of ED point-of-care ultrasound for pediatric testicular torsion?

BEEM Bottom Line

Why is this study important? Testicular torsion is an acute time-dependent surgical emergency, requiring rapid diagnosis. ED bedside point-of-care ultrasound (POCUS) can expedite timely diagnosis if performed with high accuracy.

What, if any, threats to validity are most likely to have an impact on the results and how? Limited numbers of studies in Pediatric EM settings, different age groups (varied differential diagnoses), and limited descriptions of US use/provider training limit the generalizability of findings.

How do the key results compare with the current evidence? The pooled results here show high diagnostic accuracy of bedside POCUS scans compared to formal radiologist scans (including a single ED-based study). Larger prospective trials needed to confirm theses findings, with focus on training requirements, scanning protocols and optimal scanning modalities.

How should this study impact the care of ED patients? With proper training and experience, ED physicians should be able to use bedside POCUS to accurately diagnose testicular torsion and expedite timely urological referral.

Study Summary

Article	Mori T, Ihara T, Nomura O. Diagnostic accuracy of point-of-care ultrasound for paediatric testicular torsion: a systematic review and meta-analysis. Emerg Med J. 2022 May 6:emermed-2021-212281. doi: 10.1136/emermed-2021-212281.
Design	Systematic review with meta-analysis; registered CRD42021208684.
Population	***Included:*** Studies with children <19yo visiting hospital with symptoms suggestive of acute scrotum. ***Excluded:*** Case reports/series with <10pts, animal studies, commentaries.
Index Test	Point of care ultrasound (POCUS) by diagnosing physician.
Reference Standard	Formal US by radiologist and/or intraoperative findings during exploratory surgery and/or clinical follow-up.
Diagnoses of Interest	***Primary:*** Diagnostic accuracy of POCUS for testicular torsion. Subgroup *a priori*: accuracy of POCUS by different US providers.
Key Results	**4 studies (n=748pts) included.** 202 true positive, 3 false positive results. 3 studies had POCUS by urologists, 1 study (n=120) by Peds EM physician. ***Pooled Dx test characteristics (Table 3):*** Sensitivity 98.4% (95% CI: 88.5% to 99.8%) **LR+ 34.7 (95% CI: 7.4 to 164.4)** Specificity 97.2% (95% CI: 7.2% to 99.4%) **LR- 0.017 (95% CI: 0.002 to 0.12)** ***Single PED study (Friedman 2019):*** Sens 100.0 (83.1 to 100.0), Spec 99.1 (97.2 to 99.1) LR+ 108.0 (29.6 to 108.0), LR- 0.0 (0.0 to 17.4) Unable to complete subgroup analyses due to limited inclusion of studies.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible. **No comment re: duplicate searches**	?	?
4. The selection of studies was unbiased and reproducible. **Dual independent screening**	✓	✓
5. The data abstraction was unbiased (e.g., conducted **independently by 2 researchers**).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high. **GRADE rating "moderate" for evidence quality.**	?	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	✓	✓
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Reported; no funding for this study.
Conflict of interest	Reported; no conflicts of interest declared.

Potential threats to viability

Chance	N/A.
Selection bias	*Specify comprehensive searches; publication bias?* Use of Deeks funnel plot for assessment of publication bias; could not be assessed (only 4 studies included).
Measurement bias	Quality of evidence assessed using GRADE methods. Most studies had low risk of bias, although 2 had high RoB for patient selection (Fig 3).
Analysis bias	*Fixed/random effects? Heterogeneity mgt?* Clinical heterogeneity discussed, but no statistical heterogeneity presented in forest plots. Summary ROC curve presented in Appendix 2; visually high accuracy, but no AUC value reported.
Confounding	*Enter independent factors affecting the outcome; clinicians to comment.* Operator training, experience and use of probes can affect diagnostic accuracy (as with most POCUS studies).

Administrative details

Key words	Pediatric, point-of-care, testicular torsion, ultrasound
Reference(s)	Friedman N, Pancer Z, Savic R, et al. Accuracy of point-of-care ultrasound by pediatric emergency physicians for testicular torsion. J Pediatr Urol 2019;15:608.e1–608.e6. Sheth KR, Keays M, Grimsby GM, et al. Diagnosing testicular torsion before urological consultation and imaging: validation of the twist score. J Urol 2016;195:1870–6.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Rahim Valani, MD, MBA, M Med Ed, LLM *Associate Professor of Medicine, University of Toronto*	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

What is the efficacy of single vs. 2-dose dexamethasone for mild/moderate asthma exacerbations?

BEEM Bottom Line

Why is this study important? Asthma exacerbation is a common reason for ED visits. Oral steroids are frequently prescribed upon discharge for mild to moderate exacerbations. Dexamethasone is a long-acting steroid, more potent than prednisone and has putative antiemetic effects, which make it an attractive alternative to prednisone. However, the optimal dosing for Dexamethasone is still debated. This single-site study aimed to explore single- vs. double-dosing regimens at 0.6mg/kg/dose.

What, if any, threats to validity are most likely to have an impact on the results and how? There is no difference in treatment effects presented, including the lower boundary of the 95%CI which is necessary to ensure a non-inferiority claim. This was also a single site centre and a non-blinded study.

How do the key results compare with the current evidence? Multiple prior studies support the use of Dexamethasone over prednisone for pediatric asthma, and that a single dose of dexamethasone is non-inferior to a 5day course of Prednisone. This study supports the same.

How should this study impact the care of ED patients? A single dose of Dexamethasone given in the ED for mild/ moderate pediatric asthma is non-inferior to a 2-dose regimen.

Study Summary

Article	Martin M, Penque M, Wrotniak BH, Qiao H, Territo H. Single-Dose Dexamethasone is Not Inferior to 2 Doses in Mild to Moderate Pediatric Asthma Exacerbations in the Emergency Department. Ped Emerg Care 2022; 38(6): e1285-1290. DOI: 10.1097/PEC.0000000000002727
Design	Randomized controlled trial (non-inferiority). Single childrens hospital ED (Buffalo NY)
Population	***Included:*** Children aged 2-20yo with known asthma, and mild/moderate exacerbations (defined by Pediatric Asthma Scores: mild 5-7, moderate 8-11). ***Excluded:*** Severe asthma (PAS>12), oral steroid use prior 2wks, known chronic lung dz (eg. CF), received parenteral steroids, or vomited 2 doses oral steroids in the ED.
Intervention	Dexamethasone 0.6mg/kg (max 16mg) single dose in ED
Comparison	Dex same dose in ED, and script for same dose to be consumed 24hrs later at home.
Outcomes	All patients contacted by phone on day6 post ED discharge by research assistants. ***Clinical:*** Symptom changes & duration, unscheduled medical visits, additional treatments needed, compliance with Rx plan, vomiting/other side effects (appetite, insomnia, mood) ***Social:*** Missed school days
Key Results	**308pts randomized (154 each arm).** No differences between groups based on age, gender, or race. Mean age 7.5yo, females 40%. Mild asthma 64%, moderate 28% (19pts not scored). 81% of Int group pts completed a 2nd Dex dose (94/116). ***No Differences:*** 1) Unplanned return visits: Ctrl 12.1% vs Int 10.3% (OR 0.892, 95%CI 0.377-2.11); 1 admission from Ctrl group, no PICU admissions. Mild asthma returns 13.5%, moderate 7.7%. 2) Days to symptoms resolution: Ctrl 2.4d vs Int 2.5 (OR 0.927, 0.830-1.13). No differences in mild vs moderate pts. 3) Missed any school: Ctrl 47.6% vs Int 48% (OR 1.114, 0.613-2.02) 4) Vomiting post ED DC: Ctrl 8.6% vs Int 3.4% (OR 2.42, 0.637-9.23) 5) Any adverse effects: Ctrl 14.7% vs 15.5%

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively. **Convenience sampling; Research Assistants available 8am-11pm, 7days**	X	X
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed. **Impractical with take home script**	X	X
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Research assistants not blinded.**	?	X
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up). **LTFU 18%**	X	X
8. The patients were analyzed in the groups to which they were randomized (ITT).	X	X
9. All patient-important outcomes were considered.	?	?
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Reported; not funded
Conflict of interest	Reported; no conflicts of interest declared

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Sample size calculated based on non-inferiority limit of 11% and presumed 12% ED return rate; 216pts needed (108 per arm).
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Yes. Many patients given prednisone prior to enrollment (as per hospital ED protocol), so couldn't be recruited to this study.
Measurement bias	Lost to followup about 18% in each group; sample size requirements still satisfied. **There is not treatment <u>difference</u> presented between 2 groups for all outcomes, including lower boundary of 95%CI which is needed to ensure non-inferiority accuracy.**
Analysis bias	*ITT, Per Protocol, As Treated.* ITT
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Lack of blinding could have skewed reporting of outcomes, but this would usually be towards rejecting null hypothesis (not confirming it). Potential reporting bias on completed/consumed fills for 2nd Dex dose (not confirmed with pharmacies).

Administrative details

Key words	Asthma, dexamethasone, exacerbation
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Rahim Valani, MD, MBA, M Med Ed, LLM *Associate professor of Medicine, University of Toronto*	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

What are the latest recommendations in the management of Kawasaki disease?

BEEM Bottom Line

Why is this study important? Kawasaki disease (KD) is a common pediatric vasculitides, with an incidence of 25-50cases/100K children annually in USA. It is the most common cause of acquired heart disease in childhood, with 25% untreated children getting coronary aneurysms if left untreated (50% infants <6mo). Accurate diagnosis and early treatment is critical to reduce this risk.

What, if any, threats to validity are most likely to have an impact on the results and how? The consensus is developed by rheumatologists. There was no Emergency physician input.

How do the key results compare with the current evidence? These Recs build on prior guidance, and updates definitions of KD to be more practical (Yellen et al 2010, McCrindle et al 2017).

How should this study impact the care of ED patients? In patients with suspected KD/incomplete KD (+/- MAS), a broad workup and expetious referral to pediatic/rheumatologic consultants is warranted to prevent serious complications.

Study Summary

Article	Gorelik M, Chung SA, Ardalan K, Binstadt BA, *et al.* 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Kawasaki Disease. Arthritis Rheumatol. 2022 Apr;74(4):586-596. doi: 10.1002/art.42041.
Design	Clinical Practice Guideline
Population	***Included:*** Not clearly specified ***Excluded:*** Not clearly specified
Scope of Recs	Guideline aimed at providers who care for suspected KD/vasculitis patients.

Key Recommendations (LoE = Level of Evidence)

Recommendation	*Strength (LoE)*
Diagnostics: For children with suspected incomplete KD and fever, obtaining an echocardiogram with coronary artery measurements without delay is strongly recommended over not obtaining an echocardiogram.	Strong (Very Low)
For children with unexplained shock physiology, obtaining an echocardiogram with coronary artery measurements is strongly recommended. (Image coronary arteries also)	Strong (Very Low)
For children with unexplained MAS, obtaining an echocardiogram with coronary artery measurements is strongly recommended.	Strong (Very Low)
Therapeutics: For patients with incomplete KD, prompt treatment with IVIG at the time of diagnosis is strongly recommended over delaying treatment until day 10 or later.	Strong (Low)
For patients with acute KD and suspected or diagnosed MAS*, treatment with IVIG for KD and additional agents to treat MAS is strongly recommended.	Strong (Very Low)
For patients with acute KD, using aspirin is strongly recommended over no aspirin.	Strong (Very Low)
	Strong (Very Low)

For patients with acute KD with subsequent resolution of fevers, continued daily monitoring for fevers is strongly recommended over not monitoring for fevers.	
Therapeutics: For patients with acute KD who are at high risk of IVIG resistance or developing coronary artery aneurysms, use of IVIG with adjunctive glucocorticoids as initial therapy is conditionally recommended over treatment with IVIG alone. For patients with acute KD who are at high risk of IVIG resistance or developing coronary artery aneurysms, using IVIG with other nonglucocorticoid immunomodulatory immunosuppressive agents as initial therapy is conditionally recommended over treatment with IVIG alone. For patients with acute KD and persistent fevers after initial treatment with IVIG, a second course of IVIG is conditionally recommended over the use of glucocorticoids. For patients with acute KD who have arthritis that persists after IVIG treatment and who do not have coronary artery aneurysms, using NSAIDs to treat arthritis is conditionally recommended over not using NSAIDS.	Conditional (Low) Conditional (Very Low) Conditional (Very Low) Conditional (Very Low)
IVIG is the standard-of-care therapy for the initial treatment of KD. For patients with acute KD and persistent fevers after repeated treatment with IVIG, either nonglucocorticoid immunosuppressive therapy or glucocorticoids may be used.	Good Practice Statement (High) Ungraded Position Statement

***MAS = Macrocyte Activation Syndrome; may be suspected in KD patients with persistent fever, splenomegaly, elevated ferritin levels, and thrombocytopenia.**

BEEM Critique

Risk of bias assessment (amalgamated from AGREE-II/NEATS instruments)

	A1	A2
1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.	✓	✓
2. Financial conflicts of interest of guideline development group (GDG) members have been disclosed and managed. **Online Supplement has disclosures available.**	✓	✓
3. The CPG development group includes all of the relevant multidisciplinary stakeholders, including clinicians, methodologists and patients/caregivers. **2 patients on Initial Voting Panel. No ER physicians**	✓	X
4. The CPG objectives, health questions, scope of relevant providers and target recipients of care are clearly defined.	✓	✓
5. Values/preferences of patients, caregivers, advocates and/or the public with experience with the clinical disease management has been sought/integrated into CPG development (reported clearly). **Separate patient panel convened to explicitly outline values/preferences.**	✓	✓
6. The search strategy for evidence is thoroughly developed and described. **Online Appendix1**	✓	✓
7. The criteria for selecting relevant studies/evidence are clearly described. **Online Appendix 1**	✓	✓
8. The quality, strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.). Summaries of evidence tables are provided. **GRADE tables Appendix 2**	✓	✓
9. The health benefits, side effects, and risks were considered in formulating the recommendations.	?	?
10. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
11. The strength of recommendations is clearly reported, including confidence in underlying evidence. **Table 2**	✓	✓
12. Recommendations are clear and unambiguous, and easily identified in the CPG publication. **Table 2**	✓	✓
13. Different options for management for managing the health questions are clearly presented.	X	✓
14. Experts externally reviewed the guideline prior to its publication. **Different ACR committees only**	X	X
15. The CPG describes a procedure to update the guideline.	X	X
16. The CPG provides advice, tools and/or clinical pathways for easy adoption/adaptation into practice. **Figure 1**	?	✓
17. The CPG describes barriers and facilitators to implement recommendations.	X	X
18. Performance metrics for monitoring implementation of recommendations for audit/feedback have been defined appropriately.	X	X
19. Resource implications for implementing CPG recommendations have been discussed.	X	X

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Reported. Funding from American College of Rheumatology & Vasculitis Foundation.
Conflict of interest	Reported; minimal (online Supp materials)

Potential threats to viability

Development	*Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible?* Broad teams of clinical panels, Evidence panels and patient panels all used. Reporting in various online Appendices
Presentation	*Well organized with easy to find recommendations?* YES; Table 2
Comprehensive	*Was the information to inform decision-making complete?* Yes? Some basic Recs relevant to ED practice; majority of Recs more appropriate for consulting Peds/Rheum/other specialists.
Clinical Validitiy	*Are the recommendations clinically sound and appropriate for the intended patients?* YES

Administrative details

Key words	Emergency department, IVIG, Kawasaki disease, unexplained fever, vasculitis
Reference(s)	McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation 2017;135:e927–99. Yellen ES, Gauvreau K, Takahashi M, Burns JC, Shulman S, Baker AL, et al. Performance of 2004 American Heart Association recommendations for treatment of Kawasaki disease. Pediatrics 2010; 125:E234–41.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Rahim Valani, MD, MBA, M Med Ed, LLM Associate Professor of Medicine, University of Toronto	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

Is combination IV ketorolac + metoclopramide superior to metoclopramide alone for pediatric migraine?

BEEM Bottom Line

Why is this study important? Metoclopramide and ketorolac are commonly prescribed in the ED for migraine treatment, but the efficacy of combination vs. monotherapy has not yet been determined.

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. It is possible that this trial was under-powered to detect smaller improvements in headache scores, but prior pilot work established an MCID of 20mm (20%) on 100mm VAS scale.

How do the key results compare with the current evidence? Neither agent (alone/combined) showed as much benefit as use of prochlorperazine (50% reduction in a prior trial); may be higher risks of akathisia/dystonic reactions with this agent (9x higher?).

How should this study impact the care of ED patients? ED physicians may continue to use metoclopramide monotherapy in treating pediatric migraines, and use combination with ketorolac for rescue?

Study Summary

Article	Richer LP, Ali S, Johnson DW, Rosychuk RJ, Newton AS, Rowe BH. A randomized trial of ketorolac and metoclopramide for migraine in the emergency department. Headache 2022; Jun;62(6):681-689. doi: 10.1111/head.14307.
Design	Randomized Controlled Trial. 2 Cdn Peds ED sites (Edmonton, Calgary). ClinicalTrials.gov (NCT01596166).
Population	***Included:*** Children 6-17yo who failed usual home Rx or at least one dose of ibuprofen or acetaminophen in the ED. ***Excluded:*** Presence of VP shunt, fever >38.5^{o}C, meningismus/clinical suspicion of meningitis, prior head trauma <7days, allergy/contraindications to study meds, inability to complete headache pain assessments.
Intervention	IV metoclopramide 0.2mg/kg (max 10mg) + ketorolac 0.5mg/kg (max30mg) with 10ml/kg normal saline over 30min (MetKet)
Comparison	IV metoclopramide 0.2mg/kg (max 10mg) with 10ml/kg saline over 30min (Met)
Outcomes	***Primary:*** Mean change in pain intensity from baseline to 120min; measured every 30min using VAS scale (age 8-17yo), or FPS-R (age <8yo) scales. ***Secondary:*** (1) pain-free = VAS score of 0; (2) headache relief = 33% or 50% reductions in the VAS score from baseline; (3) presence of nausea or emesis; (4) use of rescue medication at the discretion of the treating ED physician after last assessment period; (5) participant responses to the questions: "I would take the medication again," and "my headache is a bit better/ worse" or "my headache is a lot better/worse" which were used as surrogates for "minimum clinically significant difference"; and (6) "I would take this medication again." All outcomes measured at 120min, or prior to earlier ED discharge. ***Follow-up (24hrs after ED discharge):*** Follow-up outcome measures included: (1) discharged from ED within 24 h; (2) sustained pain-freedom = no recurrence of headache or use of rescue medication within 24 h if pain-free in the ED; (3) headache recurrence = no moderate or severe headache if the child's headache was reported as "a lot better" or had decreased by 33% or 50% from baseline on the VAS in the ED; (4) presence of nausea or vomiting; (5) return to ED within 24 h; (6) satisfaction with treatment in ED; and (7) use of rescue medication in last 24 h. ***Adverse outcomes (24hrs after ED discharge):*** Akithisia, acute dystonic reactions, any other significant/persistent disability or incapacity, prolonged ED stay or hospital admission attributed to study meds.
Key Results	**53 pts enrolled; mean age 13yo, 66% females.** Mean duration migraine attack 24hrs prior to ED visit. Migraine prevention meds 28% used, and 89% used home meds prior to ED visit.

	Mean PedMIDAS score 21 at enrollment ("mild" disability), and overall baseline pain severity VAS 67/100. ***Primary (VAS changes at 120min):*** Met -44mm vs MetKet -36mm; Difference 8mm (95%CI -9 to 25, p=0.355) favouring Met alone. ***VAS changes <120min (22pts who left before 2hrs):*** Met -38mm vs MetKet -42mm; Difference 4mm (-16 to 8, p=0.525). **No significant differences in VAS changes at any time point 0-120min.** ***Secondary:*** **No statistically significant differences** for any outcomes. **(Table 2**) ***Safety:*** **No statistically significant differences** in safety outcomes (**Table S1**). Rare AE's noted in Met (5) and MetKet (4) groups. 1 patient hospitalized; deemed unrelated to study meds. No definite akathisia or dystonic events recorded in either group. More "probable" akathisia events in Met alone (36%) vs MetKet (9%); most mild/moderate and subjective (not corroborated by ED physician). ***Follow up 24hrs:*** 61% reported improved headache ("a lot") by ED discharge, but 87% still were not pain-free at 24hrs, and 10% returned to ED. Non-significant trend to better 24hr pain-free status in MetKet group (22%) vs Met alone (4%). (**Table 3**)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively. **Not reported**	?	?
2. The patients were adequately randomized (allocation sequence adequately generated). **1:1 permuted block randomization at each site**	✓	✓
3. The allocation sequence was adequately concealed. **Treatment code kept with study pharmacists**	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **All blinded**	✓	✓
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Reported; study funded by CIHR.
Conflict of interest	Reported; multiple authors supported by CIHR/other public grants. Otherwise, no conflicts of interest declared.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Sample size of 25pts per arm needed for 90% power to detect a 20% change in pain scores. Minimum clinically important difference (MCID) 20% established in pilot study conducted prior to designing this trial. Not powered to detect smaller differences.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Yes
Measurement bias	Study not powered to detect differences in follow-up.
Analysis bias	*ITT, Per Protocol, As Treated.* ITT.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* IV hydration in both arms may have "diluted" any treatment benefits/differences between study meds.

Administrative details

Key words	emergency department, headache, migraine, pediatrics
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Rahim Valani, MD, MBA, M Med Ed, LLM *Associate Professor of Medicine, University of Toronto*	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

Is wrist bandaging equivalent to rigid immobilization for torus fracture in children?

BEEM Bottom Line

Why is this study important? Minimally intrusive treatment of pediatric torus (buckle) fractures can lead to optimal patient/ caregiver outcomes and minimal disruption of function, satisfaction and quality of life. Simple wrist bandages with elective follow-ups (compared to rigid immobilization and formal clinic follow-up) offer such alternatives.

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal; allocation concealment/blinding is impractical in this equivalence trial design. No other significant biases/confounders noted.

How do the key results compare with the current evidence? Results of this large pragmatic multi-centre trial are congruent with prior Cochrane 2010 evidence summaries showing no significant differences between the two interventions.

How should this study impact the care of ED patients? Children/caregivers can be offered a choice between simple bandages/self-management or rigid immobilization/fracture clinic follow-up with distal radius torus fractures.

Study Summary

Article	Perry DC, Achten J, Knight R, *et al*; FORCE Collaborators in collaboration with PERUKI. Immobilization of torus fractures of the wrist in children (FORCE): a randomized controlled equivalence trial in the UK. Lancet. 2022 Jul 2;400(10345):39-47. doi: 10.1016/S0140-6736(22)01015-7.
Design	Randomized controlled equivalence trial, 23 hospital EDs in United Kingdom; ISRCTN registry, ISRCTN13955395.
Population	***Included:*** Children aged 4–15 years with a radiologically confirmed torus fracture of the distal radius, +/- any concomitant fracture of ipsilateral ulna. ***Excluded:*** Injury 36hrs old, other radial fracture (eg. greenstick) or fractures outside of affected wrist, parental inability to adhere to trial procedures (language, developmental delay, no internet access).
Intervention	Soft bandage and immediate discharge. Subsequent use at family discretion, no planned ortho clinic follow-up.
Comparison	Rigid immobilization (RI; commercial, custom) & standard clinic follow-up (as per local recruiting centre).
Outcomes	***Primary:*** Pain at 3days post ED visit using Wong-Baker FACES scale (MCID 1 face = 2pts). ***Secondary:*** PROMIS Upper Extremity Score for Children Computer Adaptive Test, collected at baseline, days 3/7, 3 and 6 weeks; health-related quality of life EuroQol EQ-5DY-3L. Proxy reports for children <8yo, self-reporting for children 8+. Analgesia type & use at 1/3/7 days. Days of school/child-care missed at 3 & 6 weeks. Hospital return at 1/3/7days, 3 & 6 weeks. Satisfaction with treatment at 1 day & 6 weeks. **Subgroup:** Treatment equivalence between 2 age groups: 4-7yo, and 8-15yo.

Key Results	**965 patients included; 489 in bandage arm (51%), 476 RI arm (49%). Females 379 (39%), males 586 (61%). 69% patients aged 8-15yo, 31% aged 4-7yo.** Median use bandage = 7days; median use RI splints/casts = 18days. At 3 weeks, 10% bandages were still used, 37% RI splints/casts used. ***Crossovers:*** Day 3 primary outcome assessment: 36 bandage pts (7%) changed to RI splints, 1 RI pt changed to bandage option offered (0.2%). After day 3, 21 more bandage pts (4%) changed over to RI. Overall 53 bandage pts changed over to RI (11%), and 22 in RI pts returned for a splint/cast change. ***Primary (908 [94%] completed; 100% ITT):*** Equivalence confirmed (Figure 2); pain score difference -0.10pts (-0.37 to 0.17) ITT, -0.16 (-0.34 to 0.21) per protocol. Equivalence confirmed in age subgroup strata (4-7, 8-15). ***Secondary:*** Equivalence of pain outcomes at all other time points (Table 3, Figure 3). No significant difference in PROMIS scores at any time point; scores improved markedly between day 7 and 3 weeks in both groups; generally higher in older vs younger age groups. No significant difference in EQ-5DY-3L scores from baseline to 6wks, with higher overall scores in younger vs older age subgroups. Parental satisfaction higher in RI group at day 1, but equivalent by 6 weeks. School absences no difference; median 1.5days in each arm. Small but significant analgesia (acetaminophen, ibuprofen) use in RI arm vs bandage on day 1 (83% vs 78%), but no differences at any other time points. No serious adverse events noted in either arm. Complication rate very low (5pts bandage, 3 RI); formal comparison not possible. No intervention beyond plaster cast application needed.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?✓X	?
2. The patients were adequately randomized (allocation sequence adequately generated). **Block randomization (2/4/6), stratified by age & recruitment center.**	✓	✓
3. The allocation sequence was adequately concealed. **Irrelevant**	X	X
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Impractical**	X	X
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	UK National Institute for Health and Care Research. No role in study design, data management/analysis, or writing manuscript.
Conflict of interest	Reported; all authors received an NIHR HTA programme grant. No commercial interests declared.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Sample size for EQ margin set at 278pts total (139 per arm); recruiting targets met.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Yes.
Measurement bias	Equivalence margin set at half-MCID (half face, 1pt) as per std EQ trial practices.
Analysis bias	*ITT, Per Protocol, As Treated.* Both ITT and per protocol analyses conducted; no significant differences noted between the two.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Inability to blind patients/families to intervention received may have influenced outcome assessments based on pre-conceived biases (eg. better outcomes for those who strongly believed in RI vs bandages); demonstrated equivalence of outcomes overcomes such potential preferential reporting biases.

Administrative details

Key words	Children, bandage, emergency department, rigid immobilization, splint, torus fracture
Reference(s)	Kaji AH, Lewis R. Are We Looking for Superiority, Equivalence, or Noninferiority? Asking the Right Question and Answering It Correctly. Annals Emerg Med 2010; 55:408-411. doi:10.1016/j.annemergmed.2010.01.024

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Rahim Valani, MD, MBA, M Med Ed, LLM *Associate Professor of Medicine, University of Toronto*	**No conflicts of interest/Identify conflicts (ICMJE)**

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Research Question

How useful are the PECARN & CATCH rules for pediatric minor head injuries presenting to ED >24hrs post-injury?

BEEM Bottom Line

Why is this study important? Minor head trauma (MHT) is a very common pediatric ED presentation, and risk-stratifying for clinically important/intervenable head injuries based on CT imaging is important in order to identify higher-risk injuries that merit the CT radiation risk. Clinical decision rules (CDRs) that reliably assess risk can improve practice.

What, if any, threats to validity are most likely to have an impact on the results and how? The retrospective nature of this study precludes confirmation of uniform understanding and application/interpretation of predictor variables, and documentation. It is also not clear if clinicians applying predictor variables were blinded to outcomes. There is no comparison with children assessed who did not have a CT scan for same outcomes.

How do the key results compare with the current evidence? These results are congruent with limited studies of children with MHT >24hrs that show that these CDRs have predictive value for serious outcomes.

How should this study impact the care of ED patients? Use of a validated CDR, coupled with clinical judgement, can be useful to risk-stratify children with MHT for need of CT scanning and/or neurosurgical intervention.

Study Summary

Article	Sert ET, Mutlu H, Kokulu K. The Use of PECARN and CATCH Rules in Children with Minor Head Trauma Presenting to Emergency Department 24 Hours After Injury. Peds Emerg Care 2022; 38(2): e524-e528. doi: 10.1097/PEC.0000000000002011.
Design	Clinical Decision Rule
Population	***Included:*** Patients <18yo who underwent CT scanning for blunt MHT (minor = GCS 13+) ***Excluded:*** Children scanned for nontraumatic reasons, GCS <13 (not minor HT), incomplete records, uncertain injury times recorded.
Predictor Variables	Components of the CATCH and PECARN rules.
Comparison	CT Head findings.
Outcomes	***Primary:*** Presence of new traumatic intracranial injury on CT scan in early (<24hrs) and late (>24hrs) ED admission groups. New traumatic intracranial injury in CBT included linear or nonlinear skull fracture, any intracranial hemorrhage (epidural, subdural, subarachnoid, intracerebral), pneumocephalus, contusion, or cerebral edema. ***Secondary:*** Sensitivity of PECARN & CATCH rules to identify clinically important MHT. Neurosurgical outcomes were defined as invasive intracranial pressure measurement by any method, burr hole procedure, craniotomy, hematoma removal, surgical repair of displaced skull fracture, and dura repair.
Key Results	**2490 children with MHT included; 70% male. 168 (6.75%) attended ED >24hrs after injury.** Majority (90%) had GCS 15 at ED presentation; majority of those with GCS 14 presented within 24hrs (only 2 presented >24hrs). Traumatic HT with abnormal CT (abCT): 168pts (6.7%); 6.9% in early group, 4.2% in late group. **NeuroSx intervention: Overall 0.7% pts; Late group 2.4% >> early group 0.6% (p=0.02).** 4 pts died; 3 early, 1 late (NSS). ***PECARN <24hrs:*** Sens for abCT: 96.3% (91.7-98.5%), Sens for NeuroSx Int: 100% (71.6-100%) ***PECARN >24hrs:*** Sens for abCT: 85.7% (42.0-99.2%), Sens for NeuroSx Int: 100% (39.6-100%) ***CATCH <24hrs:*** Sens for abCT: 91.9% (86.3-95.4%), Sens for NeuroSx Int: 100% (71.7-100%) ***CATCH >24hrs:*** Sens for abCT: 85.7% (42.0-99.2%), Sens for NeuroSx Int: 100% (39.5-100%) PECARN misclassified 6 early patients (0.4%) and 1 late patient (0.8%) as no-CT indication who ultimately had an intracranial injury. CATCH misclassified 13 early patients (0.9%) and 1 late patient (0.6%) as no-CT indication with subsequent intracranial injury. There were NO deaths nor NeuroSx interventions in either misclassified group. **Table 4**

	Regardless of early vs late assessment, a positive screen on PECARN had a strong predictive value for finding intracranial injury on imaging (OR 33.47, 95%CI 10.55-106.20).

BEEM Critique

Risk of bias assessment

	A1
1. The patients were representative of those with the problem.	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample. **Retrospectively enrolled from hospital records database.**	?
3. All patients underwent the same clinical evaluation. **Retrospective design.**	?
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	?
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	?
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	?
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓
8. All patient-important outcomes were considered.	✓
9. The follow-up was complete.	✓
10. The point estimates and respective precisions are clinically significant.	✓

A1 = S. Upadhye

Funding and conflicts of interest

Funding	None reported.
Conflict of interest	Reported; no conflicts of interest declared.

Potential threats to viability

Chance	*Type I & II errors?* Children who were NOT scanned during the study period are not included, so there is no clinical comparison available for CDR application in this group.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Unknown; patients retrospectively sampled from database of children who all received CT scanning. Exclusion of those records with missing information may also contribute to selection bias.
Measurement bias	Retrospective design makes it difficult to ascertain uniformity of predictor variable training, application/interpretation and documentation. Without specificity measures, authors are unable to calculate likelihood ratios for these "diagnostic tests."
Analysis bias	*Are the results data- or hypothesis-driven? Is the model over fitted and not applicable?* Models showed a good fit (Hosmer-Lemeshow test 0.56).
Confounding	*Residual confounding as with all observational studies because of unknown prognostic factors that cannot be controlled for; Independent factors affecting the outcome; clinicians to comment.*

Administrative details

Key words	Minor head trauma, traumatic brain injury, computed tomography, CATCH, PECARN
Reference(s)	Cheng et al, 2019. Choosing Wisely Canada's emergency medicine recommendations: Time for a revision. CJEM 2019; 21(6):717–720.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC	**No conflicts of interest/Identify conflicts (ICMJE)**
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University	

Research Question

What is the optimal duration of antibiotic therapy for pediatric community acquired pneumonia (CAP)?

BEEM Bottom Line

Why is this study important? Antibiotic stewardship principles advocate for the shortest effective duration of infection treatment, with the goal of reducing adverse effects and antibiotic resistance. Duration of treatment has been based on historic notions by preceptors that have continued. Very few studies have identified the minimum duration of antibiotics needed for treatment.

What, if any, threats to validity are most likely to have an impact on the results and how? Not all children had microbiology/CXR confirmation of CAP. Furthermore, many patients would likely have viral infections that would not necessitate treatment.

How do the key results compare with the current evidence? These results are congruent with past shorter-duration CAP antibiotics trials (including SAFER 2021), and WHO guidelines for treating non-severe CAP in children.

How should this study impact the care of ED patients? For pediatric patients with uncomplicated CAP, 5 days of antibiotics is appropriate duration of treatment.

Study Summary

Article	Williams DJ, Creech B, Walter EB, et al. Short- vs Standard-Course Outpatient Antibiotic Theraphy for Community-Acquired Pneumonia in Children (SCOUT-CAP Randomized Clinical Trial). JAMA Peds 2022; DOI: 10.1001/jamapediatrics.2021.5547
Design	Randomized controlled trial, in 8 US community clinics, urgent care or emergency department. Registered at: ClinicalTrials.gov Identifier: NCT02891915.
Population	**Children initially received 3-6d of Abx for CAP with some demonstrated clinical improvement, then considered for trial enrollment. ***Included:*** Children aged 6-71mo, otherwise healthy. Fever >38.3C in prior 24hrs, tachypnea (>50bpm if <2yo, >40bpm if >2yo), and severe cough. ***Excluded:*** Systemic Abx <7d prior to CAP Dx, initial CAP Abx combination Rx, beta-lactam allergy/anaphylaxis, concomitant bacterial infection needing >5d Abx Rx, CAP complications/ hospitalization, Hx of CAP/bronchodilator/inhaled steroid use within past 6mo, CAP S. Aureus/GAS on culture/PCR, Dx aspiration/bronchiolitis/bronchitis/acute asthma, airway intervention/surgery within 7days of CAP Dx, immunocompromise, complex chronic medical conditions, other safety concerns as per enrolling physician.
Intervention	Antibiotics (Abx) for 5 additional days; beta-lactam of choice (amoxicillin, clavulin 80-100mg/kd/day, max 2000mg/day OR cefdinir 12-16mg/kd/day, max 600mg, divided BID)
Comparison	Matching placebo for 5 days.
Outcomes	***Primary:*** Response Adjusted for Duration of Antibiotics Risk (RADAR) at OAV1; clinical outcomes ranked on an 8pt ordinal scale of desirability of outcome ranking (DOOR) encompassing adequate clinical response (absence of a medically attended visit, surgical procedure, or receipt of non-study antibiotics for persistent or worsening pneumonia after randomization), symptom resolution (absence of fever, elevated respiratory rate, and moderate or severe cough) and adverse effects (presence/severity of irritability, vomiting, diarrhea, allergic reaction, stomatitis, or candidiasis). ***Secondary:*** RADAR at OAV2, DOOR components at OAV1 & OAV2. DNA resistome substudy of Antibiotic-Resistance Genes (ARGs) at OAV2. Outcomes assessment visits (OAVs): OAV1 6-10 days, OAV2 19-25days (all in-person)

Key Results	380 participants analyzed via ITT analysis. Mean age 35.7mo, 51% male. **21% recruited/treated from ED.** Int arm (192 pts, 189 ITT analyzed): OAV1 170, OAV2 163 (**overall LTFU 15%).** 84% completed the placebo Rx schedule. Comp arm (193 pts, 191 ITT analyzed): OAV1 174, AOV2 167 (**LTFU 14%**). 80% completed the extended Abx Rx schedule. **No significant differences:** 1) Clinical response at OAV1 [0.5% (95%CI -2.4 to 3.7)] or OAV2 [-0.5% (-3.9 to 2.8)] 2) Persistent symptoms at OAV1 [-1% (-6.8 to 4.9)] or OAV2 [0.1% (-5.3 to 5.4)] 3) Adverse effects at OAV1 [3% [-7.0 to 13.0]; most AE's mild (irritability, diarrhea), 11% in both arms experienced mod/severe AE's. OAV2 [2.6% (-7.7 to 12.9)]; 19% in both groups had mod/severe AE's. 4) DOOR at OAV1: 0.48% probability of more desirable DOOR (0.42-0.53). 5) Cumulative risk at any DOOR rank. 6) DOOR at OAV2: 0.48% probability of a more desirable DOOR (0.42-0.54). **Significant differences:** 1) Short course RADAR superior at OAV1: probability of more desirable RADAR 0.69 (0.63-0.75). 2) Short course RADAR superior at OAV2: 0.63 (0.57-0.69). 3) Lower resistome genes identified in shorter course group (median 1.17, range 0.35-2.43) vs std course group (median 1.33, 0.46-11.08); p=0.01 **No deaths, hospitalizations or surgery for persistent/worsening CAP.**

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively. **Not reported.**	X	X
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Supp1 Protocol**	✓	✓
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	X	X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = Rahim Valani

Funding and conflicts of interest

Funding	Various US gov't grants (NIAID, NIH, DHHS), Duke University, and Cincinnati Children's Hospital.
Conflict of interest	Many authors had gov't grant support. Some industry supports related/unrelated to current work for some authors.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* **Superiority design**, sample size 180pts/arm needed, >180 recruited each arm.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* **Yes**
Measurement bias	Null hypothesis: No difference in RADAR = 50% probability of more desirable RADAR for the short-course strategy. Alternate hypothesis: 60+% probability of a more desirable RADAR for short course strategy.
Analysis bias	*ITT, Per Protocol, As Treated.* ITT analysis. **ITT analysis. No difference in outcomes in sensitivity analyses based on per protocol, complete case and worst-case analyses.**
Confounding	*Independent factors affecting the outcome; clinicians to comment.*

Administrative details

Key words	Community-acquired pneumonia, emergency department, pediatric
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest (ICMJE)**
Rahim Valani, MD, MBA, LLM, M Med Ed *Associate Professor of Medicine, University of Toronto*	**No conflicts of interest (ICMJE)**

Research Question

Can use of multi-species probiotics help reduce the risk of antibiotic-associated diarrhea in children?

BEEM Bottom Line

Why is this study important? Antibiotics-associated diarrhea (AAD) is a common complication of antibiotics (Abx) use. Probiotics may have a protective role in reducing the risk of AAD.

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. Stringent vs relaxed definitions of outcomes can change interpretation of effect estimates, and real-world generalizability.

How do the key results compare with the current evidence? Cochrane review suggests that probiotics can reduce risk of AAD (Guo et al, 2019), but this study (using strict definitions of AAD) did not show the same benefit.

How should this study impact the care of ED patients? There may a role in suggesting a course of probiotics for concomitant use with Abx to minimize risk of "any" diarrhea (not necessarily AAD).

Study Summary

Article	Lukasik J, Dierikx T, Besseling-van der Vaart I, de Meij T, Szajewska H; Multispecies Probiotic in AAD Study Group. Multispecies Probiotic for the Prevention of Antibiotic-Associated Diarrhea in Children. JAMA Pediatr. 2022 Jun 21:e221973. doi: 10.1001/jamapediatrics.2022.1973.
Design	Randomized controlled trial; multi-centre (3 Dutch, 2 Polish). ClinicalTrials.gov Identifier: NCT03334604
Population	***Included:*** Children 3mo-18yrs, recruited within 24hrs of Abx initiation (oral, IV). ***Excluded:*** Use of antibiotics <prior 4wks, use of probiotics/proton pump inhibitors/ laxatives/antidiarrheal drugs within the previous 2 weeks; severe infection or life-threatening illness at recruitment (ie, indicated/probable admission to PICU); preexisting diarrhea <4wks based on patient/caregiver report; severe chronic disease (eg, cancer, inflammatory bowel disease, short-bowel syndrome); diagnosed primary/secondary immunodeficiency; required tube-feeding; exclusive breastfeeding; and known allergy or hypersensitivity to any component of the study product.
Intervention	Multispecies probiotics (ProBx) mix; 2 sachets daily for duration of Abx Rx + 7 more days, start within 24hrs of 1st Abx dose. Total dose of 10Billion CFU daily. Data collected with study diaries. Stool consistency reported via Bristol or Amsterdam scales. Routine stool cultures at baseline, end of Abx usage, end of intervention period, and 1mo. Each acute diarrhea event fully cultured for multiple pathogens (including C. Difficile).
Comparison	Placebo matched mix; same dosing/data collection as above.
Outcomes	***Primary:*** Incidence of AAD = 3+ loose/watery stools (a score of A on the AISS, or 5-7 on the BSFS) per day in a 24hr period, caused either by C difficile/otherwise unexplained etiology, after testing for common, predefined diarrheal pathogens. ***Secondary:*** Diarrhea = 3+ loose/watery stools per day in a 24hr period regardless of the etiology; mild AAD = 2+ loose/watery stools per day for a minimum of a 24hr period caused by C difficile/otherwise unexplained etiology; severe AAD = 3+ loose/watery stools per day for a minimum of a 48hr period caused by C difficile/otherwise unexplained etiology; diarrhea duration = interval until normalization of stool consistency according to the BSFS (1, 2, 3, or 4) or AISS (B, C, or D) and the presence of normal stools for 48 hours; diarrhea caused by C difficile; discontinuation of the Abx Rx/hospitalization/need for IV rehydration owing to diarrhea; and adverse events.

Key Results	**350pts recruited (55% male, median age 28mo).** Outpatient Rx setting 22.6%. Oral Abx Rx 41%. Majority of Abx = beta-lactam monotherapy (>90%). ***Primary (ITT):*** AAD incidence ProBx 14.6% vs. Plac 18.1%; RR 0.81 (95%CI 0.49-1.33); similar results for mild & severe AAD. **Table 2** ***Secondary (ITT):*** Diarrhea (any) incidence ProBx 20.9% vs Plac 32.3%; RR 0.65 (95%CI 0.44-0.94, **NNT 9**, p=0.02) **in favour of ProBx.** Reduced need for IV rehydration **in favour of ProBx?** ProBx 0% vs Plac 5%; NNT 32, p=0.03. No other significant differences for any other outcomes. Similar findings in per protocol analyses; none statistically significant due to smaller sample sizes/LTFU. **Supp 2, eTable 4.** No differences between Poland vs Netherlands. *Sensitivity analyses*: AAD more likely in younger patients, and any diarrhea associated with younger age, placebo group or use of amoxicillin-clavulanic acid. Highest benefits found in children with rotavirus diarrhea. Results may change minimally based on assumptions/imputations of LTFU patients.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	✓	✓
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	X	X
8. The patients were analyzed in the groups to which they were randomized (ITT). **ITT, per protocol**	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Reported. Probiotics/placebos provided free of charge by commercial manufacturer. University received a statutory donation for study. Sponsor had no role in study design, data management nor manuscript preparation.
Conflict of interest	Reported. Various authors received grants and other non-financial supports from sponsor.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Required sample size 350 (175/arm), with 20% LTFU built-in buffer.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Yes; Table 1.
Measurement bias	N/A.
Analysis bias	*ITT, Per Protocol, As Treated.* ITT analysis planned. Lost to follow up Poland 15.1% vs Netherlands 4.1%; children LFTU were demographically similar to those included/analyzed.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Similarities in ITT vs per protocol outcomes may reflect some misclassification of compliance data.

Administrative details

Key words	Antibiotics, Clostridium difficile, diarrhea, probiotics
Reference(s)	Leal, J., Heitman, S., Conly, J., Henderson, E., & Manns, B. (2016). Cost-Effectiveness Analysis of the Use of Probiotics for the Prevention of Clostridium difficile–Associated Diarrhea in a Provincial Healthcare System. *Infection Control & Hospital Epidemiology,37*(9), 1079-1086. doi:10.1017/ice.2016.134

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Rahim Valani, MD, MVA, M Med Ed, LLM *Associate Professor of Medicine, University of Toronto*	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

Does Point-of-Care-Testing for viral respiratory pathogens change antibiotic prescribing for children?

BEEM Bottom Line

Why is this study important? Acute respiratory infections are the most common reason for ED visits in children, and many (70%) receive antibiotics (Abx) for uncertain reasons, leading to over-consumption and increasing antibacterial resistance. This study examined the role of point-of-care-testing (POCT) for respiratory pathogens on Abx prescribing rates in the peds ED.

What, if any, threats to validity are most likely to have an impact on the results and how? A high degree of pathogen and CRP testing (both groups) may have influenced Abx prescribing rates. Positive viral test results do not necessarily rule out concomitant bacterial infection (warranting use of Abx)?

How do the key results compare with the current evidence? Recent similar trials show mixed outcomes re: POCT for respiratory pathogen testing on targeted Abx prescribing rates. (Supp eTable 3).

How should this study impact the care of ED patients? Use of POCT for respiratory pathogens did not influence ED Abx prescribing rates. Other drivers of prescribing need to be addressed in order to optimize Abx stewardship.

Study Summary

Article	Mattila S, Paalanne N, Honkila M, Pokka T, Tapiainen T. Effect of Point-of-Care Testing for Respiratory Pathogens on Antibiotic Use in Children: A Randomized Clinical Trial. JAMA Netw Open. 2022 Jun 1;5(6):e2216162. doi: 10.1001/jamanetworkopen.2022.16162.
Design	Randomized Controlled Trial (Diagnostic); single-site Peds ED (Finland). ClinicalTrials.gov Identifier: NCT03932942.
Population	***Included:*** Children (aged 0-17yrs) with fever (>38.^{o}C) and/or any respiratory signs or symptoms (tachypnea, shortness of breath, apnea, wheezing, cough, rhinitis, croup, sneezing, earache, sore throat, or some other suspicion of respiratory infection) ***Excluded:*** Need for CPR or immediate ICU transfer
Intervention	Multiplex PCR point-of-care testing (18 respiratory viruses and 3 bacteria with results ready within 70 minutes) upon arrival at the ED
Comparison	Routine care; resp testing at physician discretion, results next day.
Outcomes	***Primary:*** Proportion of children receiving antibiotics (Abx) therapy ***Secondary:*** Diagnostic test rates, chest X-rays performed, and costs for same. Proportion of macrolide Rx in ED, and mean time for starting targeted Rx for influenza or Mycoplasma. ED length of stay, hospitalizations, subsequent ED visits and outpatient telephone contacts also reported. Abx script within 1 week, ICU admissions/deaths within 1mo also noted.
Key Results	**1417 children screened, 1350 randomized. 1243 included in final ITT population (829 Int, 414 controls).** Males 56%. Mean age 3yo. In intervention group, 1.9yrs in controls. Multiplex PCR testing rates: Int 99.8%, Ctrl 1.4%. Ctrl tests for next-day results 62.3% (Int 0). ED RSV, Influenza 3hr tests: Int 3.1%, Ctrl 39.9% CRP POCT tests: Int 69%, Ctrl 70.8%. Mean level 6.3 & 6.6 respectively. ***Outcomes: (Table 2)*** Most common resp viruses = Rhino-enterovirus, RSV, adenovirus. Abx prescribing highly concordant with national guidelines: Int 95.4% vs Ctrl 93.9% Abx not recommended by guidelines: Int 16% vs Ctrl 15.9%. Inappropriate Abx most commonly prescribed for viral wheezing, croup and viral tonsillitis. Duration of Abx Rx: Int 2.5d vs Ctrl 2.6d (NSS). ***Primary (ITT):*** **No reduction in Abx prescribing Int (27.3%) vs Ctrl (28.5%), RR 0.96** (95%CI 0.79-1.16). **Table 3.** No subgroup differences in non- vs. pathogen-targeted Abx use. ***Secondary (ITT):*** **No differences in all secondary outcomes/subgroups** (Abx script within 1 week, macrolides in ED or age<3mo, hospital admissions/ED revisits within 1 week, CXR in

	ED/1week, PICU admissions <30days). No deaths within 30d either group. Total ED tests, ED LOS, and related costs not significantly different.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively. **Not specified**	?	?
2. The patients were adequately randomized (allocation sequence adequately generated). **2:1 ratio to intervention arm**	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Impractical in this pragmatic real-world design**	X	X
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Reported; study supported by public/foundation research grants (no commercial support). Sponsors had no role in study design, data collection/analysis or manuscript preparation.
Conflict of interest	Reported; lead author had public/foundation grant support, no industry funds. No other conflicts declared.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Required sample size 1177pts; recruited 1350 before trial stopped due to COVID19 pandemic.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?*
Measurement bias	None noted.
Analysis bias	*ITT, Per Protocol, As Treated.* ITT analyses for all outcomes.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Both groups allowed to have ED influenza, RSV and CRP testing (results done within 3hrs). Antibiotic Rx rates are generally low in high-income European countries (legislated stewardship?). High rates of CRP testing in both groups may have influenced Abx Rx rates.

Administrative details

Key words	Antibiotics, point-of-care testing, respiratory tract infections, viral pathogens.
Reference(s)	Cheng et al, 2019. Choosing Wisely Canada's emergency medicine recommendations: Time for a revision. CJEM 2019; 21(6):717–720.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Rahim Valani, MD, MBA, M Med Ed, LLM *Associate professor of Medicine, University of Toronto*	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

Can bruising patterns be useful in predicting abuse in young children?

BEEM Bottom Line

Why is this study important? Bruising is a common feature of injury, including non-accidental injuries, in the pediatric population. Failure to recognize child abuse can lead to poor outcomes for the child, including death. While there are risk factors based on history, physical exam, and social interactions, many of these are either not seen or can be difficult to elicit. Distinct bruising locations can help identify abuse with the potential to improve patient outcomes.

Which, if any, threats to validity are most likely to have an impact on the results and how? Spectrum bias may attenuate utility of such Clinical Decision Rules (CDR), since all patients recruited from 5 Peds ED study sites (i.e. higher prevalence of abuse given that they are referral centres?).

How do the key results compare with the current evidence? An earlier version of the TEN4 rule had a Sens 81%, which missed 19% of abused children. The refined rule performs better. The strongest characteristic of abuse was the location of the bruise (the torso, ear, and neck identified 81% of abuse patients).

How should this study impact the care of ED patients? The refined TEN4-FACESp bruising CDR has strong discriminatory ability for differentiating abuse from non-abused children <4yo.

Study Summary

Article
Pierce MD, Kaczor K, Lorenz DJ, *et al*. Validation of a Clinical Decision Rules to Predict Abuse in Young Children Based on Bruising Characteristics. JAMA Netw Open 2021; Apr 1;4(4):e215832. doi: 10.1001/jamanetworkopen.2021.5832.

Design
Prospective refinement and validation of a bruising CDR for children seen in Peds ED (5 test sites).

Population
Included: Children <4yo.
Excluded: Children with injuries from MVA, known coagulopathy, preexisting neuromuscular dz from known spasticity, severe skin disorders that may distort bruising characteristics.

Predictors
TEN4-FACESp score (torso/ear/neck/any bruising on infant<4.99mo., frenulum, angle of jaw, cheek [fleshy], eyelids, subconjunctiva). Any positive criterion is considered "positive" for abuse classification. Patterned bruising = bite, loop, hand slap, squeeze/grab, or multilinear.

Comparison
Expert consensus panel (98% agreement).

Outcomes
Primary: Performance characteristics of refined TEN4-FACESp rule.

Key Results
N = 21123 children screened, 2161 enrolled. Mean age 2.1yrs, 60% male. 410 cases determined as abuse (19%). Higher likelihood of abuse in non-white or Hispanic ethnicity, and have gov't insurance compared to non-abused children.
Median bruise count in abused children = 3; generally higher in all age strata. Patterned bruising generally uncommon (8%), but much higher in abused children (39%) vs non-abused (0.6%).
Children with patterned bruising were highly categorized as abuse (94%).

CDR	*Outcome*	*Sensitivity (95% CI)*	*Specificity (95% CI)*
TEN4-FACESp	Child abuse	95.6% (93-97.3%) LR+ 7.41	87.1% (85.4-88.6) LR- 0.05

Test characteristics did not vary significantly based on skin tone.
TEN bruises alone correctly identified 81% of abuse patients.
Most specific bruises for abuse = buttocks, perineum/anus, jaw angle, neck, subconjunctiva.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those with the problem.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	✓	✓
3. All patients underwent the same clinical evaluation.	✓	✓
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	✓	?
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	✓	✓
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	?	?
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓	✓
8. All patient-important outcomes were considered.	✓	✓
9. The follow-up was complete.	✓	✓
10. The point estimates and respective precisions are clinically significant.	✓	✓

A1 = S. Upadhye A2 = R Valani

Funding and conflicts of interest

Funding	Not specifically reported.
Conflict of interest	Most authors have NIH grant support. One author (JML) reported being a medicolegal expert/court testimony.

Potential threats to validity

Chance	Not every child in the cohort may have received a complete head2toe examination, which may lead to misclassification bias.
Selection bias	Children recruited from Peds ED's, where prevalence of abuse may be higher than general ED settings.
Measurement bias	None?
Analysis bias	CDR outcomes performed better with actual study data than boot-strapping with 10000 iterations (Sens 91.5%, Spec 84.5%, LR+ 5.90, LR- 0.11).
Confounding	Non-abused children with darker skin tone had significantly lower bruise counts than those with lighter tone; risk of under-estimating abuse in darker skin children?

Administrative details

Key words	Bruising, abuse, non-accidental
Appraisers	Upadhye S, Valani R
Reference(s)	Pierce MD, Kaczor K, Lorenz DJ, Bertocci G, Fingarson AK, Makaroff K, Berger RP, Bennett B, Magana J, Staley S, Ramaiah V, Fortin K, Currie M, Herman BE, Herr S, Hymel KP, Jenny C, Sheehan K, Zuckerbraun N, Hickey S, Meyers G, Leventhal JM. Validation of a Clinical Decision Rules to Predict Abuse in Young Children Based on Bruising Characteristics. JAMA Netw Open 2021; Apr 1;4(4):e215832. doi: 10.1001/jamanetworkopen.2021.5832.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

Can infants/young children with fractures be identified for potential maltreatment?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? Identification of abuse is difficult to determine without a formal assessment and having high vigilance to consider this in the differential diagnosis. Certain fractures can prompt the clinician to have a high index of suspicion for non-accidental trauma.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? Lack of patient/caregiver stakeholder involvement and external review risk missing key patient-related outcomes. The search strategies seem limited, and no explicit quality assessment of the methods/results erode confidence in the evidence supporting their recommendations.

How should this guideline, and specifically which recommendations should impact the care of ED patients? The author indicate that this guideline is intended to complement the American Academy of Pediatrics; Committee on Child Abuse and Neglect position statement. Specific fractures in infants/young children (ribs, humerus, and femur) should prompt further investigations for suspected child abuse.

Study Summary

Article Mitchell IC, Norat BJ, Auerbach M, *et al*. Identifying Maltreatment in Infants and Young Children Presenting with Fractures: Does Age Matter? Acad Emerg Med 2021 Jan;28(1):5-18. doi: 10.1111/acem.14122

Design Systematic Review/Clinical Practice Guideline

Population Children with various fractures, suspected victims of child abuse.

Scope This guideline is intended for practitioners/facilities who evaluate injured children for potential child abuse.

Key Results

Recommendation	*Strength*	*Quality of Evidence*
"In children presenting to a health care facility with a rib fracture, who were not in an independently verified incident, we strongly recommend routine child abuse evaluations for patients younger than 3 years of age."	Recommendation (Strong); incidence of abuse 96% (random effects); RE)	Moderate
"In children presenting to a health care facility with a **humeral fracture**, who were not in an independently verified incident, we strongly recommend routine child abuse evaluations for patients younger than 18 months of age."	Recommendation (Strong); 48% incidence of abuse (RE)	Moderate
"In children presenting to a health care facility with a **femoral fracture** aged less than 18 months, who were not in an independently verified incident, we strongly recommend routine evaluation to identify child abuse."	Recommendation (Strong); Abuse incidence (<12mo) 34%, incidence <18mo 25% (RE)	Moderate

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	X
2. Systematic methods were used to search for evidence.	X	X
3. The criteria for selecting the evidence are clearly described.	?	?
4. The strengths and limitations of the body of evidence are clearly described (e.g., **GRADE**, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	X	X
8. The content of the guideline is free of influence by the views of the funding body.	?	X
9. Competing interests of guideline development group members have been recorded and managed.	✓	✓
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	None reported.
Conflict of interest	None (reported).

Potential threats to validity

Development:	**Limited search of electronic databases, English only articles. Unclear quality assessment of included articles. No parents/caregiver stakeholders included on CPG panels.**
Presentation:	Well organized with easy to find recommendations? **No. EM physicians prefer all CPG Recs to be summarized at beginning of publications (Aboulsoud et al 2011).**
Comprehensive:	Was the information to inform decision-making complete? **Yes.**
Clinical Validity:	Are the recommendations clinically sound and appropriate for the intended patients? **Yes**

Administrative details

Key words	Child abuse, fractures, risk stratification.
Appraisers	Upadhye S, Valani R
Reference(s)	Mitchell IC, Norat BJ, Auerbach M, Bressler CJ, Como JJ, Escobar Jr MA, Flynn-O'Brien KT, Lindberg DM, Nickoles T, Rosado N, Weeks K, Maguire S. Identifying Maltreatment in Infants and Young Children Presenting with Fractures: Does Age Matter? Acad Emerg Med 2021 Jan;28(1):5-18. doi: 10.1111/acem.14122

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

What is the utility of the Infant Scalp Score (ISS) for infants with traumatic scalp hematoma for risk of traumatic brain injury?

BEEM Bottom Line

Why is this study important? Risk stratification of infants with isolated scalp hematoma for potential traumatic brain injury is important to determine which infants need CT scanning, and which can be spared unnecessary ionizing radiation.

Which, if any, threats to validity are most likely to have an impact on the results and how? This is a secondary exploratory analysis of the original PECARN database to generate a CDR relevant to infants ≤1 year. The predictor variables are limited to those data points already collected, and therefore may be missing other important predictors.

How do the key results compare with the current evidence? The ISS score consists of points assigned to the patient age, hematoma size, and location. This CDR was derived using administrative database, and prospective validation is required. This CDR is not appropriate for infants who are victims of potential child abuse (higher incidence of CT TBI).

How should this study impact the care of ED patients? The new ISS may be a useful tool to risk stratify CT imaging needs for infants ≤1 year with isolated traumatic scalp hematoma.

Study Summary

Article	Schutzman SA, Nigrovic LE, Mannix R. The Infant Scalp Score: A Validated Tool to Stratify Risk of Traumatic Brain Injury in Infants with Isolated Scalp Hematoma. Acad Emerg Med. 2021 Jan;28(1):92-97. doi: 10.1111/acem.14087. PMID: 32673432.
Design	This is a CDR derivation study using the original PECARN TBI database as source material.
Population	*Included:* Infants <1yo with an isolated scalp hematoma (ISH) without other clinical findings/bulging fontanel. *Excluded*: Missing clinical variables, uncertain diagnosis of isolated scalp hematoma (ISH).
Predictors	Age (months), hematoma size, hematoma location.
Comparison	CT findings, or structured follow-up for clinical status 7d after initial ED head injury assessment (not scanned).
Outcomes	*Primary:* Clinically important TBI (ciTBI) = death from TBI, need for neurosurgical procedure, intubation for 24hrs, or hospitalization for 2+ nights. Incidence: 2.1% of imaged children, 0.9% of all infants. *Secondary:* Any TBI on CT scan = any intracranial bleed, pneumocephalus, cerebral edema, depressed skull fracture, or skull diastasis. Incidence: 12.7% imaged infants, 4.6% total cohort.

Key Results

N = 1289 infants included (43904 in parent study, 5441 infants <1yo). 36% of infants had cranial CT

Outcome	*Area Under Curve*	*Outcomes*
ciTBI	0.916	Cutoff 4/8: No ciTBI/any TBI missed. 52% infants imaged (669/1289)
Any CT TBI	0.807	Cutoff 5/8: No ciTBI/3 any TBI missed. 32% infants imaged (417/1289)

CI = confidence interval; *N* = number of patients; N/A = not applicable; NSS = not statistically significant; *p* = probability; OR = odds ratio (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those with the problem.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	X	✓
3. All patients underwent the same clinical evaluation.	✓	✓
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	✓	✓
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	?	?
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	✓	✓
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓	✓
8. All patient-important outcomes were considered.	✓	✓
9. The follow-up was complete.	✓	X
10. The point estimates and respective precisions are clinically significant.	?	?

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	None (reported).
Conflict of interest	None (reported).

Potential threats to validity

Chance	None?
Selection bias	Publicly available PECARN TBI dataset was sampled.
Measurement bias	Successful follow-up in 79% of parent study.
Analysis bias	No CI's around individual ROC point estimates.
Confounding	Long-term impact of any CT TBI on future developmental/neurocognitive outcomes not clear.

Administrative details

Key words	Clinical decision rule, infant scalp hematoma, traumatic brain injury.
Appraisers	Upadhye S, Valani R
Reference(s)	Schutzman SA, Nigrovic LE, Mannix R. The Infant Scalp Score: A Validated Tool to Stratify Risk of Traumatic Brain Injury in Infants with Isolated Scalp Hematoma. Acad Emerg Med. 2021 Jan;28(1):92-97. doi: 10.1111/acem.14087. PMID: 32673432

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

Do children with a stable distal radial buckle need primary care physician follow-up?

BEEM Bottom Line

Why is this study important? Most pediatric distal radial buckle fractures have excellent healing, and there is little value added of orthopedic follow-up. This study examined the benefits/outcomes of primary care physician follow-up vs. self-care.

Which, if any, threats to validity are most likely to have an impact on the results and how? Minimal crossover between groups that may have biased results towards confirming noninferiority; mitigated by similar results in ITT vs per protocol analyses. Also, the comparison is with primary care follow up, and the PCP may not have the expertise for evaluation or provide appropriate anticipatory guidance to the patient or family.

How do the key results compare with the current evidence? These results build on prior work suggesting that simple distal radial buckle fractures in children do not require physician follow-up.

How should this study impact the care of ED patients? ED physicians can educate patients/parents on the post-immobilization care of distal radial buckle fractures, and provide specific instructions on when physician follow-up may be needed (otherwise just complete home management).

Study Summary

Article	Colaco K, Willan A, Stimec J, *et al*. Home Management Versus Primary Care Physician Follow-up of Patients with Distal Radius Buckle Fractures: A Randomized Controlled Trial. Annals Emerg Med 2021; 77: 163-173. https://doi.org/10.1016/j.annemergmed.2020.07.039
Design	Parallel 2-arm double-blinded randomized noninferiority trial. (Single urban tertiary children's hospital {Toronto Hospital for Sick Children], sees approximately 300 buckle fractures annually).
Population	*Included:* Children (5-17yo) within 3days of isolated wrist injury and confirmed diagnosis of distal radial buckle fracture (with/without ulnar buckle/styloid fracture). All children treated with prefabricated removable splint. *Excluded*: Ipsilateral forearm fracture in preceding 3mo, risk of pathologic fractures or known congenital wrist anomalies. Significant cognitive/developmental delay, insurmountable language barrier or no phone/email access for follow-up.
Intervention	Home removal of splint and self/parental assessment.
Comparison	Primary care physician (PCP) follow-up 1-2 weeks after ED visit.
Outcomes	*Primary:* Change in modified ASKp-38 score from ED visit to 3 weeks. *Secondary:* Functional recovery, use of splint, parental satisfaction. Data on health care use.

Key Results

N = 149 patients; mean age 9.5yrs, 54% male, 40% injury to dominant wrist. 73 pts home mgt, 76 to PCP. 86% completed the study protocol by 6 weeks.

Sig.	*Outcome*	*Intervention*	*Control*	*Outcome Measure (95% CI)*
NSS	Primary modASKp-38	N/A	N/A	Mean Diff -0.5% (**-2.6** to 1.3)
	ITT	N/A	N/A	Mean Diff 0.4% (**-1.9** to 2.8)
	Primary (Per Protocol, PP)	N/A	N/A	Mean Diff 0.8% (**-1.4** to 2.9)
	PP, radiologically confirmed buckle fractures			No significant differences for all secondary outcomes.
	Splint Use, Parental satisfaction			No differences in child care or medications costs.
SS	Total costs (Cdn$)			-122.30 (-169.1 to -75.5) favouring home mgt
	Total health system costs			-100.1 (-130.0 to -70.2) favouring home mgt
	Total parental costs			- 28.2 (-49.6 to -7.0) favouring home mgt
	Parental wage loss			-29.6 (-45.0 to -14.2) favouring home mgt

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	X
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = R. Valani ITT = intention to treat.

Funding and conflicts of interest

Funding PSI (gov't) grant.
Conflict of interest None (reported).

Potential threats to validity

Chance Allowances made for ED Xray discrepancies and management change at ED physician discretion; patients still included in final analyses. 4 missed Salter-Harris II fractures later treated in orthopedics clinic/ED.

Selection bias Patients recruited during Research Assistant working hours (0830-2300) daily, making it a sample of convenience. Recruited to exceed calculated sample size by 20% (SS 110, recruited 140). Patient groups otherwise properly balanced for clinical features and parental education level.

Measurement bias Non-inferiority (NI) margin set a 5% difference between two mgt options, based on prior research. Impossible to blind patients to intervention allocation, but 3wk outcomes assessment blinded.

Analysis bias ITT, Per Protocol, As Treated for radiologically confirmed distal buckle fracture. Noninferiority margin was not crossed in any calculation variation.

Confounding Crossover: 8/66 (12.1%) home mgt pts visited PCP for minor splint issues/misunderstanding of discharge follow-up instructions. 56/67 (83.6%) of PCP follow-up patients actually complied; remaining 11 did not bother. No impact on final ITT or per protocol outcomes.

Administrative details

Key words Buckle fracture, distal radius, follow-up, primary care physician
Appraisers S. Upadhye, R. Valani
Reference(s) Colaco K, Willan A, Stimec J, Barra L, Davis A, Howard A, Boutis K. Home Management Versus Primary Care Physician Follow-up of Patients with Distal Radius Buckle Fractures: A Randomized Controlled Trial. Annals Emerg Med 2021; 77: 163-173. https://doi.org/10.1016/j.annemergmed.2020.07.039

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

Is POCUS useful to diagnose skull fractures in children?

BEEM Bottom Line

Why is this study important? Children with skull fractures are at increased risk of traumatic brain injury (TBI). CT is the imaging of choice to identify TBI, but is associated with the risk of ionizing radiation. If ED POCUS can reliably rule out a skull fracture, then it can reduce CT imaging if other high-risk features of head injury are absent.

Which, if any, threats to validity are most likely to have an impact on the results and how? ED POCUS skills/experience will influence test performance characteristics.

How do the key results compare with the current evidence? Most clinical decision rules (CATCH, CHALICE, PECARN, NICE) include skull fracture as a predictor for TBI. A recent review confirmed the findings of this study (Gordon 2020).

How should this study impact the care of ED patients? ED POCUS can be a valuable adjunct for diagnosing childhood skull fracture. However, it is operator dependent. If a skull fracture can be ruled out with POCUS and there are no other high-risk features on history or physical exam to suggest TBI, then a CT-sparing strategy may be employed.

Study Summary

Article Alexandridis G, Verschuuren EW, Rosendaal AV, Kanhai DA. Evidence base for point-of-care ultrasound (POCUS) for diagnosis of skull fractures in children: a systematic review and meta-analysis. Emerg Med J 2020 Dec 3:emermed-2020-209887. doi: 10.1136/emermed-2020-209887.

Design Systematic review and meta-analysis of prospective studies evaluating POCUS diagnosis for child skull fracture.

Population *Included:* Children <18yo diagnosed with skull fracture using point-of-care ultrasound (POCUS). *Excluded*: Studies not using CT scan as reference standard. Also excluded review articles, conference abstracts and case reports.

Index Test POCUS. All scans performed by ED physicians/fellows (varied levels of training).

Reference Test CT scan of skull.

Diagnosis of Interest Pediatric skull fracture.

Key Results *N* = 7 studies, 925 patients included. ALL PATIENTS RECRUITED FROM ED SETTINGS ☺ Age range 2mo-17yrs; average 7-17yrs.

Fracture incidence 10-77%. 75% injuries due to mechanical fall.

Measure (95% CI)		I^2
Sensitivity = 91% (67-100)	Specificity = 96% (85-100)	32%
LR+ = 22.75 LR– = 0.09	*2.9% false positives, 2.2% false negatives	
AUC = Not calculated	** Results similar with high vs low fracture incidence groups, ages	

AUC = area under the curve; CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); *N* = number of patients; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search included all languages, databases, abstracts, bibliographies, and expert contact.	X	X
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	?	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	✓	✓
9. The subgroups were stated a priori and appropriate.	?	?
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = R. Valani

QUADAS = quality assessment of diagnostic accuracy studies; ROC = receiver operating characteristic curve.

Funding and conflicts of interest

Funding	None reported.
Conflict of interest	None declared.

Potential threats to validity

Chance	None?
Selection bias	None or specify comprehensive searches; publication bias. Search of various electronic databases, reference lists of included articles. No language restrictions. Assessment of publication bias by Egger's test; none detected.
Measurement bias	Overall risk of bias (RoB) for included studies: 2/7 low RoB, 5/7 some RoB (patient selection domain).
Analysis bias	Two subgroups (based on high vs low fracture %) assigned during study visual inspection. Moderate heterogeneity amongst included studies (I2 = 32%).
Confounding	Most studies (5/7) used convenience sampling, which may lead to recruiting bias. Knowledge of anatomic suture lines is essential to avoid false positives.

Administrative details

Key words	Blunt childhood head injury, point-of-care ultrasound, skull fracture.
Appraisers	Upadhye S, Valani R
Reference(s)	Alexandridis G, Verschuuren EW, Rosendaal AV, Kanhai DA. Evidece base for point-fo-care ultrasound (POCUS) for diagnosis of skull fractures in children: a systematic review and meta-analysis. Emerg Med J 2020 Dec 3:emermed-2020-209887. doi: 10.1136/emermed-2020-209887.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

Is an apple juice/preferred fluids strategy more cost-effective than electrolytes for pediatric gastroenteritis?

BEEM Bottom Line

Why is this study important? Gastroenteritis is a common presentation to the emergency department. The current recommendations are to use oral balanced rehydration solutions as part of the treatment strategy. Unfortunately, these solution is not very palatable and therefore can result in failed oral rehydration treatment. This study looked at the economic benefits of half apple strength apple juice as an alternate for oral hydration in mild cases.

What, if any, threats to validity are most likely to have an impact on the results and how? This economic analysis was based on a single non-inferiority RCT (not multiple similar trials) conducted at a single Canadian tertiary Peds ED. One of the primary end-points was physician request to cross over which would impact the results. In addition, the original trial did not use balanced solution popsicles / freezies which are more readily acceptable. These results may be less applicable to community hospitals as well as low- or middle-income countries. Subsequent unplanned health visits relied on parental self-reporting/diaries (recall bias?).

How do the key results compare with the current evidence? These economic results reinforce the prior clinical evidence supporting use of half strength apple juice /preferred fluids (+/- ondansetron), as the dominant strategy for managing gastroenteritis. Previous economic evaluations also support the use of ondansetron in ED settings to reduce vomiting.

How should this study impact the care of ED patients? Minimally/mildly dehydrated children can be started with half strength apple juice/preferred fluids (+/- ondansetron) to promote ORT and avoid IV starts/hospital admissions in a cost-effective manner.

Study Summary

Article	Schuh S. Cost-effectivenss of preferred fluids versus electrolytes in pediatric gastroenteritis. Can J Emerg Med 2021; https://doi.org/10.1007/s43678-021-00108-9
Design	Cost-effectiveness analysis (CEA) of a prior randomized controlled trial (Freedman 2016; ClinicalTrials.gov: NCT01185054)
Population	*Included:* Children aged 6-60months with acute gastroenteritis (AGE) & minimal/mild dehydration on ED presentation. Dehydration measured using Clinical Dehydration Score. *Excluded:* History of chronic gastrointestinal disease (eg, IBD, celiac disease) or other diseases (eg, DM, inborn errors of metabolism) that complicated the clinical picture; prematurity with corrected postnatal age of less than 30 weeks; bilious vomiting, hematemesis, hematochezia, or clinical concern for acute abdomen; or a need for immediate intravenous rehydration
Costing of Main Interventions	All patients treated ("no treatment" option not included) in decision analytic model. Costs calculated from local ED pricing, OHIP MD fee schedules, Ontario Case Costing Initiative (OCCI), Ontario Drug Benefits Formulary, and Statistics Canada (Table 2).
Reference Case Perspective	Societal; includes the importance of parent productivity losses in peds settings. Health system perspective also examined (excludes parent productivity losses).
Time Horizon Studied	ED discharge to 14days
Outcomes of Interest	Societal, health care system cost effectiveness

Key Results

Apple juice/preferred fluids: Societal mean cost per patient $638 ($196, $1424), health care system $402 ($114, $1146). Mean Rx failure per pt 0.17 (0.13, 0.21)

Electrolyte maintenance solution: Societal $808 ($247, $2253), health care system $550 ($155, $1974). Mean Rx failure 0.25 (0.20, 0.30)

Mean Rx failure difference: 8% (2-15%) in favour of AJ/preferred fluids

Incremental cost: Societal − $171 (− $1097, − $22), Health care system − $147 (− $1056, − $23). Mean Rx failure − 0.08 (− 0.15, − 0.02)

Apple juice/preferred fluids is **DOMINANT (less costly, more effective) vs electrolytes solutions.

Results stable to all sensitivity analyses across clinical effect and cost estimate ranges. Largest cost savings ranges noted for hospital admissions, days of admission and return ED visits.

BEEM Critique

Risk of bias assessment

	A1	A2
1. Is there a well-defined question?	✓	✓
2. Has clinical effectiveness been established?	✓	✓
3. Is there a comprehensive description of alternatives?	✓	X
4. Are all relevant costs and outcomes for each alternative identified?	✓	✓
5. Are costs and outcomes measured accurately?	✓	✓
6. Are costs and outcomes valued credibly?	✓	✓
7. Are costs and outcomes adjusted for differential timing?	?	?
8. Is there an incremental analysis of costs and consequences?	✓	✓
9. Were sensitivity analyses conducted to investigate uncertainty in estimates of costs/consequences?	✓	✓
10. Do study results include all of issues of concern to users?	✓	X
11. Are the results generalizable to the setting of interest in the study?	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Various authors have CIHR-SPOR supports. Original trial supported by PSI grant. No personal industry relationships reported.
Conflict of interest	None (reported)

Potential threats to viability

Chance	N/A. Sampling issues addressed in original trial.
Selection bias	N/A. This is a secondary analysis of a primary RCT (Freedman 2016).
Measurement bias	Use of a probabilistic analysis to account for clinical/cost estimate uncertainty; 10K Monte Carlo simulations completed to determine incremental CE point estimates/95%CI's.
Analysis bias	No ICER calculated, as AJ was dominant over electrolytes as more effective and less costly.
Confounding	*Clinicians to comment.* EE based on a single trial (no other comparable trials reviewed/meta-analyzed to increase generalizability). Subsequent unplanned health care visits relied on parental recall/diary recording (shown to be reliable for up to 1yr post ED visit).

Administrative details

Key words	Gastroenteritis . Child health . Oral rehydration therapy . Cost-effectiveness analysis
Appraisers	S. Upadhye, R. Valani
Reference(s)	1. Freedman SB, Willan AR, Boutis K, Schuh S. Effect of dilute apple juice and preferred fluids vs electrolyte maintenance solution on treatment failure among children with mild gastroenteritis: a randomized clinical trial. JAMA. 2016;315(18):1966–74. 2. Freedman SB, Steiner MJ, Chan KJ (2010) Oral Ondansetron Administration in Emergency Departments to Children with Gastroenteritis: An Economic Analysis. PLoS Med 7(10): e1000350. doi:10.1371/journal.pmed.1000350 3. Gomersall JS, Jadotte YT, Xue Y, Lockwood S, Riddle D, Preda A. Conducting systematic reviews of economic evaluations. Int J Evid Based Healthc. 2015;13(3):170–178.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the optimal dose & duration of amoxicillin to treat pediatric community-acquired pneumonia (CAP)?

BEEM Bottom Line

Why is this study important? Duration and doses of antibiotics for the treatment of infections have been arbitrary and passed down as dogma over the years. In the era of over-utilization and antibiotic resistance, there is a need to limit unnecessary use or prolonged duration. This study examined the optimal dose and duration of amoxicillin for pediatric community acquired pneumonia (CAP).

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. This was a 2x2 noninferiority design, in order to optimize treatment compliance and clinical effectiveness (avoiding need for re-treatment, CAP symptoms, adverse effects, and *S. Pneumo* resistance). Well executed factorial NI design in a pragmatic real-world multicentre setting.

How do the key results compare with the current evidence? This report summarizes a larger study published elsewhere (Barratt 2021), and mirrors findings in the Canadian 2021 SAFER study (McMaster, CHEO) that found that shorter course amoxicillin (5d vs 10d) was not superior to longer durations.

How should this study impact the care of ED patients? A shorter course and dose of amoxicillin (3 days, 35-50mg/kg daily) should be sufficient to treat uncomplicated CAP in children diagnosed in the ED.

Study Summary

Article	Rodriguez-Ruiz JP, Malhotra-Kumar S, Powell C, Faust SN, Alcock AE, Hall D, Robinson G, Hawcutt DB, Lyttle MD, Bigg DM, Sharland M, for the PERUKI, GAPRUKI, and the CAP-IT Trial Group. Effect of Amoxicillin Dose and Treatment Duration on the Need for Antibiotic Re-treatment in Children With Community-Acquired Pneumonia. The CAP-IT Randomized Clinical Trial. JAMA. 2021;326(17):1713-1724. doi:10.1001/jama.2021.17843
Design	Multi-center 2x2 noninferiority RCT, 29 hospitals (28UK, 1 Ireland). ISRCTN Identifier: ISRCTN76888927
Population	*Included:* Children 6mo (6-24kg) with clinical Dx of CAP needed amoxicillin monoRx after discharge. CAP defined as per British Thoracic Society guidelines (cough <96hrs, fever <48hrs, laboured breathing/chest signs as reported by parents) *Excluded:* (1) Uninterrupted prior β-lactam antibiotic treatment for more than 48 hours or any prior non-β-lactam treatment; (2) Severe underlying chronic disease; (3) Any contraindications to amoxicillin, including allergy; (4) Complicated pneumonia (defined as signs of sepsis or local parenchymal or pleural complications); or (5) Bilateral wheezing without focal chest signs.
Intervention	2x2 factorial trial comparing 1) Dose amoxicillin 35-50mg/kg vs 70-90mg/kg daily, and 2) 3 vs 7 day duration of Rx. Amoxil daily doses divided BID.
Comparison	N/A
Outcomes	*Primary:* Clinically indicated antibiotic (Abx) re-treatment within 28days post-randomization. NI margin set at 8%. *Secondary:* Severity/duration of 9 pt-reported CAP symptoms (fever, cough, phlegm, fast breathing, wheezing, disturbed sleep, eating/drinking less, interference with normal activity, vomiting), 3 Abx-related adverse effects (diarrhea, thrush, skin rash), *S. Pneumo* isolate resistance. Pre-specified sensitivity analyses: (1) re-treatment regardless of reason or indication; (2) retreatment specifically for CAP or chest infection; and (3) for duration, considering only re-treatments after 3days from randomization.

Key Results

824 pts randomized, 814 received 1 dose of trial medication. Median age 2.5yrs, 52% males/48% female. 591 (73%) children were discharged directly from the ED.

Primary (97%): 139 children received non-trial systemic antibiotic treatment by day 28, with criteria for the primary endpt (PEP) met in 100 (12.5% [90% CI, 10.7% to 14.6%])

a) Low vs High dose groups meeting PEP: 12.6% vs 12.4% (Diff 0.2%, -∞ to 4%)
b) Short vs Longer duration for PEP: 12.5% vs 12.5% (Diff 0.1%, -∞ to 3.9%)

Both lower dose and shorter duration was satisfied the NI criterion.

Secondary: No significant difference in cough severity, vomiting, fever, fast breathing, wheezing, interference with normal activity, appetite reduction, phlegm production between groups by dose or duration.
Cough longer in the shorter- vs longer-duration groups (median, 12 days vs 10 days; hazard ratio 1.2 [90% CI, 1.0-1.4]; P = .04).
Sleep disturbed by cough (median, 4 days vs 4 days; hazard ratio 1.2 [90% CI, 1.0-1.3]; p=0.03).
S. Pneumo isolates tested (n=647), 42% overall colonized and 16.9% had Pen-nonsusceptibility at baseline, and 29% colonized and 5% Pen-nonsusceptible at final visit (21/437). No Pen-R isolates identified in either group. No significant difference at day 28 for Pneumo colonization or nonsusceptibility based on amoxicillin dose or duration.

Adverse effects: Diarrhea 44%, skin rash 24%, oral thrush 7%. Rash more frequent with longer vs shorter Rx (27% vs 23%). No deaths.
Therapy non-completion overall 6%, and 14% took fewer doses/lower volumes than prescribed. Children receiving shorter duration more likely to complete full course (98% vs 91% longer duration Rx).
43 children (5%) ended up hospitalized, majority (87%) for respiratory illness.

Sensitivity analyses: PEP for severe CAP lower vs higher dose = 17.3% vs 13.5% (Diff 3.8%, -∞ to 10%). PEP for shorter vs longer duration = 16% vs 14.8% (Diff 1.2%, -∞ to 7.4%).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	?	?
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	X	X
8. The patients were analyzed in the groups to which they were randomized (ITT).	X*	?
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = R. Valani *Per protocol analysis required for NI trial analysis.

Funding and conflicts of interest

Funding	NIHR HTA grant; sponsor had no role in study administration.
Conflict of interest	PI spouse is senior corporate counsel at Novartis Intl (stock/stock options). Other investigators have various grants, some industry relationships outside of submitted work.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Sample size 800 needed to meet one-sided 8% NI margin, assuming 15% Rx failures and 15% loss to follow-up; recruitment goal met. No comments on consecutive vs convenience sampling, as eligible children were screened by trained staff (24hr availability?), so possible (likely) risk of sampling bias in 29 different sites.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Patients randomized in blocks of 8 into 4 different dose/duration groups; stratified by study site.
Measurement bias	Multiple tests for interactions (dosing, scheduling) did not show significant effects.
Analysis bias	*ITT, Per Protocol, As Treated.* Per protocol, analyzed in groups based on Rx received. Secondary analyses not adjusted for multiple comparisons.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Study meds blinded to all by independent repackaging, labelling, meds/placebo suspension weighting to be identical in all groups. No other cointerventions of interest described in paper/supplements. Some children with primarily obstructive airways disease may have been included, and were unlikely to respond to amoxicillin, thereby receiving re-treatment (ie. failed PEP); 16% of children received bronchodilators/steroids (distribution not specified), which may have influenced PEP.

Administrative details

Key words	Amoxicillin, community acquired pneumonia, dose/duration
Appraisers	S. Upadhye, R. Valani
Reference(s)	Barratt S, Bielicki JA, Dunn D, Faust SN, Finn A, Harper L, et al. Amoxicillin duration and dose for community-acquired pneumonia in children: the CAP-IT factorial non-inferiority RCT. Health Technol Assess 2021;25(60). Pernica JM, Harman S, Kam AJ, et al. Short-Course Antimicrobial Therapy for Pediatric Community-Acquired PneumoniaThe SAFER Randomized Clinical Trial. JAMA Pediatr. 2021;175(5):475-482. doi:10.1001/jamapediatrics.2020.6735.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the latest guidelines for the management of a well looking febrile infant (aged 8-60days)?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? Pediatric fever is a common presentation in the ED. Evaluation of febrile infants <60 days is a challenge given the risk of a serious bacterial infection balanced with invasive testing such as catheter urine specimen or lumbar puncture. These guidelines provide a good framework for investigating well appearing infants between 8 and 60 days old.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? This is a strong guideline that meets NEATS trustworthiness standards. The involvement of parents/caregivers in the guideline development process would have made this publication even more credible. Defining QI performance metrics would make these pathways easier to implement, and monitor for audit/feedback purposes.

How should this guideline, and specifically which recommendations should impact the care of ED patients? In light of changing bacterial pathogens with immunization, the need to decrease unnecessary testing, and avoid missing occult infections, these guidelines provide clear evidence-based evaluation/management algorithms for a well appearing infant between 8-60 days.

Study Summary

Article	Pantell RH, Roberts KB, Adams WG, *et al*, for the Subcommittee on Febrile Infants. Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old. Pediatrics 2021; 148(2):e2021052228
Design	Clinical Practice Guideline.
Population	Well-looking febrile infants (temp ≥ 38°C/100.4°F) aged 8-60days, with gestational birth age of 37-42 weeks. Guideline not to be used with infant is not "well-appearing." Excluded = preterm infants (<37weeks GA), infants <2weeks age with complicated perinatal course (infection/surgery), high suspicion of HSV, focal bacterial infection identified (treat as indicated), clinical bronchiolitis, documented/suspected immune compromise, congenital/chromosomal anomalies, tech intervention to sustain life, immunized within last 48hrs.
Scope	This guideline is intended for clinicians taking care of febrile infants aged 8-60days.
Key Results	42 recommendations total, stratified for infants 8-21d, 22-28d, and 29-60d.

Strength of Recommendations (Grade of Evidence Quality*) – "Clinicians should…"

Infant Age Group	Strong	Moderate	Weak
8-21days	**KAS 1**: Should obtain urine specimen by catheterization or suprapubic aspiration (SPA) of bladder for urinalysis and, if urinalysis result is positive, for culture. (A) **KAS 2**: Should obtain a blood culture. (A) **KAS 4**: Should obtain CSF for analysis (WBC, protein, glucose, Gram stain) and culture for bacteria. (A)	**KAS 6**: Should actively monitor infants while awaiting results of bacterial cultures in a hospital setting with nurses and staff experienced in the care of neonates/young infants. (B) **KAS 7a**: Should discontinue parenteral antimicrobial agents and discharge hospitalized patients when all of the following criteria are met: (1) culture results are negative for 24–36 h or only positive for contaminants; (2) the infant continues to appear clinically well or is improving (eg, fever, feeding); (3) there no other reasons for hospitalization. (B)	**KAS 3**: May assess IM**s. (B)

	KAS 5: Should initiate parenteral antimicrobial therapy. (A) **KAS 7b**: Should treat infants' positive bacterial pathogens in urine, blood, or CSF with targeted antimicrobial therapy for the duration of time consistent with the nature of the disease, responsible organism, and response of the infant to treatment. (A)		
22-28days	**KAS 8**: Should obtain urine specimen by catheterization or SPA of bladder forurinalysis and, if urinalysis result is positive, for culture OR Should obtain urine specimen by bag, spontaneous void, or stimulated void for urinalysis and, if urinalysis result is positive, obtain a catheterization or SPA specimen for culture. (A) **KAS 9**: Should obtain a blood culture. (A) **KAS 12a**. Should administer parenteral antimicrobial therapy in a hospital if either of the following apply: (1) CSF analysis suggests bacterial meningitis; (2) urinalysis result is positive. (A) **KAS 14c**: Should treat infants' positive bacterial pathogens in urine, blood, or CSF with targeted antimicrobial therapy for the duration of time consistent with the nature of the disease, responsible organism, and response of the infant to treatment. (A)	**KAS 10**: Should assess IMs. (B/Strong) **KAS 11b**. Should obtain CSF for analysis (WBC, protein, glucose, Gram stain), and bacterial culture if any IM obtained is positive. (B) **KAS 12b**. May administer parenteral antimicrobial therapy in a hospital if ALL of the following apply: (1) CSF analysis is normal; (2) urinalysis is normal; (3) Any IM obtained is abnormal. (B) **KAS 12c**. May administer parenteral antimicrobial therapy to hospitalized infants even if ALL of the following are met: (1) urinalysis is normal; (2) no IM obtained is abnormal; (3) CSF analysis is normal or enterovirus-positive. (B/Weak) **KAS 13a**: May manage infants at home if all of the following criteria are met: (1) Urinalysis is normal; (2) No IM obtained is abnormal. (3) CSF analysis is normal or enterovirus-positive. (4) Verbal teaching and written instructions have been provided for monitoring throughout the period of time at home. (5) Follow-up plans for reevaluation in 24 h have been developed and are in place. (6) Plans have been developed and are in place in case of change in clinical status, including means of communication between family and providers and access to emergency medical care. (B) **KAS 13b**: Should hospitalize infants in a facility with nurses and staff experienced in the care of neonates/young infants when CSF is not obtained or is uninterpretable. (B/Weak) **KAS 14a**: Should discontinue antimicrobial agents and discharge hospitalized infants after 24 to 36 h	**KAS 11a**: Clinicians may obtain a CSF analysis on infants 22–28 d of age even if all of the following criteria are met: (1) urinalysis result is negative or positive; (2) no IM obtained is abnormal; (3) blood and urine cultures have been obtained; (4) infant is hospitalized. (C/Mod) **KAS 12d**: Should administer parenteral antimicrobial therapy for infants who will be managed at home even if ALL of the following are met: (1) urinalysis is normal; (2) No IM obtained is abnormal; (3) CSF analysis is normal. (C/Mod)

		of negative culture results if both of the following are met: (1) the infant is clinically well or improving (eg, fever, feeding); (2) there are no other reasons for hospitalization. (B/Strong) **KAS 14b**: Should discontinue antimicrobial agents on infants managed at home when all of the following criteria are met: (1) infant is clinically well or improving (eg, fever, feeding) at time of reassessment; (2) all culture results are negative at 24–36 h; (3) there is no other infection requiring treatment (eg, otitis media). (B/Strong)	
29-60days	**KAS 15**: Should obtain urine specimen by bag, spontaneous void, or stimulated void for urinalysis and, if urinalysis result is positive, obtain a catheterization or SPA specimen for culture, OR Should obtain urine specimen by catheterization or SPA of bladder for urinalysis and, if result is positive, for culture. (A) **KAS 19a**: Should use parenteral antimicrobial therapy if CSF analysis suggests bacterial meningitis. (A) **KAS 20a**: Should hospitalize infants in a unit with nurses and staff experienced in the care of 29- to 60-d-old infants if CSF analysis, if obtained, is abnormal. (A) **KAS 21d**: Should treat infants' positive bacterial pathogens in urine, blood, or CSF with targeted antimicrobial therapy for the duration of time consistent with the nature of the disease, responsible organism, and response of the infant to treatment. (A)	**KAS 16:** Should obtain a blood culture. (B) **KAS 17:** Should assess IMs. (B) **KAS 18b**: Need not obtain CSF for analysis and culture if all IMs obtained are normal. (B) **KAS 19b**: May use parenteral antimicrobial therapy if both of the following apply: (1) CSF analysis (if CSF obtained) is normal; (2) any IM obtained is abnormal. (B) **KAS 19c**: Should initiate oral antimicrobial therapy if all of the following apply: (1) CSF analysis (if CSF obtained) is normal; (2) urinalysis result is positive; (3) no IM obtained is abnormal. (B) **KAS 19d**: Need not use antimicrobial therapy while awaiting bacterial culture results if all of the following are met: (1) CSF analysis, if obtained, or normal or enterovirus-positive; (2) urinalysis result is negative; (3) no IM obtained is abnormal. (B) **KAS 20b**: May hospitalize infants in a unit with nurses and staff experienced in the care of 29- to 60d-old infants if any IM obtained is abnormal. (B) **KAS 20c**: Should manage patients at home if all of the following criteria are met: (1) CSF analysis, if CSF obtained, is normal; (2) urinalysis result is negative; (3) all IMs obtained are normal; (4) appropriate parental education has been provided; (5) follow-up plans for reevaluation in 24 h have been developed and are in place (6) plans have been developed and are in place in case of change in clinical status, including means of communication between family and providers and access to emergency medical care. (B)	**KAS 18a**: May obtain CSF for analysis (WBC, differential, protein, glucose, Gram stain), culture for bacteria, and test for enterovirus when CSF pleocytosis is detected or during enterovirus season if any IM is abnormal. (C) **KAS 20e**: Need not treat with antimicrobial therapy if all of the following apply: (1) CSF analysis (if CSF obtained) is normal; (2) urinalysis result is negative; (3) no IM obtained is abnormal. (C/Mod)

		KAS 20d: May manage infants without antimicrobial treatment at home without having obtained interpretable CSF if all of the following are met: (1) urinalysis result is negative; (2) all IMs obtained are normal; (3) parents can return promptly if there is a change in infant condition and agree to follow-up in 24 to 36 h. Infants monitored at home should be reassessed in the following 24 h. (B) **KAS 21a**. Should discontinue antimicrobial agents when all of the following are met: (1) all bacterial culture results are negative at 24–36 h; (2) infant is clinically well or improving (eg, fever, feeding); (3) there is no other infection requiring treatment (eg, otitis media). (B/Strong) **KAS 21b**: Should discharge hospitalized patients with positive urine culture (UTI) results if all of the following are met: (1) blood culture result is negative; (2) result of CSF culture, if obtained, is negative; (3) infant is clinically well or improving (eg, fever, feeding); (4) there are no other reasons for hospitalization. (B/Strong) **KAS 21c**: Should discontinue parenteral antibiotics (if started) and begin or continue oral antimicrobial for infants with UTIs managed at home when all of the following are met: (1) urine culture result is positive; (2) all other bacterial culture results are negative at 24–36 h; (3) infant is clinically well or improving (eg, fever, feeding). (B/Strong).	

*Evidence Quality: A=Strong, B=Moderate, C=Weak unless otherwise specified.

**IM = Inflammatory Mediators (CRP, Procalcitonin, WBC/ANC)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	✓
2. Systematic methods were used to search for evidence.	✓	✓
3. The criteria for selecting the evidence are clearly described.	✓	✓
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	✓	✓
8. The content of the guideline is free of influence by the views of the funding body.	✓	✓
9. Competing interests of guideline development group members have been recorded and managed.	✓	✓
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	None (reported).
Conflict of interest	3 subcommittee members had some commercial/industry disclosures. No members of the writing committee had reported conflicts.

Potential threats to validity

Development	Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible? **Extensive 2021 systematic review (300pgs) published in support of these CPG recommendations. No patient/parent stakeholders in working groups.**
Presentation	Well organized with easy to find recommendations? **Yes; Key Action Statements summarized in Table 1.**
Comprehensive	Was the information to inform decision-making complete? **Yes; benefits, harms/risks, costs detailed for each Key Action Statement.**
Clinical Validity	Are the recommendations clinically sound and appropriate for the intended patients? **Yes**

Administrative details

Key words	Clinical practice guideline, febrile illness, infants 8-60days.
Appraisers	Upadhye S, Valani R
Reference(s)	Pantell RH, Roberts KB, Adams WG, Dreyer BP, Kupperman N, O'Leary ST, Okechukwu K, Woods CR, for the Subcommittee on Febrile Infants. Pediatrics 2021; 148(2):e2021052228 PMID: 34281996 Hui C, Neto G, Tsertsvadze A, et al. Diagnosis and management of febrile infants (0-3 months). Evid Rep Technol Assess (Full Rep). 2012;205(205):1–297.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

Can parental medical education improve safety of fever medications administered to children?

BEEM Bottom Line

Why is this study important? Pediatric fever is a common presentation to the Emergency Department (ED). Appropriate management with antipyretics helps with symptom management. Unfortunately, dosing errors are common (70%) with acetaminophen and ibuprofen, leading to health-care overutilization (both under- and over-dosing). A multimodal teaching intervention at ED discharge could reduce the risk of medication errors.

Which, if any, threats to validity are most likely to have an impact on the results and how? Substantial loss to follow-up threatens the statistical significance of primary outcome (explored in online appendices). Unclear how long it takes to deliver the teaching intervention, which may be a barrier to implementation.

How do the key results compare with the current evidence? These results build on prior work that support the same conclusions.

How should this study impact the care of ED patients? There is a need for appropriate discharge instructions that include dosing of antipyretics for febrile children. A multimodal caregiver teaching intervention that includes lay language, providing handouts, and a teach back process for weight based antipyretic medication administration reduces early dosing errors.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article Naureckas C, Camargo CA, Faridi M, *et al*. Medication Education for Dosing Safety: A Randomized Controlled Trial. Annals Emerg Med 2020; 76: 637-645. https://doi.org/10.1016/j.annemergmed.2020.07.007

Design Enter text here. State true design not what the investigators call it.

Population *Included:* Parents of febrile children (age 90d-11.9yrs) being discharged from ED with plan to use liquid antipyretics, fluent in English/Spanish, and reachable for telephone follow-up within 7days. *Excluded*: Children with complex chronic medical conditions, planned use of nonstandard weight-based meds, children not accompanied by parent/legal guardian.

Intervention Standard discharge teaching PLUS child-specific dosing algorithm, demonstration of meds loading in syringe by RA, "teach-back" cycles where parent demonstrated appropriate skills acquisition of meds loading/ administration, then parent sent home with same syringe.

Comparison Standard discharge teaching.

Outcomes *Primary:* Parent/guardian report of safe dosing at first f/u call (defined as within 20% of weight-based dose at ED discharge). Correction of dosing information by RA if needed.
Secondary: Safe dosing report at 2nd f/u call.

Key Results *N* = 149 patients. 66 allocated to intervention, 83 to controls. 35 analyzed at both calls in Int group; 62 and 41 analyzed at 1st and 2nd calls in controls.

Sig.	*Outcome*	*Intervention*	*Control*	*Outcome Measure (95% CI)*
NSS	Secondary: Call 2			aRR* 0.97 (0.74-1.27)
SS	Primary: Call 1			RR 1.58 (1.12-2.24) aRR* 1.50 (1.06-1.23) favouring intervention

*aRR = adjusted relative risk for health literacy, parental language

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The patients were recruited consecutively.	?	X	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓	?✓X
3. The allocation sequence was adequately concealed.	✓	✓	?✓X
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓	?✓X
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓	?✓X
6. All groups were treated equally except for the intervention.	✓	✓	?✓X
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	X	X	?✓X
8. The patients were analyzed in the groups to which they were randomized (ITT).	?	✓	?✓X
9. All patient-important outcomes were considered.	✓	✓	?✓X
10. The effect size of the primary outcome is clinically significant.	?	?	?✓X

A1 = S. Upadhye A2 = R Valani A3 = ITT = intention to treat.

Funding and conflicts of interest

Funding This work was supported by the Massachusetts General Hospital Department of Emergency Medicine Fellowship Eleanor and Miles Shore 50th Anniversary Fellowship Program for Scholars in Medicine, the National Center for Advancing Translational Sciences, and National Institutes of Health Award UL 1TR002541.

Conflict of interest None (not explicitly reported?).

Potential threats to validity

Chance Appropriate sample size calculations based on prior research done in investigators workplace. Low response to initial follow-up calls led to protocol change to send text messages before phone calls; improved call responses seen thereafter. Single site intervention may limit generalizability to other workplaces.

Selection bias Patients recruited during work hours when bilingual research assistants available.

Measurement bias None?

Analysis bias ITT vs per protocol analyses not specified. Substantial loss to follow-up in both arms; first phone call responses = 53% in Int arm, 75% in control arm. Various impacts of LTFU explored in online Appendices.

Confounding Unable to blind patients/RA's to allocation, but treating providers & outcomes assessors were blinded.

Administrative details

Key words Enter up to 5 key words here (in alphabetical order, separated by semicolons and a period at the end).

Appraisers Upadhye S,

Reference(s) Naureckas C, Camargo CA, Faridi M, Espinola JA, Hayes BD, Porter S, Cohen A, Sameuls-Kalow M. Medication Education for Dosing Safety: A Randomized Controlled Trial. Annals Emerg Med 2020; 76: 637-645. https://doi.org/10.1016/j.annemergmed.2020.07.007

Clinical Appraisal faculty

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Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

What is the efficacy and safety of ibuprofen vs acetaminophen for treating febrile children <2yo?

BEEM Bottom Line

Why is this study important? Mild to moderate pain and fever is effectively treated in children < 2 years old with ibuprofen or acetaminophen. This study compared these two agents at fours hours from time of administration, as well as any serious adverse events related to their use.

Which, if any, threats to validity are most likely to have an impact on the results and how? Single author abstract screening may lead to a selection bias of articles included. All studies under-powered for pain/safety outcomes. The clinical significance f

How do the key results compare with the current evidence? These results are congruent with evidence of efficacy/safety from studies in older children.

How should this study impact the care of ED patients? Ibuprofen was found to be better at reducing fever in <4 hrs, and was better for fever and pain reduction in the 4-24hr window. Beyond 24 hrs, there was little difference in pain control between the two agents. There was no difference in the safety profile between the two agents.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Tan E, Braithwaite I, McKinlay JD, Salziel SR. Comparison of Acetaminophen (Paracetamol) with Ibuprofen for Treatment of Fever or Pain in Children Younger Than 2 Years. A Systematic Review and Meta-analysis. JAMA Netw Open 2020; 3(10): e2022398. doi: 10.1001/jamanetworkopen.2020.22398.
Design	Systematic review and meta-analysis of all studies comparing acetaminophen with ibuprofen.
Population	*Included:* All studies (any design) comparing acetaminophen vs ibuprofen in children <2yo. *Excluded*: Case series, studies with other medical cointerventions.
Intervention	Ibuprofen (various doses).
Comparison	Acetaminophen (various doses).
Outcomes	*Primary:* Pain or fever within 4hrs of initial Rx. *Secondary:* Fever/pain at 4-24hrs, 1-3days, and >3days. Safety outcomes (< and >28d) = renal impairment, GI bleeds, hepatotoxicity, severe soft tissue infection, empyema, asthma/wheeze,

Key Results

19 studies, 241138 children. NO INCLUDED STUDIES for Primary Pain<4hrs outcome.

Sig.	*Outcome*	*Quality of Evidence*	*Outcome Measure (95% CI)*	I^2
NSS	Primary: Fever<4hrs (nonRCT)	Very Low	SMD -0.04 (-0.40 to 0.31)	0%
	Sec: Serious A/E <28d	Mod to Very Low	VERY LOW rates of any serious A/E's (most studies had zero). No significant differences for overall/individual A/E's.	
	Sec: Fever Red	Mod to Low	No difference fever 1-3 days, and >3days	
	Sec: Pain >24hrs	Low	No difference pain 1-3days, and >3days	
SS	Primary: Fever reduction <4hrs (RCTs)	Moderate	SMD 0.38 (0.08-0.67) favours ibuprofen*	49%
	Sec: Afebrile<4hrs (RCT)	Moderate	OR 1.86 (1.01-3.44) favours ibuprofen	
	Sec: Fever Red 4-24hrs	Moderate	SMD 0.24 (0.03-0.45) favours ibuprofen	
	Sec: Pain 4-24hrs	Moderate	SMD 0.20 (0.03-0.37) favours ibuprofen	

*No difference on higher or lower doses of antipyretics, nor on sensitivity analyses of excluding RCTs with high RoB (all prespecified subgroup analyses).

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	✓	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓	?✓X
3. The search for studies was unbiased and reproducible.	✓	✓	?✓X
4. The selection of studies was unbiased and reproducible.	?	✓	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓	?✓X
7. The quality of the primary studies is high.	X	X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓	?✓X
9. The outcomes are clinically relevant.	✓	✓	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	?	?✓X

A1 = S. Upadhye A2 = R Valani A3 =

Funding and conflicts of interest

Funding	Support by several New Zealand university fellowship/govt grants.
Conflict of interest	Support by national govt grants.

Potential threats to validity

Chance	None?
Selection bias	Thorough unrestricted search of electronic and other evidence sources. Titles/abstracts screened by a single author. No analysis for publication bias described/reported.
Measurement bias	None or enter text here (e.g., missing details on study selection; missing results of quality assessments). Quality appraisal with Cochrane Risk of Bias (RoB) tool (RCTs), ROBIN-I (non-RCTs). Overall evidence review with GRADE. High RoB for 2 RCTs, all non-RCTs considered moderate/serious RoB.
Analysis bias	None.
Confounding	Randomized studies of higher quality were more likely to show significant benefits compared to non-randomized trials. Potential classification bias of outcomes based on definitions used in individual studies.

Administrative details

Key words	Acetaminophen, febrile child, ibuprofen.
Appraisers	Upadhye S, Valani R
Reference(s)	Tan E, Braithwaite I, McKinlay JD, Salziel SR. Comparison of Acetaminophen (Paracetamol) with Ibuprofen for Treatment of Fever or Pain in Children Younger Than 2 Years. A Systematic Review and Meta-analysis. JAMA Netw Open 2020; 3(10): e2022398. doi: 10.1001/jamanetworkopen.2020.22398.

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Associate Professor of Medicine, University of Toronto

Research Question

What exam features or diagnostic tests are useful to diagnose septic arthritis in limping children?

BEEM Bottom Line

Why is this study important? Septic arthritis (SA) is a rare yet critical diagnosis to exclude in the limping child. Early identification and treatment ≤ 4 days from onset is the most important prognostic factor in preventing complications. This study updates current evidence on clinical examination and investigations for SA in limping children.

Which, if any, threats to validity are most likely to have an impact on the results and how? Inconsistent definitions and reporting of clinical findings, spectrum bias, and uncertain time intervals between index and reference tests erode the already weak performance characteristics of various clinical, lab and imaging modalities for diagnosing pediatric septic arthritis.

How do the key results compare with the current evidence? These results mirror the relative paucity of reliable clinical markers for adult septic arthritis (Carpenter et al, 2011).

How should this study impact the care of ED patients? While the Kocher (Kocher, 2004) and Caird (Caird, 2006) criteria have been used to help identify patients at high risk, there are no clinical/lab/imaging features that can reliably rule out SA in febrile limping children. This may necessitate moving onto joint aspiration for definitive diagnosis.

Study Summary

Article	Tu J, Gowdie P, Cassar J, Craig S. Test characteristics of history, examination and investigations in the evaluation for septic arthritis in the child presenting with acute non-traumatic limp: A systematic review. BMJ Open 2020;10:e038088. doi:10.1136/bmjopen-2020-038088.
Design	Systematic review of diagnostic studies for pediatric septic arthritis.
Population	*Included:* All studies describing pediatric patients with monoarticular complaints (limp, altered gait, non-weight bearing, limb pain/swelling) with suspicion of septic arthritis (SA). *Excluded*: Patients without monoarticular complaint, adult/mixed populations, no extractable data determining test characteristics, no reference standard for SA Dx.
Index Test	History/physical exam findings, lab investigations, imaging results.
Reference Test	Abnormal synovial fluid findings (macroscopic appearance, elevated WBC count, fluid/blood culture results).
Diagnosis of Interest	Septic arthritis.

Key Results

N = 18 studies, 2672 children; 560 confirmed septic arthritis.

	Index Test Likelihood Ratio (95% CI)
Useful	Fever (any level): LR+ 2 to 25.2 (1.7-78), LR- 0.2-0.8 Joint tenderness: LR+ 11.4 (5.9-22.0), LR- 0.3 (0.2-0.5); single study Labs (7 studies): ESR LR+ 2 to 12, LR- 0.1-0.9; CRP LR+ 1.2-12.3, LR- 0.1-0.7 Imaging: US joint effusion LR+ 8.4 (4.1-17.1), LR- 0.2 (0.1-0.3); single study n=30 kids
Not useful	Clinical: Male gender, history of tick bites, prior antibiotic use, history of chills, joint pain, recent illness Laboratory: WBC count, procalcitonin (single small study) Imaging: Plain radiographs of joint
Unknown	Kocher CDR (non-weightbearing status, fever, WBC>12, ESR>40mm/hr): AUC 0.96 derivation, 0.80 and 0.86 on validation. Caird CDR (Kocher criteria + CRP>20mg/L): PPV (5 criteria positive) 98% derivation, 60% external validation?

AUC = area under the curve; CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); *N* = number of patients; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search included all languages, databases, abstracts, bibliographies, and expert contact.	X	X
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	X	X
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	X	X
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = R. Valani

QUADAS = quality assessment of diagnostic accuracy studies; ROC = receiver operating characteristic curve.

Funding and conflicts of interest

Funding	None (reported).
Conflict of interest	None (declared).

Potential threats to validity

Chance	Spectrum bias likely had an impact (over-estimation) of index test performance in study samples.
Selection bias	Limited electronic search (MedLine, EMBASE); no mention of gray literature, conference abstracts, article reference lists. English language articles only. No mention/reporting of publication bias analysis.
Measurement bias	Lack of blinding in outcome assessors between index and reference tests. Unknown times between index and reference tests can affect index test performance (eg. CRP, ESR).
Analysis bias	Unable to pool data for meta-analysis due to widespread heterogeneity between included studies.
Confounding	A number of clinical, exam and radiographic variables did not share the same definition, which could affect how variable outcomes are interpreted. Also, there was variability in the definition of SA, which would affect diagnostic test outcomes. No time interval reporting between index and reference tests.

Administrative details

Key words	Limping child, septic arthritis
Appraisers	S Upadhye, R Valani
Reference(s)	Tu J, Gowdie P, Cassar J, Craig S. Test characteristics of history, examination and investigations in the evaluation for septic arthritis in the child presenting with acute non-traumatic limp: A systematic review. BMJ Open 2020;10:e038088. doi:10.1136/bmjopen-2020-038088. Kocher MS, Zurakowski D, Kasser JR. Differentiating between septic arthritis and transient synovitis of the hip in children: an evidence-based clinical prediction algorithm. J Bone Joint Surg Am 1999;81:1662–70. Caird MS, Flynn JM, Leung YLEO, et al. Factors distinguishing septic arthritis from transient synovitis of the hip in children. J Bone Joint Surg Am 2006;88:1251–7.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

What are the predictors of severe illness in community children with fever?

BEEM Bottom Line

Why is this study important? Pediatric fever is a common presentation to the Emergency Department (ED). Early recognition of serious illness is important to prevent significant morbidity and mortality. Predictors that can help identify sick children early can enable the clinician to aggressively manage these patients and mitigate poor outcomes.

Which, if any, threats to validity are most likely to have an impact on the results and how? Most studies were too heterogeneous to pool results. Spectrum bias with mostly hospitalized children limit generalizability to community settings (validity in ED?).

How do the key results compare with the current evidence? These results are congruent with prior reviews, especially with children from low/middle-income countries.

How should this study impact the care of ED patients? The most valuable predictors were poor nutritional status, altered level of consciousness, acidosis, and poor peripheral perfusion. The heterogeneity of studies precluded conclusive evaluation of items such as hypoglycemia. Due to the heterogeneity of where the studies originated from, it is difficult to generalize the findings.

Study Summary

Article	Chandna A, Tan R, Carter M, *et al*. Predictors of disease severity in children presenting from the community with febrile illnesses: a systematic review of prognostic studies. BMJ Global Health 2021;6:e003451. doi:10.1136/bmjgh-2020-003451.
Design	Systematic review of prognostic studies in pediatric febrile illness severity.
Population	*Included:* Prognostic studies with children >28days and <19yrs old with community acute febrile illness and suspected sepsis. *Excluded*: No pediatric prognostic data reported in included studies, or patients recruited from admitted inpatients. No specific clinical syndromes or pathogens included. Variables not available at time of presentation also excluded.
Index Test	Various clinical predictor variables for febrile illness at community presentation.
Reference Test	Hospital/ICU admission, mortality.
Diagnosis of Interest	Suspected sepsis/severe illness requiring admission, death.

Key Results

N = 18 studies, 24530 children evaluated.

Prognostic Group	*Prognostic Variable (n=studies), Likelihood Ratios (95% CI)*	
Clinical	Malnutrition; n=5	LR+ 1.56-11.13, LR- 0.87-0.95
	Prostration; n=2	LR+ 0.87-3.88, LR- 0.18-1.23
	Resp distress; n=5	LR+ 1.36-7.71, LR- 0.28-0.64
	Jaundice; n=1	LR+ 5.42 (3.65-8.06), LR- 0.78 (0.70-0.88)
	Comorbidity; n=6 (4 HIV+)	LR+ 1.35-12.48, LR- 0.12-0.97
	Oxygen Sat (<90%); n=3	LR+ 2.10-9.49, LR- 0.73-0.86
	Bradycardia (80-105bpm); n=3	LR+ 5.95-14.59, LR- 0.91-0.94
	Peripheral hypoperfusion; n=6	LR+ 1.78-17.38, LR- 0.61-0.93
	Hypotension; n=4	LR+ 1.89-9.57, LR- 0.79-0.92
	Decreased LOC; n=11	LR+ 0.95-14.02, LR- 0.27-1.04
Lab	Elevated Lactate (>4mM); n=6	LR+ 2.28-5.13, LR- 0.13-0.87
	Hypoglycemia (<2.5mM); n=3	LR+ 5.10-13.36, LR- 0.75-0.87
	Hyperkalemia; n=1	LR+ 6.64 (4.46-9.89), LR- 0.84 (0.78-0.89)
Clinical prediction models	Outcome: Mortality, organ support, PICU admit (n=28)	AUROC 0.55-0.97
	Hospital LOS, symptom duration (n=5)	AUROC 0.49-0.64

AUC = area under the curve; CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); LR = likelihood ratio (because this is a ratio, if the value of the range includes 1, there is no difference); *N* = number of patients; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	X	X
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	X	X
9. The subgroups were stated a priori and appropriate.	X	X
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = R. Valani

QUADAS = quality assessment of diagnostic accuracy studies; ROC = receiver operating characteristic curve.

Funding and conflicts of interest

Funding	Government/university research trust funding.
Conflict of interest	None (declared).

Potential threats to validity

Chance	Most of the studies included hospitalized children, not community-based (spectrum bias).
Selection bias	Search of electronic databases (no language restrictions) with "snowballing" of reference lists. No gray literature/conference abstracts mentioned. No mention of publication bias analysis.
Measurement bias	Quality assessment completed independently using QUIPS/PROBAST tools. Only two studies considered low risk of bias.
Analysis bias	High heterogeneity precluded meta-analysis.
Confounding	A number of studies from sub-Saharan Africa (higher rates of malaria, HIV) contributed to specific predictor variables (eg. malnutrition) that may not be generalizable to higher-income countries.

Administrative details

Key words	Community, febrile illness, severity prediction.
Appraisers	S. Upadhye, R. Valani
Reference(s)	Chandna A, Tan R, Carter M, Van Den Bruel A, Verbakel J, Koshiaris C, Salim N, Lubell Y, Turner P, Keitel K. Predictors of disease severity in children presenting from the community with febrile illnesses: a systematic review of prognostic studies. BMJ Global Health 2021;6:e003451. doi:10.1136/bmjgh-2020-003451.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

How accurate is point-of-care ultrasound (POCUS) in diagnosing clinically important pediatric intussusception?

BEEM Bottom Line

Why is this study important? Intussusception is the most common cause of bowel obstruction in children <6 yo. Ultrasound is the preferred Dx diagnostic test of choice, prior to radiologic/surgical reduction. ED-based POCUS may be a diagnostically accurate alternative to traditional radiologist ultrasound (RADUS). This study is a prospective global Peds pediatric ED-based noninferiority project examining the diagnostic accuracy of ED POCUS for clinically important intussusception.

What, if any, threats to validity are most likely to have an impact on the results and how? Convenience sampling at study centres may lead to selection bias and spectrum bias. The study was slightly underpowered for sample size requirements needed.

How do the key results compare with the current evidence? Prior small studies support the accuracy/safety of ED POCUS as a RADUS alternative, although these are small trials, and/or retrospective studies. This prospective study reinforces past retrospective findings. The likelihood ratios for ED POCUS show outstanding/demonstrate clinically useful test performance characteristics (LR+ >10, LR- <0.05).

How should this study impact the care of ED patients? With training/experience, ED sonologistsemergency physicians can likely use POCUS to make accurate and faster earlier diagnoses diagnosis of pediatric intussusception, and timely referral to pediatric surgeons for management.

Study Summary

Article	Bergman KR, Arroyo AC, Tessaro MO, et al, on behalf of the P2Network. Diagnostic Accuracy of Point-of-Care Ultrasound for Intussusception: A Multicenter, Noninferiority Study of Paired Diagnostic Tests. Annals Emerg Med 2021; 78: 606-616. https://doi.org/10.1016/j.annemergmed.2021.04.033
Design	Prospective multicentre cohort noninferiority trial in 17 pediatric EDs in North/Central America, Europe and Australia.
Population	*Included:* Children aged 3mo-6yo with clinical suspicion of intussusception and RADUS orders. *Excluded:* Children with imaging results from referring facilities.
Index Test	Point of care ultrasound (POCUS)
Reference Standard	Radiology-performed US (RADUS)
Diagnoses of Interest	*Primary:* Diagnostic accuracy to detect clinically important intussusception (defined as needing radiographic or surgical reduction). *Secondary:* Agreement between POCUS and RADUS, serious complications (peritonitis, bowel perforation, intestinal obstruction, or death). Planned sensitivity analyses: proportion of correct POCUS interpretations in children with/ without intussusception, and diagnostic accuracy of POCUS after eliminating one study site.

Key Results

(LR calculated from reported Sens, Spec, Prev & sample size data at: http://araw.mede.uic.edu/cgi-bin/testcalc.pl)

262 children enrolled, 256 included in primary analysis. Median age 21.1 mo (IQR 8.9-40.6mo), CC abdominal pain (82.8%) or fussiness (80.5%). Median enrollment per site = 15 cases.
96.9% had POCUS before RADUS, and 94.9% had at least 8 images/clips per scan.

58 children had primary outcome (22.7%); 21.5% radiographically reduced, 6.3% surgically reduced.

POCUS identified 60 cases (23.4%) for primary outcome; 4 false positives, 2 false negatives. Similar results with RADUS.

POCUS (vs clinical Dx confirmation): Overall accuracy 97.7% (94.9-99.0), Sens 96.6% (87.2-99.1), Spec 98.0 (94.7-99.2); LR+ 48, LR- 0.03

RADUS (vs clinical Dx confirmation): Overall accuracy 99.3 (96.8-99.9), Sens 98.3 (88.7-99.8), Spec 99.5 (96.5-99.9); LR+ 58, LR- 0.01

POCUS (vs RADUS): Overall accuracy 97.0 (94.0-98.6), Sens 94.8 (85.1-98.3), Spec 97.5 (94.1-99.0); LR+ 38, LR- 0.05. Agreement = 96.9% (Cohen's kappa 0.911).

Absolute difference POCUS vs RADUS: 1.5% (-0.6 to 3.6); within NI margin of 4%

Site B removed: POCUS accuracy 97.5%, Sens 92.9%, and Spec 97.9%. No differences in POCUS interpretations with/without prior intussusception in the previous 14 d.

Median POCUS scan time: 6min (IQR 4-9), median time to RADUS 65min (40-106).

Telephone f/u 190 children (74.2%); those lost to follow-up were demographically similar to those during index visit.
Return to ED within 7d of discharge = 14 children (7.4%).
Serious complications in 5 children (2%); all correctly identified by POCUS at index visit.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those likely to undergo testing in the ED.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	?	X
3. All patients underwent the same diagnostic evaluation.	✓	✓
4. All tests were conducted within similar time frames to preclude changes in disease status.	✓	✓
5. The reference standard criteria for the candidate diagnoses are explicit and reproducible.	✓	✓
6. The reference standard was applied regardless of and blinded to the index test result.	✓	✓
7. The assignment of the candidate diagnoses was explicit and reproducible.	✓	✓
8. Most (> 80%) patients received a diagnosis.	✓	✓
9. Undiagnosed patients received adequate clinical follow-up.	✓	?
10. The estimates of disease probability are clinically significant.	✓	✓

A1 = S. Upadhye A2 = D. Kim

Funding and conflicts of interest

Funding	Partial grant from Research Committee of Children's Hospitals and Clinics of Minnesota.
Conflict of interest	Ron Berant provides consulting services to GE.

Potential threats to viability

Chance	Children recruited consecutively when study sonologist available (risk of sampling and spectrum bias). Sample size was slightly underpowered (<90% planned sample size). If RADUS was completed first, child got POCUS ASAP afterwards (blinded to RADUS results).
Selection bias	Is the sampling method representative of the target population; are the groups balanced? Site B: higher proportion of intussusception transfers, more bloody stool presentations (late finding). Enrolled patients on a convenience basis when a study sonologist was present.
Measurement bias	Noninferiority margin set at 4% a priori; 258 children sample size required.
Analysis bias	
Confounding	35 trained POCUS sonologists (PEM physicians who had: completed a POCUS fellowship, held RDMS designation, or had completed at least 20 abdominal POCUS scans with at least 1 positive intussusception study).

Administrative details

Key words	Clinically important intussusception, POCUS, RADUS
Appraisers	Upadhye S; Kim D.
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Daniel Kim, MD FRCPC
Clinical Associate Professor, Department of Emergency Medicine, University of British Columbia
Medical Advisory Board, Clarius Mobile Health (no relevance to current appraisal)

Research Question

Is intranasal ketamine noninferior to intravenous ketorolac for treating pediatric migraines?

BEEM Bottom Line

Why is this study important? Intranasal (IN) route of medication administration has become increasingly popular for a variety of clinical situations. Several medications such as benzodiazepines and opioids have been shown to provide the necessary effect and without the need for delay in treatment or the need for IV insertion. This study examined the possibility of using IN ketorolac for pediatric migraine treatment.

What, if any, threats to validity are most likely to have an impact on the results and how? The investigators did not achieve their required sample size (80, 59 enrolled, 56 analyzed), so one can't be confident of possible Type II error. Trial also not powered to detect differences in secondary outcomes. In addition, a higher IN dose was given compared to IV which questions the equivalency of the two therapies. Finally, since all patients received a 20mL/kg bolus of normal saline IV, the study did not avert the need for IV insertion.

How do the key results compare with the current evidence? These results suggest that intranasal medications have a role in treatment. However, the need for IN route should be to provide immediate treatment or avoid IV insertion, both of which were not shown in this study.

How should this study impact the care of ED patients? Intranasal ketorolac can be a useful alternative for treating pediatric migraines. It does not replace concurrent therapy with IV fluids, and therefore does not offer additional clinical benefit.Further confirmatory research is required.

Study Summary

Article	Tsze DS, Lubell TR, Carter RC, *et al*. Intranasal ketorolac versus intravenous ketorolac for treatment of migraines in children: A randomized clinical trial. Acad Emerg Med 2021. Nov 25. Online ahead of print. DOI: 10.1111/acem.14422
Design	Double-blind non-inferiority randomized controlled trial
Population	*Included:* Children aged 8–17yrs with migraine headaches (meeting Irma's ED criteria), moderate to severe pain, and requiring parenteral analgesics *Excluded:* any contraindication to receiving ketorolac; receipt of any NSAID within previous 6h; presence of IN obstruction that could not be readily cleared; inability to complete self-report measures of pain or questionnaires (e.g. developmental delay, autism spectrum disorder, neurological impairment); history of intracranial surgery, structural abnormalities, or risk factors for intracranial abnormality (e.g. coagulopathy; pseudotumor cerebri; pregnancy); chronic disease associated with pain other than migraine headaches (e.g. sickle cell disease, fibromyalgia); underlying medical condition necessitating multiple painful procedures (e.g. malignancy, complex congenital heart disease); known liver or kidney problems; critical illness; use of any medication for headaches on more than 10 days per month; or did not speak English or Spanish.
Intervention	Intranasal ketorolac (1 mg/kg, max 30mg) with IV NS placebo; INK. Meds delivered via a mucosal atomization device (Wolfe-Tory Medical Inc).
Comparison	Intravenous ketorolac (0.5 mg/kg, max 30mg) with IN NS placebo; IVK
Outcomes	*Primary*: Reduction in pain at 60 min after administration measured using the Faces Pain Scale-Revised (scored 0–10). Non-inferiority margin was 2/10. *Secondary*: Time to onset of clinically meaningful decrease in pain; ancillary emergency department outcomes (e.g. receipt of rescue medications, headache relief, headache freedom, percentage improvement); 24-h follow-up outcomes; functional disability; and adverse events

Key Results

59 children enrolled, 56 analyzed at end (27 in INK, 29 in IVK). Required sample sizes 40 per group not met.

Primary: Mean Diff 0.2pts (95%CI -0.9 to 1.3). Treatment success (pain reduction 50% or more at 30 or 60min after study meds administration) achieved in 88.9% of INK and 93.1 IVK pts (MD 4.2%, -19.2 to 10.8)

Secondary: Pain at 10min (MD 0.9, -0.4 to 2.2)*, 30min (MD 0.8, -0.4 to 1.9), 120min (MD 0.0, -1.3 to 1.2)
No difference in rescue meds used prior to 60min (approx. 20% in each group).
All patients achieved minimally clinically important pain improvement by 60min.
No difference between groups at 24hr follow-up.
No difference in patients with none/mild functional disability at 60 & 120min, and at 24hr follow-up.
No serious adverse events in either group. Milder adverse events in both groups, most commonly nausea & dizziness (4 in INK, 6 in IVK).
Pain intensity of INK administration 6.7 (6.5-6.9) vs placebo 0.6 (0.5-0.7).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	X
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	X	X
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	✓	X

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding Columbia University's CTSA grant No. UL1TR000040 from NCATS/NIH and the Migraine Research Foundation (New York, NY).

Conflict of interest None (reported)

Potential threats to viability

Chance *Sample size, Type I & II errors?* Required sample sizes not met due to funding limitations (May 2016-March 2018) and COVID research restrictions from March 2020. Study terminated in March 2021 due to persistent decline in overall PEM visits/study eligible visits.

Selection bias *Is the sampling method representative of the target population; are the groups balanced?* Single site Peds ED limits generalizability? No comments on consecutive vs. convenience sampling.

Measurement bias Use of FPS-R scale, with MCID 2/10 points; validated for ED use.

Analysis bias *ITT, Per Protocol, As Treated.* Missed eligible patients identified by chart review, confirmed to be not different than those enrolled (Table S3). Results analyzed per protocol completions (56/59), as 3 patients randomized did not receive allocated interventions.

Confounding *Independent factors affecting the outcome; clinicians to comment.* None.

Administrative details

Key words Ketorolac, non-inferiority, pediatric migraine, intranasal vs intravenous

Appraisers S. Upadhye; R. Valani.

Reference(s)

1. Bailey et al, J Emerg Med 2017. Review of Intranasally Administered Medications for Use in the Emergency Department. PMID: 28259526. DOI: 10.1016/j.jemermed.2017.01.020
2. Tamayo-Sarver et al, Acad Emerg Med 2008. *Advanced Statistics:* How to Determine Whether Your Intervention Is Different, At Least As Effective As, or Equivalent: A Basic Introduction. **https://doi.org/10.1197/j.aem.2005.01.010**

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the latest guidelines for the management of pediatric cardiac arrest?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? These guidelines update the prior recommendations on the management of pediatric cardiac arrest, in order to optimize survival to hospital discharge with meaningful neurologic recovery.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? Minimal. Lack of patient/parent/public engagement is problematic to maintain focus on patient-relevant outcomes (PRO's). Use of multiple strata of recommendation classes (1-2a-2b-3Mod-3Harm)/levels of evidence (A-BR-BNR-CLD-CEO may leave readers confused, as opposed to a more intuitive framework (e.g. GRADE).

How should this guideline, and specifically which recommendations should impact the care of ED patients? These updated guidelines provide the standard of care for pediatric cardiac arrest. The top ten take home messages from the article provide a synopsis of the relevant recommendations.

Study Summary

Article Topjian AA, Raymond TT, Atkins D, *et al*, on behalf of the Pediatric Basic and Advanced Life Support Collaborators. Part 4: pediatric basic and advanced life support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Pediatrics. 2021 Jan;147(Suppl 1):e2020038505D. doi: 10.1542/peds.2020-038505D.

Design Clinical Practice Guideline.

Population Infants/children in pre/intra/post-arrest states. Excludes neonates up to 28days.

Scope This guideline is intended to be a resource for lay rescuers and healthcare providers to identify and treat infants and children in the pre-arrest, intra-arrest, and post-arrest states.

Key Results

Recommendation	*LoE*
Provide continuous core temp measurement during TTM post-arrest	A
Initiate bystander chest compressions (+/- rescue breaths) in out-of-hospital arrest.	B-NR
Avoid sodium bicarb, unless known hyperkalemia/Na channel blocker OD (eg TCA). **CoR 3 Harm**	B-NR
Avoid calcium administration (routine) unless known hypocalcemia/CCB OD/hypermagnesemia or hyperkalemia. **CoR 3 Harm**	B-NR
Provide family members the option of being present during resuscitation, and designate a team member to provide answers, comfort and support.	B-NR
Use inhaled nitric oxide/prostacyclin for initial Rx of pulmonary HTN crises/acute right heart failure d/t increased pulmonary vascular resistance. Provide ongoing respiratory monitoring/care.	B-R
Lay rescuers should start CPR in unresponsive/nonbreathing/VSA children (no pulse check).	C-LD
Use 2 finger sternum (single)/2 thumb encircling hands (2 rescuers) for infants.	C-LD
Activate "CPR mode" to stiffen mattress bed during in-hospital arrest.	C-LD
Use a head-tilt/chin-lift maneuver to open airway (unless suspected C spine injury; use jaw thrust)	C-LD
Use a pediatric attenuator for AED on infants/child <8yo.	C-LD
Use parenteral fluids/vasopressors to maintain sBP >5th percentile for age after ROSC.	C-LD
	C-LD

Use continuous EEG monitoring for seizure detection in post-arrest persistent encephalopathy (if resources available). Trat clinical seizures post arrest.	C-LD
If family presence is detrimental during resuscitation, ask respectfully to leave the room.	C-LD
Reassess patient after each fluid bolus for response/signs of volume overload.	C-LD
In severe foreign body airway obstruction, perform abdominal thrusts/5 back-blow cycles repeatedly until object expelled or victim goes unresponsive; once unresponsive, start CPR and clear visible obstructions when opening airway. Do not perform blind finger sweeps.	C-LD
Provide rescue breathing/BVM support until spont breathing restored in opioid-related arrest, and use standard BLS/ALS protocols prior to naloxone administration (C-EO).	C-LD
Discontinue cricoid pressure during intubation if it interferes with ventilation/intubation (**Cor 3 Harm).** For intubated children with perfusing rhythm, use colorimeter/capnography to confirm ETT placement.	C-LD
For bradycardia <60bpm with CV compromise & effective ventilation/oxygenation, start CPR. If due to primary AV block or increased vagal tone, give atropine.	C-LD
Give IV/IO adenosine for SVT treatment. If refractory SVT to adenosine/vagal maneuvers, seek expert consultation (C-EO).	C-LD
For stable wide-complex tachycardia, seek expert advice prior to administering antiarrhythmic meds.	C-LD
Consider ICU transfer for children with acute myocarditis showing arrhythmias, ST changes or low cardiac output.	
With each chest compression, allow chest to recoil completely.	C-EO
Use child weight-based dosing for resuscitation drug dosing (not exceed adult doses).	C-EO
Use a manual defibrillator for shockable rhythms in infants under trained HCP care.	C-EO
Use largest paddles/self-adhering electrodes on child's chest while maintaining good separation. Continue CPR between shocks (minimize interruption of chest compressions).	
Use continuous arterial pressure monitoring (if resources available) to identify/treat hypotension.	C-EO
For non-survivors of unexpected arrest, provide access to pathologist/autopsy and preserve biological materials for genetic analysis/inherited cardiac disease testing.	C-EO
For survivors of unexpected cardiac arrest, get a new ECG/compare to prior ECG's, and get a complete personal/family history of syncopal events/arrhythmias/other cardiac disease.	C-EO
For patients with cardiogenic shock, get early expert consultation.	C-EO
Provide rescue breathing for patients with a pulse but inadequate/absent respiratory efforts.	C-EO
Pay attention to cuffed ETT size, position & inflation pressure.	C-EO
Give epinephrine IV/IO/ETT if persistent bradycardia (after correcting hypoxia)	C-EO
Provide analgesia/sedation/neuromuscular blockade for children at high risk of pulmonary HTN crisis.	C-EO
In traumatic arrest, evaluate/treat correctible causes (eg. bleeding, tamponade, tension PTX).	C-EO

Only Class 1 or 3 (Strong) recommendations summarized here. See publication for CoR 2a/2b/3 Mod recommendations

Class of Recommendation (CoR)	*Level of Supporting Evidence (LoE)*
1 (Strong): Benefits >>> Risk. "Recommended, indicated, useful, effective, beneficial." 2a (Moderate): Benefits >> Risk. "Reasonable, can be useful/ effective/beneficial." 2b (Weak): Benefit ≥ Risk. "May/might be reasonable, considered. Unknown/unclear/uncertain usefulness or effectiveness 3 No Benefit (Moderate): Benefit = Risk. "Not recommended/indicated/ useful/effective/beneficial. Should not be performed/administered." 3 Harm (Strong): Risk > Benefit. "Potential/actual harm, excessive morbidity/mortality, should not be performed/ administered."	Level A = High quality evidence from >1 RCT, meta-analyses of high quality RCTs, corroborating registry studies Level B-R (Randomized) = Moderate quality evidence from 1+ RCTs, SR/MA of moderate quality RCTs Level B-NR (Nonrandomized) = Mod quality evidence from 1+ nonrandomized/observational studies, or registries Level C-LD (Limited Data) = non/randomized (or registry) studies with design/execution limitations, or SR/MA of same. Physiologic/mechanistic studies of human subjects. Level C-EO (Expert Opinion) = Consensus of expert opinion based on clinical experience.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	✓
2. Systematic methods were used to search for evidence.	✓	✓
3. The criteria for selecting the evidence are clearly described.	✓	✓
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	✓	✓
8. The content of the guideline is free of influence by the views of the funding body.	✓	✓
9. Competing interests of guideline development group members have been recorded and managed.	✓	✓
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	None reported. All volunteers with no conflicts of interest.
Conflict of interest	None (reported in Appendix 1 & 2).

Potential threats to validity

Development	Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible? **No patient/parent stakeholders involvement reported. Linkage of evidence base with strength of recommendations is explicit.**
Presentation	Well organized with easy to find recommendations? **Yes; key recommendations summarized at top of article (Top Ten list). Coloured recommendation boxes scattered throughout manuscript.**
Comprehensive	Was the information to inform decision-making complete? **Yes. Clinical pathways/algorithms included in body of text.**
Clinical Validity	Are the recommendations clinically sound and appropriate for the intended patients? **Yes**

Administrative details

Key words	Guidelines, advanced/basic life support, pediatric resuscitation.
Appraisers	Upadhye S; R Valani.
Reference(s)	Topjian AA, Raymond TT, Atkins D, Chan M, Duff JP, Joyner BL Jr, Lasa JJ, Lavonas EJ, Levy A, Mahgoub M, Meckler GD, Roberts KE, Sutton RM, Schexnayder SM; on behalf of the Pediatric Basic and Advanced Life Support Collaborators. Part 4: pediatric basic and advanced life support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Pediatrics. 2021 Jan;147(Suppl 1):e2020038505D. doi: 10.1542/peds.2020-038505D.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the optimal management of stable/non-critical pediatric intussusception?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? Ileocolic intussusception is one of the most common causes of small bowel obstruction in children. Failure to recognize and manage these patients can result in ischemic bowel, perforation, sepsis, and death. This review updates evidence/recommendations on antibiotics stewardship, imaging, ED discharge advice and non-surgical management for stable non-critical pediatric intussusception.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? This "systematic review" actually meets some of the standards of a clinical practice guideline (CPG). Various key elements on the evidence review and transformation into CPG recommendations are missing.

How should this guideline, and specifically which recommendations should impact the care of ED patients? ED physicians can avoid prophylactic antibiotics in children with intussusception, and if observed in ED after successful enema reduction, can be sent home after 4hrs of observation/successful trial of oral intake.

Study Summary

Article Kelley-Quon LI, Arthur LG, Williams RF, *et al*. Management of intussusception in children: A systematic review. J Peds Surg 2021; 56: 587-596. DOI: 10.1097/PEC.0000000000002224.

Design Clinical Practice Guideline.

Population Children with clinical features of intussusception.

Scope Not specified. Presumably intended for emergency physicians/other clinicians who manage children with acute abdominal pain/potential surgical emergencies.

Key Results Grade ABCD recommendations, Level of Evidence (LoE) 1-5. ED-relevant recommendations only listed.

Recommendation	*Strength*	*LoE*
None	Grade A	1
None	Grade B	2
Prophyllactic antibiotics are unnecessary prior to enema reduction.	Grade C	3-4
Children with successful enema reduction can be discharged from ED after 4hrs of observation, with appropriate parental education on recurrence symptoms*/RTER criteria.	Grade C	3-4
Have a physician present to handle pneumoperitoneum/CPR at time of enema reduction.	Grade D	5
An interval of 30min-4hrs may be reasonable/safe for delayed repeated enemas (needs further study).	Grade D	5

*Children >2yo may have a slightly higher recurrence risk compared to children <2yo.
Explanations for GRADE ABCD/Level of Evidence 1-5 strata not provided in manuscript.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	✓
2. Systematic methods were used to search for evidence.	X	X
3. The criteria for selecting the evidence are clearly described.	X	X
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	X	X
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	?	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	?	?
7. Experts externally reviewed the guideline prior to its publication.	X	X
8. The content of the guideline is free of influence by the views of the funding body.	✓	✓
9. Competing interests of guideline development group members have been recorded and managed.	✓	✓
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding Author LIK supported by NIH NCATS grant.

Conflict of interest None (reported).

Potential threats to validity

Development Limited evidence search (electronic databases only), no gray literature/article reference lists/abstracts; excluded non-English studies, animal studies, case reports, and protocol papers. Stated use of Oxford Centre for EBM Levels of Evidence for included study review. No details on quality assessment of included trials? Unclear how evidence review was linked to formulated recommendations.

Presentation Well organized with easy to find recommendations? **No.**

Comprehensive Was the information to inform decision-making complete? **Somewhat limited ED-relevant recommendations?**

Clinical Validity Are the recommendations clinically sound and appropriate for the intended patients? **Yes.**

Administrative details

Key words Antibiotics, enema, intussusception, outpatient.

Appraisers S. Upadhye, R. Valani

Reference(s)

Kelley-Quon LI, Arthur LG, Williams RF, Goldin AB, St. Peter SD, Beres AL, Hu YY, Renaud EJ, Ricca R, Slidell MB, Taylor A, Smith CA, Miniati D, Sola JE, Valusek P, Berman L, Raval MV, Gosain A, Dellinger MB, Somme S, Downard CD, McAteer JP, Kawaguchi A. Management of intussusception in children: A systematic review. J Peds Surg 2021; 56: 587-596. DOI: 10.1097/PEC.0000000000002224.

Hom J, Kaplan C, Fowler S, Messina C, Chandran L, Kunkov S. Evidence-Based Diagnostic Test Accuracy of History, Physical Examination, and Imaging for Intussusception. A Systematic Review and Meta-analysis. Ped Emerg Care 2020; DOI: 10.1097/PEC.0000000000002224. PMID: 32941364

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

What are the latest guidelines for the management of neonatal resuscitation?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? Early effective respiratory/cardiac support is essential to reduce neonatal mortality, as 10% of neonates need respiratory support at birth, and 1% require intensive resuscitative measures to restore cardiopulmonary function at birth. These guidelines update the prior recommendations on the management of neonatal resuscitation.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? Minimal. Lack of patient/parent/public engagement is problematic to maintain focus on patient-relevant outcomes (PRO's). Use of multiple strata of recommendation classes (1-2a-2b-3Mod-3Harm)/levels of evidence (A-BR-BNR-CLD-CEO may leave readers confused, as opposed to a more intuitive framework (eg. GRADE).

How should this guideline, and specifically which recommendations should impact the care of ED patients? These updated guidelines provide the standard of care for pediatric cardiac arrest. The top ten take home messages from the article provide a synopsis of the relevant recommendations.

Study Summary

Article	**See Ref below**
Design	Clinical practice guideline.
Population	Neonates (up to 28days)
Scope	"This guideline is designed for North American healthcare providers who are looking for an up-to-date summary for clinical care, as well as for those who are seeking more in-depth information on resuscitation science and gaps in current knowledge."

*****Only Class 1 or 3 (Strong) recommendations summarized here. See publication for Level 2a/2b/3 Mod recommendations***

Class of Recommendation (CoR)	***Level of Supporting Evidence (LoE)***
1 (Strong): Benefits >>> Risk. "Recommended, indicated, useful, effective, beneficial." 2a (Moderate): Benefits >> Risk. "Reasonable, can be useful/ effective/beneficial." 2b (Weak): Benefit ≥ Risk. "May/might be reasonable, considered. Unknown/unclear/uncertain usefulness or effectiveness 3 No Benefit (Moderate): Benefit = Risk. "Not recommended/indicated/ useful/effective/beneficial. Should not be performed/administered." 3 Harm (Strong): Risk > Benefit. "Potential/actual harm, excessive morbidity/mortality, should not be performed/ administered."	Level A = High quality evidence from >1 RCT, meta-analyses of high quality RCTs, corroborating registry studies Level B-R (Randomized) = Moderate quality evidence from 1+ RCTs, SR/MA of moderate quality RCTs Level B-NR (Nonrandomized) = Mod quality evidence from 1+ nonrandomized/observational studies, or registries Level C-LD (Limited Data) = non/randomized (or registry) studies with design/execution limitations, or SR/MA of same. Physiologic/mechanistic studies of human subjects. Level C-EO (Expert Opinion) = Consensus of expert opinion based on clinical experience.

Recommendation	*LoE*
Neonates >36weeks GA with evolving moderate/severe hypoxic-ischemic encephelopathy should be offered therapeutic hypothermia under clearly defined protocols.	A
Every birth should be attended by at least 1 person who can provide initial NR and initiate PPV, whose sole responsibility is care of the newborn.	B-NR
Before each birth a standardized risk factors assessment tool should be used, and a qualified team assembled based on risk stratification.	B-NR
In neonates with apnea>60sec or persistent bradycardia <100bpm despite initial stimulation, PPV should be initiated ASAP (40-60 breaths/minute, insufflation <1sec, avoid sustained/peak pressures).	B-NR, B-R
Avoid 100% oxygen in neonates >35weeks GA with PPV (CoR 3). Limit oxygen to 21-30%.	B-R
Neonatal temperature should be routine recorded, and hypothermia <36C should be prevented.	B-NR
All standardized equipment should be available (checklist) to ensure all necessary supplies are ready for complete resuscitation. Consider a preresuscitation team briefing to prepare.	C-LD
Glucose levels should be monitored ASAP after advanced resuscitation, and treated as indicated.	C-LD
If NR fails after 20min, cessation of efforts should be discussed with team/family.	C-LD
Individual/team training should be reinforced <2yrs to ensure knowledge/skills retention.	C-LD
During CPR, HR assessment should be done with an ECG.	C-EO
For neonates requiring vascular access, the umbilical vein is the recommended route (or IO if unavailable).	C-EO
Neonates receiving prolonged PPV/advanced resuscitation should be transferred/maintained in appropriate monitoring environment.	C-EO
Non-initiation of, or discontinuation of failed NR should be considered ethically equivalent.	C-EO

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	✓
2. Systematic methods were used to search for evidence.	✓	✓
3. The criteria for selecting the evidence are clearly described.	✓	✓
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	✓	✓
8. The content of the guideline is free of influence by the views of the funding body.	✓	✓
9. Competing interests of guideline development group members have been recorded and managed.	✓	✓
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	None reported. All volunteers with no conflicts of interest.
Conflict of interest	None (reported in Appendices 1&2).

Potential threats to validity

Development	Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible? **No patient/parent stakeholders involvement reported. Linkage of evidence base with strength of recommendations is explicit.**
Presentation	Well organized with easy to find recommendations? **Yes; key recommendations summarized at top of article (Top Ten list). Coloured recommendation boxes scattered throughout manuscript.**
Comprehensive	Was the information to inform decision-making complete? **Yes. Clinical pathways/algorithms included in body of text.**
Clinical Validity	Are the recommendations clinically sound and appropriate for the intended patients? **Yes.**

Administrative details

Key words	Guidelines, neonatal cardiopulmonary resuscitation.
Appraisers	S. Upadhye, R. Valani
Reference(s)	Aziz K, Lee HC, Escobedo MB, Hoover AV, Kamath-Rayne BD, Kapadia VS, Magid DJ, Niermeyer S, Schmolzer GM, Szyld E, Weiner GM, Wyckoff MH, Yamada NK, Zaichkin J. Part 5: Neonatal Resuscitation 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Pediatrics. 2021 Jan;147(Suppl 1):e2020038505E. doi: 10.1542/peds.2020-038505E.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

What is the utility in using intranasal ketamine for pediatric ED acute analgesia?

BEEM Bottom Line

Why is this study important? Management of moderate to severe pain in children can be a challenge. It often requires parenteral opioid analgesia which delays care due to the time required for IV insertion. Intranasal analgesia options can provide a bridge for pain control. Fentanyl and ketamine are two agents that have been studied for intranasal administration. Having analgesic alternatives in pediatric acute ED pain care is important, especially if there are potential safety concerns, and a desire to avoid parenteral opioids.

Which, if any, threats to validity are most likely to have an impact on the results and how? Minimal.

How do the key results compare with the current evidence? There is a growing body of evidence supporting ketamine acute analgesia options in the ED for all age groups, especially in the era of opioid stewardship.

How should this study impact the care of ED patients? Intranasal ketamine is an effective and safe alternative to opioids in acute pediatric ED pain, especially when oral/parenteral routes may be impractical.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	de Silva LOJ, Lee JY, Bellolio F, *et al*. Intranasal ketamine for acute pain management in children: A systematic review and meta-analysis. Am J Emerg Med 2020; 38: 1860-1866. https://doi.org/10.1016/j.ajem.2020.05.094
Design	Systematic review and meta-analysis of randomized controlled trials (RCTs).
Population	*Included:* RCTs of children (age <18yo) needing ED acute analgesia (moderate/severe pain). *Excluded*: Chronic pain conditions with recurrent exacerbations (eg. sickle cell disease), non-ED settings. Ketamine given for ED PSA, or alternative routes (IM, po, IV) also excluded.
Intervention	Intranasal ketamine (INK) at low/sub-dissociative doses (1-1.5mg/kg).
Comparison	Intranasal fentanyl (INF) 1.5-2ug/kg.
Outcomes	*Primary:* Pain reduction using validated pain scales at 10-15min, 30min and 60min time intervals. *Secondary:* Need for rescue analgesia, adverse events, sedation rates (UMSS scale). Minor AE's = nausea, vomiting, dizziness, drowsiness, sleepiness, dysphoria/dissociation, unpleasant taste, pruritis, visual changes, headache, rash, light-headedness, nystagmus, salivation, vivid dreams, trouble concentrating, sore throat, hallucinations. Major AE's = dysrhythmias, seizures, apnea, resp depression, anaphylaxis, hypotension, cardiac arrest.

Key Results

4 trials included, 276 patients randomized (138 to INK, 138 to INF). 3 studies included acute extremity pain, 4th study included extremity & abdominal pain.

Sig.	*Outcome*	*Outcome Measure (95% CI)*	*I^2*
NSS	Primary: pain reduction (10-15min)	WMD -1.42pts (-9.95 to 7.10)	60%
	30min	WMD 0.40 (-6.29 to 7.10)	24%
	60min	WMD -0.64 (-6.76 to 5.47)	0%
		**INK was non-inferior to INF all times (base on 10pt NI margin)	
	Need for rescue analgesia	RR 0.74 (0.44-1.25); INK 0-25%, INF 0-34%	25%
SS	Adverse events (minor)	RR 2.00 (1.43-2.00) favouring INF	49%
		**1 serious AE in INF group, none in INK	
	Sedation	RR 1.81 (1.24-2.62) favouring INF; none were deep/unarousable	0%

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.
P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.
*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	✓	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	?	X	?✓X
3. The search for studies was unbiased and reproducible.	?	?	?✓X
4. The selection of studies was unbiased and reproducible.	✓	✓	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓	?✓X
7. The quality of the primary studies is high.	✓	✓	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓	?✓X
9. The outcomes are clinically relevant.	✓	✓	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	X	?✓X

A1 = S. Upadhye A2 = R Valani A3 =

Funding and conflicts of interest

Funding	Mayo Clinic Small Grant program.
Conflict of interest	None (declared).

Potential threats to validity

Chance	None? No children <3yo in any included studies.
Selection bias	Limited search of 3 electronic databases, hand search of reference lists from retrieved articles. Contacted authors for missing data if needed. Unable to complete publication bias analysis due to small number of included articles.
Measurement bias	None or enter text here (e.g., missing details on study selection; missing results of quality assessments). Use of Cochrane Risk of Bias (RoB) tool for study quality assessments, and overall outcomes evidence evaluated using GRADE methods. All included studies had low RoB, and High GRADE certainty of evidence.
Analysis bias	Three of 4 studies reported per-protocol analyses (rather than ITT). Use of random effects models for higher heterogeneity studies appropriate.
Confounding	All patients received ibuprofen or acetaminophen prior to study drug Rx (balanced co-interventions between study groups).

Administrative details

Key words	Acute analgesia, intranasal, fentanyl, ketamine.
Appraisers	Upadhye S, Valani R
Reference(s)	de Silva LOJ, Lee JY, Bellolio F, Homme JL, Anderson JL. Intranasal ketamine for acute pain management in children: A systematic review and meta-analysis. Am J Emerg Med 2020; 38: 1860-1866.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

Research Question

What is the utility of sodium bicarbonate in pediatric in-hospital cardiac arrest?

BEEM Bottom Line

Why is this study important? While Sodium bicarbonate (SB) is not recommended for routine use in pediatric cardiac arrest, it is still commonly used. This study looked at the effects of SB given during pediatric cardiac arrest and if it made any difference in mortality or neurological outcomes for in-hospital cardiac arrest.

Which, if any, threats to validity are most likely to have an impact on the results and how? A limited number of included observational studies, with evidence of publication bias and other unreported confounders, limit the strength/generalizability of findings.

How do the key results compare with the current evidence? These results reinforce recommendations NOT to use routine SB in pediatric cardiac arrest situations.

How should this study impact the care of ED patients? Use of sodium bicarbonate in pediatric cardiac arrest is NOT routinely recommended. There was insufficient information to guide practice in specific subgroups of interest (e.g. hyperkalemia, TCA overdose, metabolic acidosis).

Study Summary

Article	Chang CY, Wu PH, Hsiao CT, *et al*. Sodium bicarbonate administration during in-hospital pediatric cardiac arrest: A systematic review and meta-analysis. Resusc 2021; 162: 188-197. https://doi.org/10.1016/j.resuscitation.2021.02.035
Design	Systematic review and meta-analysis of observational trials.
Population	*Included:* Patients <18yo with in-hospital cardiac arrest, given IV sodium bicarbonate (SB) during arrest. *Excluded*: Adults >18yo, out-of-hospital cardiac arrest (OHCA), respiratory arrest with pulse, special populations (congenital heart disease, inherited metabolic disorders). Also excluded case reports/series, unpublished reports, and animal studies.
Intervention	Sodium bicarbonate (SB) IV infusion.
Comparison	Usual PALS-driven care.
Outcomes	*Primary:* Rate of survival to hospital discharge. *Secondary:* Survival at 24hrs, and neurologic outcomes (measured by Pediatric Cerebral Performance Scale). PCPS score of 1-3 at discharge was considered a “good” neuro outcome.

Key Results

7 studies, 4877 pts included. 3168 pts received SB (65.6%).

Sig.	*Outcome*	*N/Studies*	*Outcome Measure (95% CI)*	*I^2*
NSS	Secondary (24hr survival, neuro outcomes)	1	**Insufficient data to meta-analyze outcomes	N/A
SS	Primary: survival to hospital discharge	7	OR 0.40 (0.25-0.63) AGAINST SB infusion; no difference in studies before/after 2010	73%

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	?	X
3. The search for studies was unbiased and reproducible.	?	✓
4. The selection of studies was unbiased and reproducible.	?	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	✓	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	X

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	None (reported).
Conflict of interest	None (reported).

Potential threats to validity

Chance	None? Limited number of included studies for primary outcomes, only 1 study for secondary; overall did not meet Optimal Information Size (OIS).
Selection bias	Limited electronic databases search (Pubmed, EMBASE, Cochrane Trials Registry), and bibliographies/reference lists of retrieved articles. No gray literature searches. No language or study design restrictions. Screening/selection of articles not clearly described. Publication bias analysis in Supp material; some evidence of plot asymmetry with smaller studies.
Measurement bias	Use of Newcastle-Ottawa scale to appraise observational studies; 1 moderate, 6 high quality studies included. Overall GRADE certainty of evidence was low/very low.
Analysis bias	Use of random effects analyses for high heterogeneity studies was appropriate. Insufficient studies for prespecified subgroup analyses (hyperkalemia, metabolic acidosis, TCA overdose).
Confounding	No randomized studies, so use of SB was at clinician discretion which may have led to biased interventions. Pre-existing medical conditions preceding cardiac arrest are not described in included studies, which may also lead to different eventual outcomes. Similarly, intra- and post-arrest management was not necessarily standardized within/between studies, so these variables also have potential impact on review outcomes.

Administrative details

Key words	Sodium bicarbonate, cardiac arrest, pediatric, systematic review/meta-analyses.
Appraisers	S.Upadhye, R. Valani
Reference(s)	Chang CY, Wu PH, Hsiao CT, Chang CP, Chen YC, Wu KH. Sodium bicarbonate administration during in-hospital pediatric cardiac arrest: A systematic review and meta-analysis. Resusc 2021; 162: 188-197. https://doi.org/10.1016/j.resuscitation.2021.02.035

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto

TRAUMA/CRITICAL CARE

Research Question

What is the utility of emergency resuscitative thoracotomy in thoracic trauma?

BEEM Bottom Line

Why is this study important? Emergency thoracotomy is a last-ditch effort to save lives in thoracic trauma (blunt or penetrating). Selecting the right patients for such extreme interventions requires a clear knowledge of those who may benefit the most.

What, if any, threats to validity are most likely to have an impact on the results and how? Trial examining RT for thoracic trauma are largely non-randomized, observational, and retrospective studies, such that the quality of evidence remains very low. Incomplete data on many predictors of survival such as ISS, signs of life, time from injury/transport, SBP, were not universally reported in the included trials.

How do the key results compare with the current evidence? These findings are congruent with major trauma guidelines that support RT in selected patients, particularly those with penetrating injury with signs of life. There are very few studies on pre-hospital RT and more evidence is needed. Patients with blunt trauma and longer transport time (>5-10 minutes) also is associated with higher mortality.

How should this study impact the care of ED patients? RT is a life-saving procedure for patients with thoracic trauma who meet appropriate selection criteria. While the quality of evidence is very low, RT is a necessary skill of emergency physicians and should be performed in highly selected patients.

Study Summary

Article	Liu A, Nguyen, J, Ehrlich H, Bisbee C, Santiesban L, Santos R, McKenney M, Elkbuli A. Emergency Resuscitative Thoracotomy for Civilian Thoracic Trauma in the Field and Emergency Department Settings: A Systematic Review and Meta-Analysis. J Surg Res 2022; (273) 44-55.
Design	Systematic Review/Meta-analysis
Population	***Included:*** Adult patients with thoracic trauma requiring resuscitative thoracotomy (RT) in ED or prehospital (PH) settings. ***Excluded:*** Pediatric thoracic or non-thoracic trauma, non-ED or prehospital settings. Case reports/series, questionnaires, editor letters, editorials, review articles also excluded.
Intervention	Resuscitative thoracotomy
Comparison	Usual care
Outcomes	***Primary:*** All-cause mortality in ED or prehospital thoracotomy. ***Secondary:*** Neurologic outcomes after thoracotomy. "Good" outcome = no sequelae affecting functional abilities, or GCS >13.
Key Results 6584 patients included for total analysis	***PH-RT studies (5)***: Mortality ranged from 89.7-100%. Cardiac tamponade identified in 64.9%, and exsanguination/massive hemorrhage in 28.4%. Higher mortality with responder time >10min, or ISS>25. Higher survival with penetrating stab wounds with signs of life (or single cardiac wound). Neurologic outcomes: Full recovery in 75-100% of patients (3 studies; all penetrating stab wounds, all treated within 5min of injury). All survivors treated by non-surgeons. ***ED-RT studies (45):*** Mortality range 10.8-100% (median 83.33%); 0-100% penetrating, 46.15-100% blunt. Higher risk = higher ISS>25, low GCS (<8), multiple wounds, low systolic BP, asystole/PEA rhythms, transit times >10min, blunt trauma. Better survival = younger age, organized cardiac rhythms, penetrating trauma (stabs > gunshots), measurable vitals/signs of life on scene (or witnessed loss of SoL), early intubation, shorter RT time, pericardial tamponade on ED-RT. Neurologic outcomes: Full recovery in 0-100% patients (median 86%). Better recovery with penetrating, worse with blunt trauma. **Overall Mortality:** PH-RT 93.5% vs ED-RT 81.8% (Risk Difference 11.3%; p=0.02). Penetrating 80.1% vs blunt 92.8% (RD 12.7%, p<0.001). - ED-RT penetrating 78.7% vs blunt 02.8% (RD 14.1%; p-0.0005) - Too few studies to compare PH-RT penetrating vs blunt.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **English only, limited electronic search, manual reference search.**	X	?
3. The search for studies was unbiased and reproducible.	?	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **4 authors**	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high. **Very low GRADE quality scores**	X	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant. **All-cause mortality**	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%). **Not reported**	?	?

A1 = S. Upadhye A2 = J. Owen

Funding and conflicts of interest

Funding	Not reported.
Conflict of interest	Reported; no competing interests declared.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* No RCTs included; all studies were observational, majority retrospective.
Selection bias	*Limited/incomplete search, publication bias, etc.* Limited search? No evidence of GRADE publication bias.
Measurement bias	*Missing details on study selection; missing results of quality assessments.* Quality assessments showed all evidence to have very low level of GRADE certainty.
Analysis bias	*Fixed vs. random effects, combined results of studies of different design.* Random effects analyses for forest plots with high heterogeneity (no X^2 reported).
Confounding	*List as reported.* Different countries may have different criteria/resources for PH-RT, which may confound mortality outcomes (survivor bias?). Inconsistent reporting of variables of interest (eg. ISS, GCS, SBP, etc) may limit extrapolation of risk factors for mortality/other outcomes. Non-uniform outcomes for neurologic outcomes (eg. "mild, moderate, severe") with varied definitions limit pooling/comparison for overall neurologic outcomes analyses.

Administrative details

Key words	Blunt thoracic trauma, ED thoracotomy, prehospital thoracotomy
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC **No conflicts of interest/Identify conflicts (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Julian J. Owen, MD FRCPC **No conflicts of interest/Identify conflicts (ICMJE)** *Assistant Clinical Professor, Emergency Medicine/Critical Care/Trauma, McMaster University*

Research Question

What are the latest recommendations for managing adult hip fracture?

BEEM Bottom Line

Why is this study important? Managing hip fracture quickly and effectively in the ED can improve clinical outcomes. This is particularly important in reducing patient delirium and other adverse outcomes.

What, if any, threats to validity are most likely to have an impact on the results and how? Lack of patient/caregiver stakeholder inputs may miss important patient priorities, values & preferences in hip fracture care.

How do the key results compare with the current evidence? The growing body of evidence supporting ED interventional analgesia with nerve blockade continues to grow as a positive intervention, and is opioid-sparing.

How should this study impact the care of ED patients? A hip fracture care path with prioritization of interventional nerve blockade increases patient satisfaction, reduced opioid usage and perioperative delirium.

Study Summary

Article	American Academy of Orthopaedic Surgeons Management of Hip Fractures in Older Adults Evidence-Based Clinical Practice Guideline. https://www.aaos.org/hipfxcpg.
Design	Clinical Practice Guideline
Population	***Included:*** Adults with acute hip perioperative hip fracture ***Excluded:*** Prevention of primary/secondary hip fractures, post-hospital rehabilitation
Scope of Recs	Clinicians caring for adult patients with hip fracture

Key Recommendations (LoE = Level of Supporting Evidence)

Recommendations	Rec Strength (LoE)
FOR Clinical Action	
Venous thromboembolism (VTE) prophylaxis should be used in hip fracture patients postoperatively?.	Strong (Moderate)
Multimodal analgesia incorporating preoperative nerve block is recommended to treat pain after hip fracture.	Strong (Strong)
Tranexamic acid should be administered to reduce blood loss and blood transfusion in patients with hip fractures.	Strong (Strong)
NEUTRAL Clinical Action	
A blood transfusion threshold of no higher than 8g/dl is suggested in asymptomatic postoperative hip fracture patients.	Moderate (Moderate)
AGAINST Clinical Action	Strong (Strong)
Preoperative traction should not routinely be used for patients with a hip fracture.	

BEEM Critique

Risk of bias assessment (amalgamated from AGREE-II/NEATS instruments)

	A1	A2
1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.	✓	✓
2. Financial conflicts of interest of guideline development group (GDG) members have been disclosed and managed.	✓	✓
3. The CPG development group includes all of the relevant multidisciplinary stakeholders, including clinicians, methodologists and patients/caregivers. **No patients/caregivers.**	?	?
4. The CPG objectives, health questions, scope of relevant providers and target recipients of care are clearly defined.	✓	✓
5. Values/preferences of patients, caregivers, advocates and/or the public with experience with the clinical disease management has been sought/integrated into CPG development (reported clearly). **No reps on group; obtained from literature review.**	?	?
6. The search strategy for evidence is thoroughly developed and described. **Appendix E-1?**	?	?
7. The criteria for selecting relevant studies/evidence are clearly described.	✓	?
8. The quality, strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.). Summaries of evidence tables are provided. **Used GRADE; no summary tables.**	✓	✓
9. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
10. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
11. The strength of recommendations is clearly reported, including confidence in underlying evidence.	✓	✓
12. Recommendations are clear and unambiguous, and easily identified in the CPG publication.	✓	✓
13. Different options for management for managing the health questions are clearly presented.	✓	✓
14. Experts externally reviewed the guideline prior to its publication.	✓	✓
15. The CPG describes a procedure to update the guideline.	✓	✓
16. The CPG provides advice, tools and/or clinical pathways for easy adoption/adaptation into practice.	✓	?
17. The CPG describes barriers and facilitators to implement recommendations.	✓	X
18. Performance metrics for monitoring implementation of recommendations for audit/feedback have been defined appropriately. **Not specifically stated, but Strong Recs above are easily measured with administrative data (except use of hip traction?).**	X	X
19. Resource implications for implementing CPG recommendations have been discussed. **Deliberately excluded.**	X	X

A1 = S. Upadhye A2 = E. Lang

Funding and conflicts of interest

Funding	Funding by AAOS; no external funding.
Conflict of interest	Reported (Appendix III); no significant conflicts reported.

Potential threats to viability

Development	*Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible?* One ACEP EM physician on guideline panel, no patients/caregivers.
Presentation	*Well organized with easy to find recommendations?* Yes; all listed at beginning of document
Comprehensive	*Was the information to inform decision-making complete?* Yes
Clinical Validitiy	*Are the recommendations clinically sound and appropriate for the intended patients?* Yes

Administrative details

Key words	Hip fracture, analgesia, traction, transfusion, TXA
Reference(s)	Guay J, Kopp S. Peripheral nerve blocks for hip fractures in adults. Cochrane Database of Systematic Reviews 2020, Issue 11. Art. No.: CD001159. DOI: 10.1002/14651858.CD001159.pub3. Ritcey B, Pageau P, Woo MY, Perry JJ. Regional Nerve Blocks for Hip and Femoral Neck Fractures in the Emergency Department: A Systematic Review. Can J Emerg Med 2016; 18(1): 37-47. DOI 10.1017/cem.2015.75

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Eddy Lang MD CCFP(EM) FCAHS *Professor and Department Head, University of Calgary and Alberta Health Services*	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

How accurate is portable ultrasound for detecting blunt traumatic rib fractures?

BEEM Bottom Line

Why is this study important? Blunt traumatic rib fractures are relatively common, and need to be diagnosed accurately. Bedside ultrasound (US) can be useful to detect fractures if traditional Xray or CT scanning is inaccessible/delayed.

What, if any, threats to validity are most likely to have an impact on the results and how? Patient selection bias was the highest risk domain for QUADAS testing; could adversely affect the overall pooled diagnostic accuracy in all ED chest trauma patients (attenuated?). Index test bias (i.e. operator not explicitly blinded to CT results before POCUS examination) was also high across the majority of studies and may falsely inflate the calculated test characteristics. The majority of pooled patients were male and as such applicability to the female patients (given phenotypic difference of the chest wall) may be limited.

How do the key results compare with the current evidence? There is congruence with prior reviews on the accuracy of US for detecting rib fractures, albeit with slightly different definitions and reference standards.

How should this study impact the care of ED patients? A positive US scan for rib fracture is likely diagnostic, and no further confirmatory testing is warranted. Useful in resource-limited ED settings.

Study Summary

Article	Gilbertson J, Pageau P, Ritcey B, Cheng W, Burwash-Brennan T, Perry JJ, Woo MY. Test Characteristics of Chest Ultrasonography for Rib Fractures Following Blunt Chest Trauma: A Systematic Review and Meta-analysis. Annals Emerg Med 2022; 79: 529-539. DOI: 10.1016/j.annemergmed.2022.02.006
Design	Systematic review with meta-analysis; PROSPERO reg#: CRD42021252889
Population	***Included:*** Adult ED patients with blunt chest trauma and suspected rib fractures. ***Excluded:*** Case reports/series, animal or pediatric studies, narrative reviews, studies with costal cartilage fractures.
Index Test	ED or "acute care"point-of-care ultrasound
Reference Standard	CT chest
Diagnoses of Interest	Rib fracture detection with US (Fracture = cortical discontinuity in 5 studies); 2 also reported "chimney phenomenon" (local hematoma, reverberation echoes)
Key Results	**Five of 6 included studies in ED settings;** none from North America. 668 patients included, with 663 data points available for analysis; 83.7% patients = male. Four studies had ED physicians conducting US scans, 2 with radiologists, 1 with pulmonologist + 2 radiologists. All studies used linear probes, 4 also used curvilinear probes, and 1 used phased-array probe. Most patients (71.4%) were awake and able to identify location of maximal tenderness. <u>*Pooled Diagnostic Characteristics:*</u> Sensitivity: 89.3% (81.1-94.3%) LR-: 0.11 (0.06-0.20) Specificity: 98.4% (90.2-99.8%) **LR+: 55.7** (8.5-363.4) Diagnostic Odds Ratio for positive test: 513.6 (66.4-3970.5) No significant differences between ED vs radiologist-performed US (p=0.1119)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	X
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	?	✓
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	✓	✓
9. The subgroups were stated a priori and appropriate.	X	X
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye I. Buchanan

Funding and conflicts of interest

Funding	Reported; no study funding.
Conflict of interest	Reported; no conflicts of interest stated.

Potential threats to viability

Chance	Convenience sampling in most included studies. Selection bias of patients included may over-estimate the accuracy of US results.
Selection bias	*Specify comprehensive searches; publication bias?* English-language studies only; only 4/1660 abstracts excluded on the basis of language translations. Search strategy with librarian/informatics specialist, repeated twice. Broad search from electronic databases, gray literature and conference abstracts.
Measurement bias	One author extracted study details, 2 authors independently extracted outcomes variables. High risk of bias for patient selection for index test; low risk of bias for reference standards.
Analysis bias	*Fixed/random effects? Heterogeneity mgt?* Two reviewers independently assessed study quality using QUADAS-2 tool. Unable to complete subgroup analyses on upper rib injuries (higher risk of mediastinal injury?). Some visual heterogeneity of Sens on Forest plots, but no X^2 statistics reported.
Confounding	*Enter independent factors affecting the outcome; clinicians to comment.* Heterogeneity in US operator training and experience could affect Dx test outcomes. Majority of included patients male; reluctance to expose patients breasts/anterior chest, or possibly different detection characteristics with interposing breast tissues? No international consensus criteria for diagnosing rib fractures with ultrasound.

Administrative details

Key words	Blunt chest trauma, rib fracture, ultrasound
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC **No conflicts of interest/Identify conflicts (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Ian Buchanan, MD FRCPC DipABEM DRCPSC RDMS **Educational Consulting, Pfizer Inc. (2018 & 2021)** *Asst. Professor, Emergency Medicine, McMaster University*

Research Question

What is the difference between Intravascular Cooling (IC) vs Surface Cooling (SC) in Cardiac Arrest Survivors?

BEEM Bottom Line

Why is this study important? Targeted Temperature Management (TTM) post-cardiac arrest has been shown to be beneficial for improve survival and meaningful neurologic recovery in survivors. The delivery mode of TTM, however, is uncertain, and may show important differences.

What, if any, threats to validity are most likely to have an impact on the results and how? Majority of included studies were non-RCTs, with moderate Risk of Bias.

How do the key results compare with the current evidence? Prior evidence shows that stable target temperature maintenance can enhance neurologic outcomes. The recent TTM2 trial (Dankiewicz 2021) showed no difference in death from any cause at 6 months or any difference in functional outcomes at 6 months between targeted hypothermia at 33°C and targeted normothermia with early treatment of fever (≥37.5°C). The results of this network meta-analysis focus on outcomes with targeted temperature management at 32-34°C.

How should this study impact the care of ED patients? Where possible, intravascular cooling in the ED in post-CA survivors should be initiated. In ED patients may be initiated on TTM with intravascular cooling devices (IC) or surface cooling (SC) with or without temperature feedback. If the goal of TTM is a temperature of 32-34°C, ICs may be associated with improved neurologic outcomes and survival. It is unclear how this evidence would be applied to targeted normothermia/avoidance of fever (target 36-37.5°C).

Study Summary

Article	Ramadanov N, Arrich J, Klein R, Herkner H, Behringer W. Intravascular versus Surface Cooling in Patients Resuscitated from Cardiac Arrest: A Systematic Review & Network Meta-Analysis with Focus on Temperature Feedback. Crit Care Med 2022 Jun 1;50(6):999-1009. doi: 10.1097/CCM.0000000000005463. Epub 2022 Jan 31.
Design	Systematic review with network meta-analysis. PROSPERO Reg: CRD42020166910
Population	***Included:*** Adults>18yo resuscitated from cardiac arrest (CA) undergoing TTM with target temperature 32-34°C. All study designs included. ***Excluded:*** Not reported.
Intervention	Intravascular cooling with temperature feedback
Comparison	Surface cooling with/without temp feedback
Outcomes	***Primary:*** Neurologic outcomes: Good = CPC 1-2, or modified Rankin 3 or less. ***Secondary:*** Survival (longest period of time reported in included studies).
Key Results	**14 studies included (4 RCTs), 4062 pts;** 34% received IV cooling (12 studies) and 66% received SC (14 studies). 23% of SC patients (and 15% overall) had temperature feedback info. 50% overall patients cooled without temperature feedback. ***Primary:*** IV vs SC cooling without temp feedback – OR 0.60 (95%CI 0.49-0.74) favouring IV IV vs SC cooling with temp feedback – NS difference ***Secondary:*** IV vs SC cooling without temp feedback – OR 0.80 (95%CI 0.66-0.96) favouring IV IV vs SC cooling with temp feedback – NS difference Subgroup (4 RCTs only): No change in direction, slight change in magnitude of summary effects.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Mostly electronic databases searched, some reference lists**	?	✓
3. The search for studies was unbiased and reproducible. **No duplicate search reported**	?	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible. **Duplicate?**	?	?
7. The quality of the primary studies is high. **RCTs low RoB, nonRCTs higher RoB. Included OHCA and IHCA in some studies. Studies included were from 2010-2019. Uncertain characteristics of arrest or cooling time, etc. Short outcome duration (mortality at hospital discharge).**	?	?
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	?
10. The statistical heterogeneity of the primary outcome is low (< 25%).	✓	✓

A1 = S. Upadhye A2 = J. Owen

Funding and conflicts of interest

Funding	Not reported
Conflict of interest	One author (WB) reported speaker fees from various industries. No other CoI's declared.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Variable sample sizes in included studies, which may affect outcomes of interest in pooled data.
Selection bias	*Limited/incomplete search, publication bias, etc.* No assessment of publication bias reported. No mention of grey literature searches.
Measurement bias	*Missing details on study selection; missing results of quality assessments.* Contacted authors for missing data.
Analysis bias	*Fixed vs. random effects, combined results of studies of different design.* N/A
Confounding	*List as reported.* Studies only included temp 34-36C. No analysis of duration of cooling, devices used, time to cooling initiation, rewarming rates.

Administrative details

Key words	Cardiac arrest; cooling; network meta-analysis; neurologic outcome; survival; targeted temperature management
Reference(s)	N/A

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC **No conflicts of interest/Identify conflicts (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Julian J. Owen, MD FRCPC **No conflicts of interest/Identify conflicts (ICMJE)** *Assistant Clinical Professor, Emergency Medicine/Critical Care/Trauma, McMaster University*

Research Question

What is the benefit of using fentanyl with ketamine and rocuronium during ED rapid sequence intubation (RSI)?

BEEM Bottom Line

Why is this study important? RSI is a common ED procedure and significant hemodynamic changes associated with it can contribute to adverse outcomes. This clinical trial examined hemodynamic changes with and without fentanyl for RSI with ketamine and rocuronium (KetRoc).

What, if any, threats to validity are most likely to have an impact on the results and how? The relatively small and very heterogeneous group of patients needing ED RSI precluded subgroup analyses based on diagnosis that may have shown important differences in outcomes. The primary outcome, systolic blood pressure (SBP) change outside of a pre-specified limit, is a surrogate for patient-important outcomes. Possible SBP measurement errors using non-invasive devices may introduce some variability, but likely better reflect real-world ED practice.

How do the key results compare with the current evidence? Prior trials/reviews show mixed results, based on different study design issues, patient inclusion/exclusions and other trial variables.

How should this study impact the care of ED patients? Selective use of fentanyl with KetRoc ED RSI is likely safe and useful, assuming that there is a no need to avoid episodes of hypotension.

Study Summary

Article	Ferguson I, Buttfield A, Burns B, Reid C, Shepherd S, Milligan J, Harris IA, Aneman A, for the Australasian College of Emergency Medicine Clinical Trials Network. Fentanyl versus placebo with ketamine and rocuronium for patients undergoing rapid sequence intubation in the emergency department: The FAKT study-A randomized clinical trial. Acad Emerg Med 2022; 29(6): 719-728. DOI: 10.1111/acem.14446
Design	Multi-centre RCT, 5 Australian hospital EDs. Trial Registration: ANZ Clinical Trials Registry, ACTRN12616001570471 (anzctr.org.au). Mixed academic/community centers, adults & peds.
Population	***Included:*** Adults (>18yo) needing ED RSI. ***Excluded:*** Allergy to study meds, need for "paralysis-only" or "no-drug" intubation, need for alternative induction regimen, ED "overwhelmed" or no staff available trained in study protocols.
Intervention	Fentanyl 100ug in 20ml NS; matched 1:1 with ketamine (0.5-2.0mg/kg IV) dosing volume. Drug order = Study drug *then* ketamine *then* rocuronium. Laryngoscopy initiated 60sec post Roc. Post RSI sedation continued after 10min with fentanyl and propofol.
Comparison	20ml NS, also matched to ketamine dose volume. Same drug sequence, sedation as above.
Outcomes	***Primary:*** Change in SBP outside of 100-150mmHg within 10min after induction sequence (measured every 2min). If pre-induction sBP >151mmHg, then primary outcome met if sBP rose >10% or outside limits during 10min interval. For initial sBP <99mmHg, then primary outcome met if sBP fell >10% or outside 10min interval limits. ***Secondary:*** Hypoxia (SpO_2 <93%), tachycardia (HR >120), or cardiac arrest within 10min induction interval. Airway outcomes = laryngoscopic views, first-pass intubation success, use of supraglottic airway devices (SAD), or need for surgical airway. 30day mortality, vent-free days.
Key Results	277 patients analyzed for primary outcome (95.5% recruited). ***Primary:*** Fent 66% vs Placebo 65%; Difference 1% (95%CI -10% to 12%, p=0.86). No statistically significant differences with missing 13pts added to either group. ***Secondary:*** Higher tachycardia in placebo (61%) vs fentanyl (48%); Diff 13% (2-25%). No significant differences in hypoxia (Diff 6%, 95%CI -2% to 15%), airway outcomes, 30day mortality (Fent 19%, Plac 24%; Diff 5% [-4% to 15%]), or vent-free days. Higher rates of hypertension with placebo, and hypotension with fentanyl.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively. **Multicentre trial; recruiting strategy unclear**	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	X	X
8. The patients were analyzed in the groups to which they were randomized (ITT). **Modified ITT**	✓	✓
9. All patient-important outcomes were considered.	?	?
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	Reported; internal dept funds
Conflict of interest	Reported; PhD scholarship support for lead author.

Potential threats to viability

Chance	Sample size requirements met for primary outcome but too small for patient-important outcomes and subgroup analyses. Very heterogeneous populations that precluded subgroup analyses based on RSI pathology that may have shown important differences in outcomes.
Selection bias	Unknown if consecutive sampling.
Measurement bias	Use of non-invasive BP measures may introduce some element of measurement error (but more congruent with real-world ED practices).
Analysis bias	Modified ITT.
Confounding	Study under-powered to examine clinical outcomes (mortality, vent days, hypoxias, airway interventions).

Administrative details

Key words	Fentanyl, ketamine, rocuronium, rapid-sequence intubation
Reference(s)	N/A

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC **No conflicts of interest (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Andrew Worster, MD, MSc **No conflicts of interest (ICMJE)** *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*

Research Question

Is an endotracheal intubation with a bougie superior to stylet for first attempt success?

BEEM Bottom Line

Why is this study important? Intubation failures occur in about 20% of patients in ED/ICU. It is not known if certain devices (bougies, stylets) can improve likelihood of successful intubation.

What, if any, threats to validity are most likely to have an impact on the results and how? Some discretionary exclusion or preference for devices amongst operators may lead to some selection bias. Exclusion of patients with difficult airways may also have changed outcomes (Type I error?).

How do the key results compare with the current evidence? Subsequent commentaries and past trials confirm that emergency airway management is nuanced, and very dependent on available equipment, operator training/experience, patient airway factors/urgency and teamwork. A prior study by Latimer et al (Ann Emerg Med 2021;77:296-304) demonstrated improved first pass success with use of a bougie in the out-of-hospital setting. Another RCT by Driver et al (JAMA 2018;319(21):2179-2189) also showed improved first pass success in patients with at least 1 difficult airway feature.

How should this study impact the care of ED patients? ED physicians should be familiar/experienced with all the difficult airway tools available to them, and train with their use to keep skills updated. Use of a bougie was not superior to endotracheal tube + stylet for first pass success of incidence of severe hypoxemia in this trial.

Study Summary

Article	Driver BE, Semler MW, Self WH, et al. Effect of Use of a Bougie vs Endotracheal Tube with Stylet on Successful Intubation on the First Attempt Among Critically Ill Patients Undergoing Tracheal Intubation. JAMA 2021; 326(24): 2488-2497. DOI: 10.1001/jama.2021.22002
Design	Randomized Clinical Trial (superiority), registered at: ClinicalTrials.gov Identifier: NCT03928925. Multi-centred US trial (7 EDs, 8 ICUs in 11 hospital sites)
Population	***Included:*** Adult patients needing endotracheal intubation (ET) ***Excluded:*** Patients who were pregnant, incarcerated, need for immediate ET placement prior to randomization, or if operator deemed patient needed/contraindicated from either device.
Intervention	ET with bougie (ET-B, n=556 pts)
Comparison	ET with stylet (ET-S, n=546pts)
Outcomes	***Primary:*** Successful intubation on first attempt. ***Secondary:*** Incidence of severe hypoxemia (Sat <80%)
Key Results	1106 patients recruited (1558 screened), 1102 completed (99.2%). Median age 58yo, 41% women. "Difficult airways" identified in 42% of cohort. Reasons (most common) for intubation: Altered LOC 44.6%, acute respiratory failure 31.5%. **Most common operators = emergency physicians (62.9%); mostly residents (61.6%). ED intubations in 61-63% of cases.** Video laryngoscope used in ET-B 75.7% and ET-S 73.8% patients. ***Primary OOI:*** ET-B 80.4% vs ET-S 83%.; Risk Difference -2.6% (95%CI -7.3 to 2.2, p=0.27). No differences noted in pre-specified subgroup analyses. ***Secondary OOI:*** ET-B 11% vs ET-S 8.8%; Risk Difference 2.2% (-1.6 to 6.0). ***Exploratory Outcomes:*** Time from induction to intubation: ET-B 124sec vs ET-S 112sec Airway complications (esophageal placement, injury, aspiration): 1.8% in each group Post-intubation PTX: ET-B 2.5% vs ET-S 2.7% Cardiovascular collapse: ET-B 12.2% vs ET-S 16.7%; RD -4.4% (-8.8 to -0.1) Death by 28days: ET-B 27.3% vs ET-S 33.7%; RD -6.4% (-12.0 to -0.8)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	X	X
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = J. Owen

Funding and conflicts of interest

Funding	Study funded from various public grants; no role in study development, conduct or data analysis.
Conflict of interest	Numerous authors had public/industry grants; none relevant to current work.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Unclear if patients recruited consecutively. Some discretionary inclusion/exclusion of patients based on airway difficulty, or device preferences by operators could lead to selection bias or Type I errors.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Groups seem to be well balanced (Table 1)
Measurement bias	Randomized blocks of 2/4/6 pts, stratified by site. Trial was under-powered to detect real differences in rare safety outcomes (airway injury, aspiration, PTX).
Analysis bias	*ITT, Per Protocol, As Treated.* ITT analysis.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Impossible to blind providers to intervention in this pragmatic trial. Not all operators experienced in bougie placement; did not alter outcomes in favour of ET-S groups (ie. no Type II error).

Administrative details

Key words	Bougie, endotracheal intubation, stylet
Reference(s)	Kida et al, JAMA 2022; 327(15):1503. doi:10.1001/jama.2022.2713. Brenner et al, *JAMA.* 2022;327(15):1502-1503. doi:10.1001/jama.2022.2710

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC **No conflicts of interest/Identify conflicts (ICMJE)**
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Julian J. Owen, MD FRCPC **No conflicts of interest/Identify conflicts (ICMJE)**
Assistant Clinical Professor, Emergency Medicine/Critical Care/Trauma, McMaster University

Research Question

What are the latest recommendations in transfusing critically ill patients?

BEEM Bottom Line

Why is this study important? This guideline provides evidence-based recommendations for transfusion in critically ill patients.

What, if any, threats to validity are most likely to have an impact on the results and how? Thorough search strategy, screening, data abstraction, risk of bias assessment, and evidence analysis took place. As well, formulation of recommendations followed GRADE methodology. Limitations included lack of patient/caregiver representation on panel, and lack of evidence in the literature on which to base some recommendations.

How do the key results compare with the current evidence? Restricted RBC transfusion thresholds continue to be evidence-based across various critically ill patient populations. This is supported by Choosing Wisely Canada transfusion toolkits, and other recent evidence summaries. Tranexamic acid (TXA) is beneficial if given early in trauma patients as supported by large RCTs.

How should this study impact the care of ED patients? For massively bleeding trauma patients, high ratio transfusion strategies and early use (<3 h) of TXA is recommended based on available evidence. In non-massively bleeding GI patients, a restrictive transfusion threshold for RBCs (70 mg/dL) and avoidance of high dose (4g/24h) of TXA is recommended. In non-massively bleeding post-partum hemorrhage patients, a restrictive threshold for RBCs (<60 mg/dL) and use of TXA is recommended. For patients with intracranial hemorrhage on antiplatelet therapy, a restrictive platelet transfusion strategy is recommended.

Study Summary

Article	Vlaar APJ, Dionne JC, de Bruin S, Wihnegerge M, Raasveld SJ, van Barrle FEHP, Antonelli M, Aubron C, Duranteau J, Juffermans NP, Meier J, Murphy GH, Abbasciano F, Muller MCA, Lance M, Nielsen ND, Schochl H, Hunt BJ, Cecconi M, Oczkowski S. Transfusion strategies in bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine. Intens Care Med 2021; 47, 1368–1392. https://doi.org/10.1007/s00134-021-06531-x.
Design	Clinical Practice Guideline
Population	***Included:*** Patients needing transfusions with blood products. ***Excluded:*** No Recs around BP targets, fluid resuscitation, vasopressor choices, bleeding source control.
Scope of Recs	Clinicians who care for critically ill patients needing transfusions.

Key Recommendations (LoE = Level of Evidence)

** Only ED-relevant Recs are listed here.

Recommendation	*Strength (LoE)*
1. We **recommend** the use of early (< 3 h from trauma) TXA in critically ill patients with bleeding or suspected bleeding due to trauma (Strong).	**Strong** (High)
2. We suggest the early use of TXA in critically ill patients with postpartum hemorrhage.	Conditional (High)
3. We suggest **not using** high-dose IV TXA in critically ill patients with gastrointestinal bleeding (Conditional).	Conditional (High)
1. In patients with non-massive gastrointestinal bleeding, we suggest restrictive (7 g/dL) transfusion vs. liberal (9 g/dL) RBC transfusion threshold.	Conditional (Moderate)
2. We suggest using a restrictive platelet transfusion strategy (no transfusion) in patients with intracranial hemorrhage (spontaneous or traumatic intracerebral hemorrhage) who are on antiplatelet therapy.	Conditional (Mod)
3. We suggest the use of TXA in critically ill patients with acute traumatic brain injury and bleeding due to trauma.	Conditional (Mod)

1. In patients with **non-massive postpartum hemorrhage**, we **suggest** restrictive transfusion, guided by presence of shock and symptoms potentially attributable to anemia (e.g. dyspnea, syncope, tachycardia, angina, neurological symptoms) or hemoglobin < 6 g/dL, rather than a liberal target hemoglobin of 9 g/dL.	Conditional (Low)

BEEM Critique

Risk of bias assessment (amalgamated from AGREE-II/NEATS instruments)

	A1	A2
1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.	✓	✓
2. Financial conflicts of interest of guideline development group (GDG) members have been disclosed and managed.	✓	✓
3. The CPG development group includes all of the relevant multidisciplinary stakeholders, including clinicians, methodologists and patients/caregivers. **No patients/caregivers.**	?	?
4. The CPG objectives, health questions, scope of relevant providers and target recipients of care are clearly defined.	✓	✓
5. Values/preferences of patients, caregivers, advocates and/or the public with experience with the clinical disease management has been sought/integrated into CPG development (reported clearly). **No reps on group; obtained from literature review.**	?	?
6. The search strategy for evidence is thoroughly developed and described.	X	✓
7. The criteria for selecting relevant studies/evidence are clearly described.	✓	✓
8. The quality, strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.). Summaries of evidence tables are provided.	?	✓
9. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
10. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
11. The strength of recommendations is clearly reported, including confidence in underlying evidence.	✓	✓
12. Recommendations are clear and unambiguous, and easily identified in the CPG publication. **Scattered throughout document; Summary Table 1 = nice graphics!!**	?	✓
13. Different options for management for managing the health questions are clearly presented.	✓	✓
14. Experts externally reviewed the guideline prior to its publication.	X	X
15. The CPG describes a procedure to update the guideline.	X	✓
16. The CPG provides advice, tools and/or clinical pathways for easy adoption/adaptation into practice.	X	✓
17. The CPG describes barriers and facilitators to implement recommendations.	X	✓
18. Performance metrics for monitoring implementation of recommendations for audit/feedback have been defined appropriately.	X	?
19. Resource implications for implementing CPG recommendations have been discussed.	X	✓

A1 = S. Upadhye A2 = J. Owen

Funding and conflicts of interest

Funding	Reported; CPG sponsored by ESICM. No industry involvement.
Conflict of interest	Reported; none declared.

Potential threats to viability

Development	*Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible?* See Critique above.
Presentation	*Well organized with easy to find recommendations?* Yes; Table 1 on pg 14 (Infographic)
Comprehensive	*Was the information to inform decision-making complete?* Yes
Clinical Validitiy	*Are the recommendations clinically sound and appropriate for the intended patients?* Yes

Administrative details

Key words	Bleeding, critical illness, transfusions.
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**
Julian J. Owen, MD FRCPC *Assistant Clinical Professor, Emergency Medicine & Critical Care, McMaster University*	**No conflicts of interest/Identify conflicts (ICMJE)**

Research Question

What are the latest recommendations for managing difficult airways (DA)?

BEEM Bottom Line

Why is this study important? This clinical practice guideline (CPG) updates recommendations from the American Society of Anesthesiologists Difficult Airway guidance.

What, if any, threats to validity are most likely to have an impact on the results and how? There is no clear linkage between the retrieved evidence and the strength of CPG recommendations.

How do the key results compare with the current evidence? Updated evidence searches and filtering of evidence, and support by international experts surveyed improves confidence in the recommendations.

How should this study impact the care of ED patients? Emergency departments (EDs) should create and implement DA quality improvement programs to operationalize clinical algorithms offered in this document.

Study Summary

Article	Apfelbaum JL, Hagberg CA, Connis RT, Abdelmalak BB, Agarkar M, Dutton RP, Fiadjoe JE, Greif R, Klock PA, Mercier D, Myatra SN, O'Sullivan EP, Rosenblatt WH, Sorbello M, Tung A. 2022 American Society of Anesthesiologists (ASA) Practice Guidelines for Management of the Difficult Airway. Anesthesiology 2022; 136(1): 31-81. DOI: 10.1097/ALN.0000000000004002
Design	Clinical Practice Guideline
Population	***Included:*** Adult and pediatric patients in in-patient settings, including the ED (and other critical care settings). ***Excluded:*** Pre-hospital settings. Not applicable for patients at risk of aspiration, nor physiologic (not anatomic) difficult airways.
Scope of Recommendations	CPGs are intended for adult and pediatric patients with either anticipated or unanticipated difficult airways, obstetric patients, intensive care (ICU) patients, and critically ill patients.

Key Recommendations (LoE = Level of Evidence)

Recommendations **(**Strength of Recs (LoE) NOT explicitly reported in publication!!)**

1) Evaluation for Difficult Airway (DA): The most responsible airway personnel should confirm medical, surgical, environmental and anesthetic factors that can influence patient airway outcomes. Get historical information as needed from patient, family, medical records, etc. Complete a physical exam to determine any anatomic predictors of difficult airways. Determine a risk of needing advanced airway equipment (e.g., bronchoscope, surgical airway).
2) DA Preparation: Have all equipment for advanced/emergency airway interventions on hand; consider preparing a "Difficult Airway" cart with appropriate training. Ensure proper positioning and supplement oxygen use prior to initiating DA interventions.
3) Anticipate DA: Identify step-wise strategies for awake intubation, DA patients who can be adequately ventilated, DA patients who can't be ventilated/intubated, and invasive rescue airway procedures. When appropriate, start with awake intubations if: a) difficult ventilation (face mask/supraglottic airway), (b) increased risk of aspiration, (c) DA patient is likely incapable of tolerating a brief apneic episode, or (d) there is expected difficulty with emergency invasive airway rescue. Anticipate need to vary interventions for pediatric or uncooperative patients. Be ready to used combined techniques for DA interventions as clinically warranted. Limit the number of unsuccessful intubation attempts to avoid trauma. Be wary of the passage of time with repeated attempts; monitor oxygen saturation throughout the procedure. Ensure oxygenation between attempts with BVM ventilation.
4) Unanticipated DA: Call for help as needed. Optimize oxygenation (BVM). Determine appropriateness of non-invasive vs invasive interventions. For invasive airway Rx, ensure proper training/experience for airway personnel, and complete the airway intervention as expeditiously as possible.
5) Confirmation of Tracheal Intubation: Use capnography/end-tidal CO_2 monitoring to confirm endotracheal intubation.

BEEM Critique

Risk of bias assessment (amalgamated from AGREE-II/NEATS instruments)

	A1	A2
1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.	?	?
2. Financial conflicts of interest of guideline development group (GDG) members have been disclosed and managed.	?	?
3. The CPG development group includes all of the relevant multidisciplinary stakeholders, including clinicians, methodologists and patients/caregivers.	?	?
4. The CPG objectives, health questions, scope of relevant providers and target recipients of care are clearly defined.	✓	✓
5. Values/preferences of patients, caregivers, advocates and/or the public with experience with the clinical disease management has been sought/integrated into CPG development (reported clearly).	?	?
6. The search strategy for evidence is thoroughly developed and described.	✓	✓
7. The criteria for selecting relevant studies/evidence are clearly described.	✓	✓
8. The quality, strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.). Summaries of evidence tables are provided.	✓	✓
9. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
10. There is an explicit approach linking the evidence to formulate the recommendations.	X	X
11. The strength of recommendations is clearly reported, including confidence in underlying evidence.	X	X
12. Recommendations are clear and unambiguous, and easily identified in the CPG publication.	✓	✓
13. Different options for management for managing the health questions are clearly presented.	✓	✓
14. Experts externally reviewed the guideline prior to its publication.	✓	✓
15. The CPG describes a procedure to update the guideline.	X	X
16. The CPG provides advice, tools and/or clinical pathways for easy adoption/adaptation into practice.	✓	✓
17. The CPG describes barriers and facilitators to implement recommendations.	X	X
18. Performance metrics for monitoring implementation of recommendations for audit/feedback have been defined appropriately.	X	X
19. Resource implications for implementing CPG recommendations have been discussed.	X	X

A1 = S. Upadhye A2 = A. Worster

Funding and conflicts of interest

Funding	(Reported) Support provided solely by the ASA (pg 51).
Conflict of interest	(Reported) Multiple authors had various disclosures of academic grants, and industry support. Management of those with various conflicts was not clearly disclosed.

Potential threats to viability

Development	The CPG panel had many airway experts & methodologists, but no patient, ED physician/nurse/RT stakeholders.
Presentation	Not well organized, key recommendations are buried at end of CPG, although they are reasonably identifiable in body of manuscript.
Comprehensive	The information to inform decision-making was complete.
Clinical Validity	Useful info graphics and algorithms are provided to support implementation in the workplace.

Administrative details

Key words	Difficult airway, ED.
Reference(s)	Orebaugh SL. Difficult Airway Management in the Emergency Department. J Emerg Med 2002; 22(1): 31-48. Brown NS, Chirico J, Hollidge M, Randall J. Clinical leadership in reducing risk: Managing patient airways. Healthcare Manage Forum 2019;32(2):92-96. doi: 10.1177/0840470418810678. Kornas RL, Owyang CG, Sakles JC, *et al*. Evaluation and Management of the Physiologically Difficult Airway: Consensus Recommendations From Society for Airway Management. Anesth Analg 2021 Feb 1;132(2):395-405. doi: 10.1213/ANE.0000000000005233.

Clinical Appraisal faculty

Suneel Upadhye, MD, MSc, FRCPC **No conflicts of interest (ICMJE)** *Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*
Andrew Worster, MD, MSc **No conflicts of interest (ICMJE)** *Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University*

Research Question

What is the optimal temperature for therapeutic hypothermia post cardiac arrest?

BEEM Bottom Line

Why is this study important? Most therapeutic hypothermia (TH) trials have studied temperatures at 32°C to 36°C. Small animal/human trials suggest that cooler temperatures may confer a survival advantage. This trial examined that possibility in out-of-hospital cardiac arrest (OCHA) survivors.

What, if any, threats to validity are most likely to have an impact on the results and how? A presumption of a large Rx difference driving a sample size calculation risks under-powering detection of a smaller difference that may be clinically important. Composite endpoints can sometime confuse the direction of treatment effects, but did not in this trial as each individual outcome driving the composites were also not significantly different.

How do the key results compare with the current evidence? While most TH comparison trials seem to stay in the 32°C and above range, this is the first trial reporting no advantage of cooling below 32°C.

How should this study impact the care of ED patients? There is no need to be "too cool" post OCHA. There was no difference in outcomes for 31°C vs 34°C in this trial.

Study Summary

Article	Le May M, Osborne C, Russo J, So D, Chong QY, Dick A, Froeschl M, Glover C, Hibbert B, Marquis JF, De Roock S, Labinaz M, Bernick J, Marshall S, Maze R, Wells G. Effect of Moderate vs Mild Therapeutic Hypothermia on Mortality and Neurologic Outcomes in Comatose Survivors of Out-of-Hospital Cardiac Arrest. The CAPITAL CHILL Randomized Clinical Trial. JAMA 2021 Oct 19;326(15):1494-1503. doi: 10.1001/jama.2021.15703.
Design	Randomized controlled trial; single-site (Ottawa, Canada); ClinicalTrials.gov Identifier: NCT02011568
Population	*Included:* Comatose (GCS<8) adults ≥ 18yo who survive OCHA. *Excluded:* Arrest due to intracranial bleed, severe coagulopathy with major bleeding, coma not due to OCHA, life expectancy <1yr (unrelated to cardiac arrest), or known inability to perform activities of daily living (ADLs).
Intervention	TH to a target temp of 31°C for 24hrs, then rewarmed to 37°C in a controlled fashion
Comparison	TH target temp 34°C, then rewarmed to 37°C in a controlled fashion
Outcomes	*Primary:* Composite of all-cause mortality or poor neurologic outcome at 180days post-randomization (measured on Disability Rating Scale, and Modified Rankin Scale). *Secondary:* Death or stroke (various time points), stent thrombosis, seizures, dialysis, pneumonia, cardiogenic shock/recurrent cardiac arrest, treatable arrhythmias, major bleeding, LVEF (3d, 3mo), peak CK level, ICU/hospital LOS, and proportion of survivors discharged home. Safety = IVC thrombus or leg DVT on US (day 3 and 5). *Subgroups prespecified:* age, initial rhythm, STEMI, sex, timing of PCI.

Key Results

Mean age 61yo., 81% men. Essentially equal cardiac causes of arrest, immediate angio/PCI and IABP supports between groups.

Primary: No difference RD 3.0% (-7.2 to 13.2%); RR 1.07 (0.86-1.33, p=0.56); no differences after adjusting for baseline covariates and all planned subgroups. No difference with "as treated" or ITT analyses.
Secondary: Length of ICU median difference 3days longer in 31C group (p=0.004). Otherwise no difference in all secondary outcome groups.

Survivors 180d with poor neuro outcomes (DRS>5): No difference RR 1.17 (0.47-2.91)
No difference in withdrawal of life-sustaining Rx.
No difference in DVT rates: RR 1.04 (0.59-1.86), nor IVC thrombus rates: RR 0.50 (0.21-1.20)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	?	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	X	X
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = J. Owen

Funding and conflicts of interest

Funding	University of Ottawa Heart Institute Cardiac Arrest Program
Conflict of interest	One author (So) disclosed some industry relationships (advisory boards, grants). No other conflicts declared.

Potential threats to viability

Chance	Required sample size met/exceeded in both arms. Type I error from multiple comparisons mitigated by exploratory analyses only. Sample size powered to detect a 15% risk difference, so may have been underpowered to detect a smaller one?
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Unclear consecutive vs. other sampling method.
Measurement bias	None.
Analysis bias	Primary analysis based on successful Rx completion. Secondary analysis based on ITT, and per protocol. One pt lost to follow-up in 31C arm.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* All patients treated essentially equally aside from TH Rx (Supp Table 2 and 3). Majority of enrolled patients had a primary cardiac cause of arrest; results may not be generalizable to other arrest causes.

Administrative details

Key words	Cardiac arrest, therapeutic hypothermia
Appraisers	S. Upadhye, J. Owen
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Julian J. Owen, MD FRCPC
Assistant Clinical Professor, Emergency Medicine/Critical Care, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the utility in using ED POCUS for anterior shoulder dislocation diagnosis and reduction?

BEEM Bottom Line

Why is this study important? Shoulders are the most commonly dislocated joints in the ED, and approximately 1/3 are accompanied with a fracture. A skillful physical exam (PE), with adjunct POCUS, may be useful to avoid low-value radiography (exposures, costs) when a concomitant fracture is not likely.

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. Results from a single site should ideally be validated in other settings to confirm results. Future studies should also examine reduction of x-ray rates if possible.

How do the key results compare with the current evidence? These results are congruent with prior smaller RCTs, with tighter precision/95% CIs.

How should this study impact the care of ED patients? Addition of POCUS (with appropriate standardized training and review) can dramatically improve diagnosis of anterior shoulder dislocation, proximal humeral fracture and successful reduction, and likely spare unnecessary x-rays.

Study Summary

Article	Attard Biancardi MA, Jarman RD, Cardona T. Diagnostic accuracy of point-of-care ultrasound (PoCUS) for shoulder dislocations and reductions in the emergency department: a diagnostic randomized control trial (RCT). Emerg Med J 2021;0:1–7. doi: 10.1136/emermed-2020-210947.
Design	Diagnostic RCT
Population	*Included:* Patients >16 yo with acute shoulder injury, and decreased range of motion (ROM). *Excluded:* Age <16 yo, chronic shoulder pain, unable to give consent, needing emergency surgery for polytrauma, or those referred to ED with confirmed shoulder dislocation/fracture.
Index Test	PE + POCUS vs PE alone
Reference Standard	Conventional radiography for shoulder injury (AP & axillary views)
Diagnoses of Interest	Shoulder dislocation, proximal humeral fracture, successful reduction

Key Results

1206 patients enrolled in study (600 POCUS, 606 controls). Prevalence of dislocation 24% (99% anterior), proximal humeral fracture 27%. Fracture dislocation 20% of all dislocations (n=58), of which 24% (14) needed operative reduction. Bimodal distribution of dislocations (younger males 21-30 yo, and older females 71-80 yo). Proximal humeral fractures skewed peak in older ages (F 61-70 yo, M 71-80 yo).
Overall 96% of reductions completed in the ED.
POCUS group: 158 dislocations, 178 proximal humeral fractures, 148 reductions
Control group: 132 dislocations, 154 proximal humeral fractures, 130 reductions

Dislocation Diagnosis:
PE alone: Sens 78.8% (70.9-85.4%), Spec 61.1% (56.5-65.5%), LR+ 2.0 and LR- 0.3. False positive 30%, false negative 5%
PE + POCUS: Sens 100% (97.7-100%), Spec 100% (99.2-100%), LR+ ∞ and LR- 0.0.

Proximal Humeral Fracture Diagnosis:
PE alone: Sens 83.1% (76.2-88.7%), Spec 32.7% (28.4-37.3%), LR+ 1.2 and LR- 0.5. False positive 50%
PE + POCUS: Sens 96.6% (92.8-98.7%), Spec 99.1% (97.6-99.8%), LR+ 103.9 and LR- 0.0. Missed 6 out of 178 fractures, no change in ED management.

Successful Joint Reduction:
PE alone: Spec 90.3% (83.7-94.9%), NPV 74.1%, overall accuracy 68.7% (59.9-76.5%)
PE + POCUS: Spec 100% (97.5-100%), NPV 100%, overall accuracy 100% (97.7-100%)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those likely to undergo testing in the ED.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	✓	✓
3. All patients underwent the same diagnostic evaluation.	✓	✓
4. All tests were conducted within similar time frames to preclude changes in disease status.	✓	✓
5. The reference standard criteria for the candidate diagnoses are explicit and reproducible.	✓	✓
6. The reference standard was applied regardless of and blinded to the index test result.	✓	✓
7. The assignment of the candidate diagnoses was explicit and reproducible.	✓	✓
8. Most (> 80%) patients received a diagnosis.	✓	✓
9. Undiagnosed patients received adequate clinical follow-up.	✓	N/A
10. The estimates of disease probability are clinically significant.	✓	✓

A1 = S Upadhye A2 = D Kim

Funding and conflicts of interest

Funding	None (reported)
Conflict of interest	None (reported)

Potential threats to viability

Chance	None.
Selection bias	Is the sampling method representative of the target population; are the groups balanced? Single center study, but used consecutive sampling to minimize bias.
Measurement bias	None.
Analysis bias	Lack of reporting of Sensitivity and Likelihood ratios for the successful reduction outcomes?
Confounding	ED physicians (n=21) were given standardized training for ED shoulder POCUS by expert ED PI, and regular follow-up meetings to ensure ongoing study performance. No duplicated scans of same patient to assess agreement, nor minimum number of training scans needed to demonstrate competency. The training was simply described as a 1-hr didactic session and a 1-hr practical session. No recording of scans to ensure diagnostic accuracy of ED scans by external reviewers.

Administrative details

Key words	Anterior shoulder dislocation, humerus fracture, reduction, POCUS
Appraisers	Upadhye S, Kim D
Reference(s)	Worster A, Innes G, Abu-Laban RB. Diagnostic testing: an emergency medicine perspective. CJEM 2002; 4(5): 348-354.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Daniel Kim, MD FRCPC
Clinical Associate Professor, Department of Emergency Medicine, University of British Columbia
Medical Advisory Board, Clarius Mobile Health

Research Question

What are the latest guidelines for the management of acute anaphylaxis?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? This guideline updates prior 2008 guidance on emergency anaphylaxis treatment, and provides detailed evidence reviews about effective treatments for acute anaphylaxis.

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? Enter text here. Notes: Top 3 fatal flaws in order of priority. Explain in simple terms for clinician readers. No description of the littérature search strategy is presented. Absence of selection bias thus cannot be confirmed. The recommendations are based on mostly low and the very low quality evidence. The lack of description of the populations included in the studies could threaten the external validity of the results.

How should this guideline, and specifically which recommendations should impact the care of ED patients? This evidence update supports the Resuscitation Council UK May 2021 update on emergency anaphylaxis treatment, which contains useful charts, algorithms, dosing tables, etc. for ready adaptation into ED practice.

Study Summary

Article Dodd A, Hughes A, Sargant N, Whyte AF, Soar J, Turner PJ. Evidence update for the treatment of anaphylaxis. Resuscitation 2021; 86-96. https://doi.org/10.1016/j.resuscitation.2021.04.010. PMID: 33895231

Design Clinical Practice Guideline.

Population Not specified; guidance for adults and children with anaphylaxis.

Scope This guideline is intended for ED practitioners who treat anaphylaxis.

Key Results *Updated recommendations for 2021

Recommendation	*Strength*	*Quality of Evidence*
We recommend adrenaline as the first line treatment for anaphylaxis.	Strong	Moderate
Intramuscular adrenaline should be administered at the doses listed in Table 4.	Strong	Low
Where respiratory and/or cardiovascular features of anaphylaxis persist despite 2 appropriate doses of adrenaline (administered by IM or IV route), seek urgent expert help (e.g. from experienced critical care clinicians) to establish an intravenous adrenaline infusion to treat refractory anaphylaxis.	Strong	
*We suggest that antihistamines are not used as part of the initial emergency treatment for anaphylaxis.	Low	
Adrenaline should be administered early once symptoms of anaphylaxis have been recognized or suspected.	Weak	Very Low
The intramuscular (IM) route is recommended for initial adrenaline treatment for anaphylaxis.	Strong	
Titrate the administration of adrenaline (by any route) against clinical response.	Strong	
*Subsequent doses of adrenaline should be given every 5 min, titrated to clinical response, in patients whose symptoms are refractory to initial treatment.	Weak	

Low dose intravenous adrenaline infusions appear to be effective and safe to treat refractory anaphylaxis.	Weak
For anaphylaxis refractory to initial treatment with adrenaline, an IV fluid bolus (crystalloid) is recommended as an adjunct to improve drug distribution	Weak
*We suggest against the routine use of corticosteroids to treat anaphylaxis.	Weak
*Beta-2 agonists (such as salbutamol) may be useful as an adjunct treatment for lower respiratory symptoms caused by anaphylaxis, following initial treatment with IM adrenaline.	Weak
*In the presence of persisting respiratory symptoms in anaphylaxis, beta-2 agonists (whether inhaled or parenteral) should not be used as an alternative to further parenteral treatment with adrenaline.	Strong
*We suggest a risk-stratified approach to the discharge of patients following anaphylaxis (Table 5)	Weak

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	X
2. Systematic methods were used to search for evidence.	?	?
3. The criteria for selecting the evidence are clearly described.	?	?
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	?	?
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	✓	?
8. The content of the guideline is free of influence by the views of the funding body.	?	?
9. Competing interests of guideline development group members have been recorded and managed.	✓	✓
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = J. Morris

Funding and conflicts of interest

Funding	None stated.
Conflict of interest	Declared. Some authors had govt/non-industry grants, and other academic allergy affiliations. Senior author did have some industry fees and nonfinancial supports.

Potential threats to validity

Development	Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible? **This was a GRADE-Adolopment exercise in adapting/updating pre-existing systematic reviews and guidelines (not a *de novo* literatue search). Search strategy for source materials not included in this report. The roles and the reason for choosing the internal reviewers are not detailed.**
Presentation	Well organized with easy to find recommendations? **Questions and recommendations scattered throughout the text (not summarized separately at beginning of manuscript).**
Comprehensive	Was the information to inform decision-making complete? **Yes; GRADE Adolopment framework provided.**
Clinical Validity	Are the recommendations clinically sound and appropriate for the intended patients? **Yes**

Administrative details

Key words	Anaphylaxis, adrenaline, antihistamine, corticosteroids, resuscitation
Appraisers	Upadhye S, Morris J.
Reference(s)	1. Dodd A, Hughes A, Sargant N, Whyte AF, Soar J, Turner PJ. Evidence update for the treatment of anaphylaxis. Resuscitation 2021; 86-96. https://doi.org/10.1016/j.resuscitation.2021.04.010. PMID: 33895231 2. Working Group of Resuscitation Council UK (May 2021). Emergency treatment of anaphylaxis. Available at: https://www.resus.org.uk/library/additional-guidance/guidance-anaphylaxis/emergency-treatment. 3. Beardsall I. Anaphylaxis – a Guideline Update. St. Emlyn's Emergency Medicine #FOAMed. Available at: https://www.stemlynsblog.org/anaphylaxis-a-guideline-update/

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Judy Morris, MD MSc FRCPC
Associate professor, Department of Family and Emergency Medicine
Université de Montréal
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the latest guidelines for the management of biphasic anaphylaxis?

BEEM Bottom Line

Why is this guideline and at least some of its recommendations important? Biphasic anaphylaxis occurs in 1-20% of patients, which may occur from 1-72hrs after initial anaphylaxis episode, but has been reported up to 78hrs. Risk factors for severe anaphylaxis include the following: older age, asthma Hx, and comorbid CV/other diseases. It is not clear what the optimal length of ED observation should be after initial anaphylaxis treatment to avoid biphasic reactions, but summary literature suggests that the range should be 1-5hrs (NPV range 95-97.3%).

Which, if any, threats to validity or applicability are most likely to have an impact on the recommendations and how? Lack of an explicit reported search strategy, limited to English language articles (risk of missing important information). No declaration of funding body, nor influence on guideline development/reporting. Many authors have considerable industry relationships, and it is not clear how these were managed.

How should this guideline, and specifically which recommendations should impact the care of ED patients? This guideline updates information on use of epinephrine for acute anaphylaxis, and observation for biphasic recurrence. It refutes the utility of antihistamines and glucocorticoids for biphasic anaphylaxis prevention and also recommends against routine use of those medications in patients with history of radiocontrast HSRs to prevent anaphylaxis before a radiocontrast study.

Study Summary

Article	Shaker MS, Wallace DV, Golden DBK, *et al*. Anaphyllaxis – a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. J Allergy Clin Immunol 2020; 145(4): 1082-1123. doi: 10.1016/j.jaci.2020.01.017.
Design	Clinical Practice Guideline.
Population	Not specified.
Scope	This guideline is intended for ED physicians who treat anaphylaxis **<u>EM-Relevant Questions Addressed in Guideline:</u>** Q1. What risk factors should clinicians take into consideration in determining the likelihood of biphasic anaphylaxis? Q2. Should antihistamines and/or glucocorticoids be used to prevent biphasic anaphylaxis? Q3. Should antihistamine and/or glucocorticoid premedication be used to prevent recurrent HSRs to RCM?

Key Results

Recommendation	*Strength*	*Quality of Evidence*
Rec1a: We suggest that a clinician incorporate severity of anaphylaxis presentation and/or the administration of >1 dose of epinephrine for the treatment of initial anaphylaxis as a guide to determining a patient's risk for developing biphasic anaphylaxis.	Conditional	Very Low
Rec1b: We suggest extended clinical observation in a setting capable of managing anaphylaxis (to detect a biphasic reaction) for patients with resolved severe anaphylaxis and/or those who need >1 dose of epinephrine.	Conditional	Very Low
Rec2: We suggest **against** administering glucocorticoids or antihistamines as an intervention to prevent biphasic anaphylaxis.	Conditional	Very Low
Rec3: We suggest **against** routinely administering glucocorticoids and/or antihistamines to prevent anaphylaxis in patients with prior radiocontrast HSRs when readministration of a low- or iso-osmolar, nonionic RCM agent is required.	Conditional	Very Low

Additional Good Practice Statements

GPS1: Administer epinephrine as the first-line pharmacotherapy for uniphasic and/or biphasic anaphylaxis.

GPS2: Do not delay the administration of epinephrine for anaphylaxis, as doing so may be associated with higher morbidity and mortality.

GPS3: After diagnosis and treatment of anaphylaxis, all patients should be kept under observation in a setting capable of managing anaphylaxis until symptoms have fully resolved.

GPS4: All patients with anaphylaxis should receive education on anaphylaxis, including avoidance of identified triggers, presenting signs and symptoms, biphasic anaphylaxis, treatment with epinephrine, and the use of epinephrine auto-injectors, and they should be referred to an allergist.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The guideline development group includes all of the relevant stakeholders, including patients.	✓	?
2. Systematic methods were used to search for evidence.	?	?
3. The criteria for selecting the evidence are clearly described.	X	?
4. The strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.).	✓	✓
5. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
6. There is an explicit approach linking the evidence to formulate the recommendations.	✓	✓
7. Experts externally reviewed the guideline prior to its publication.	✓	✓
8. The content of the guideline is free of influence by the views of the funding body.	?	?
9. Competing interests of guideline development group members have been recorded and managed.	✓	?
10. The strength and certainty of the key recommendations are clearly identified.	✓	✓

A1 = S. Upadhye A2 = J. Morris

Funding and conflicts of interest

Funding	Not specified.
Conflict of interest	Reported. Many industry relationships declared.

Potential threats to validity

Development:	The steering group and support collaborators all seem to be appropriate healthcare/ER/allergy experts. No patient/public stakeholders reported. The search strategy was limited and only partially reported (ie not reproducible). Use of GRADE methods to evaluate evidence and formulate recommendations is explicitly described for each relevant question.
Presentation:	Well organized with easy to find recommendations? **YES**
Comprehensive:	Was the information to inform decision-making complete? **YES**
Clinical Validity:	Are the recommendations clinically sound and appropriate for the intended patients? **YES**

Administrative details

Key words	anaphylaxis, epinephrine, antihistamines, glucocorticoids
Appraisers	Upadhye S, Morris J.
Reference(s)	1. Shaker MS, Wallace DV, Golden DBK, Oppenheimer J, Bernstein JA, Campbell RL, Dinakar C, Ellis A, Greenhawt M, Khan DA, Lang DM, Lang ES, Lieberman JA, Portnoy J, Rank MA< Stukus DR, Wang J. Anaphyllaxis – a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. J Allergy Clin Immunol 2020; 145(4): 1082-1123. doi: 10.1016/j.jaci.2020.01.017.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Judy Morris MD MSc FRCPC
Associate professor, Department of Family and Emergency Medicine
Umiversité de Montréal
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the factors associated with the need for longer ED observations periods in anaphylaxis?

BEEM Bottom Line

Why is this study important? This study reviews the literature on predictive factors associated with need for longer ED observation periods after initial anaphylaxis Rx.

Which, if any, threats to validity are most likely to have an impact on the results and how? Limited electronic database/language-restricted search (by a single searcher) could have led to missed relevant studies. The qualitative nature of data gathering precludes any concrete recommendations re: ED observation times.

How do the key results compare with the current evidence? The results of this review are congruent with similar recent reviews and guidelines addressing the ED management of severe anaphylaxis.

How should this study impact the care of ED patients? ED physicians should understand key predictors for biphasic anaphylaxis, and combine this with individual patient safety factors in making discharge decisions and in giving discharge patient instructions after treating initial severe anaphylaxis.

Study Summary

Article Simard D, Bouchard V, Plourde A, *et al*. Factors influencing emergency department observation time following anaphylaxis: a systematic review. Can J Emerg Med 2021; 23: 480-493. DOI: 10.1007/s43678-021-00112-z

Design Systematic review of studies examining factors associated with anaphylaxis severity and ED observation time.

Population *Included:* Studies including ED patients being treated/observed after initial anaphylaxis Rx. No age restrictions.
Excluded: Case studies.

Intervention Epinephrine, glucocorticoids.

Comparison N/A

Outcomes *Primary:* Factors associated with longer ED observation times.
Secondary: Variance in anaphylaxis/biphasic definitions across studies.

Key Results *N* = 21 primary studies, 22707 patients. 14 retrospective, 9 pediatric, 3 adult studies, 9 reviews, 15 guidelines/expert opinion papers

Sig.	*Outcome*	*N/Studies*	*Details*	I^2
Not Significant	Use of glucocorticoids in initial anaphylaxis Rx	N/A	Mixed results on the utility of glucocorticoids as an effective Rx, and independent predictor of biphasic anaphylaxis	
Significant	Biphasic anaphylaxis	N/A	Risk factors for BA = initial anaphylaxis severity, need for multiple epinephrine initial doses, delay in initial epinephrine dose, Hx of prior anaphylaxis, unknown triggers, and young age.	
Significant	Use of NIAID/FAAN criteria for defining anaphylaxis/BA	N/A	Most studies used these criteria; authors recommend adoption of same criteria for all future studies	

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	X	X
3. The search for studies was unbiased and reproducible.	?	?
4. The selection of studies was unbiased and reproducible.	X	X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	?	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?
7. The quality of the primary studies is high.	✓	?
8. The methods used to combine the included primary studies were reported and valid.	?	?
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	X

A1 = S. Upadhye A2 = J. Morris

Funding and conflicts of interest

Funding None.
Conflict of interest None (reported as such).

Potential threats to validity

Chance None?

Selection bias Search limited to specific electronic databases, and 2 EM textbooks. Articles in English/French only included. Search period limit 2008-2018 for a disease with little changes in disease characteristics and treatments over the years. Articles selected by a single author. Lack of detailed study review may have led to inclusion of primary studies that were also part of review articles/guidelines also included (ie. double inclusion?).

Measurement bias Data extracted singly by one author, then validated independently by another (not parallel independent abstractions with 3rd party resolution). Use of Cochrane RoB tool for study quality (reported). No attempt to quantify or pool risk factors.

Analysis bias Qualitative analysis of predictors factors based on frequency of reporting, not actual patient outcome numbers (ie. no quantitative data analyzed).

Confounding Potential confounding in the initial study themselves especially given the high number of retrospective studies included and some studies including the same study population.

Administrative details

Key words Anaphylaxis, Biphasic, ED Observation, Risk/prognostic factors
Appraisers Upadhye S, Morris J.

Reference(s)

1. Simard D, Bouchard V, Plourde A, Lefebvre S, Herman-Lemelin A, Lapointe S, Tremblay L, Desmeules C, Gagne A, Bouchard J. Factors influencing emergency department observation time following anaphylaxis: a systematic review. Can J Emerg Med 2021; 23: 480-493. DOI: 10.1007/s43678-021-00112-z

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Judy Morris MD MSc FRCPC
Associate Professor, Family and Emergency Medicine Department
Université de Montréal
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the most effective interventions for ED sciatica/nonspecific low back pain?

BEEM Bottom Line

Why is this study important? Low back pain (LBP) is a leading cause of disability and health-care costs worldwide. It is a common chief complaint in the ED, and is frequently treated with opioid analgesics. Finding effective treatments for ED LBP is important to optimize patient outcomes and reduce ED length of stay.

Which, if any, threats to validity are most likely to have an impact on the results and how? An incomplete analysis using GRADE quality domains makes the evidence evaluations and subsequent conclusions suspect. No clear definition of minimal clinically important differences on standardized pain scales make it hard to interpret clinical significance of mean score reductions.

How do the key results compare with the current evidence? The results in this review are congruent with prior literature suggesting variable comparable benefits of different medications (NSAIDs, opioids) in nonspecific LBP and sciatica, and little value in using corticosteroids and muscle relaxants.

How should this study impact the care of ED patients? Different medications (NSAIDs, opioids) may be of some use to reduce ED pain intensity in LBP (nonspecific, sciatica), but more research is needed. Interventional treatments involving trigger point injections hold considerable promise for efficacy, safety and rapid mobilization/ED discharge.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Oliveira CB, Amorim HE, Coombs DM, *et al*. Emergency department interventions for adults with low back pain: a systematic review of randomised controlled trials. Emerg Med J 2021; 38: 59-68. doi:10.1136/emermed-2020-209588
Design	Systematic review of randomized controlled trials.
Population	*Included:* Enter text here, separated by semicolons. Adults (≥ 18years) with nonspecific low back pain (nLBP) or sciatica (Sci). *Excluded*: Patients with spinal stenosis, other "red flag" conditions (infection, fracture, neoplasm, cauda equina syndrome, axial spondylarthritis), mixed studies with different diagnoses (unless 75% nonspecific LBP/sciatica).
Intervention	Mixed analgesics (NSAIDs, opioids, muscle relaxants, corticosteroids, combinations).
Comparison	Placebo, NSAIDs, "usual ED care" (variable at ED physician discretion), walking aids.
Outcomes	*Primary:* Pain outcomes during ED visit, as measured by VAS (visual analog scale) or NRS (numeric rating scale). Some trials divided into various 15min/hourly time intervals. *Secondary:* ED length of stay (LOS), functional assessment/ability to walk, adverse events, ED recidivism <48hrs.

Key Results

15 trials included = 1802 patients. Mean age 31.5-45.1yrs old. No trials reported ED recidivism rates.

Sig.	*Outcome*	*Mean Difference (0-100pt scale) [95%CI]*
NSS	Primary nLBP	Oral ketorolac vs oral acetaminophen/codeine
		IM vs oral phenarydol muscle relaxant; LoE moderate
		IV desketoprofen vs IV paracetamol
		Oral prednisone vs. placebo (ED discharge); LoE moderate
	Primary (Sci)	IV ketorolac vs IV lidocaine; LoE moderate
		IV dexamethasone vs placebo (ED discharge); LoE moderate
	Functional Walk	IV morphine vs IV morphine/promethazine; LoE moderate
	Adverse effects	Some trends towards A/E's with opioids (nausea, vomiting, sedation)
SS	Primary nLBP	Ketoprofen gel vs placebo (30min); -15pts [-21.0 to -9.0]
		Intradermal thiocolchicoside/tenoxicam/lidocaine vs IV desketoprofen (all time points); -8.1 to -17.1
		IV morphine vs IV desketoprofen (15 & 30min); -15.3 to -11.2
		Trigger point injections vs IV desketoprofen (5-60min); -21.8 to -37.7
		Physiotherapy vs std care (ED discharge): -16.0 (-22.4 to -9.6)
	Primary (Sci)	IV paracetamol vs placebo (15 to 30min): -8.8 to -15.7, LoE moderate
		IV morphine vs placebo (15 to 30min): -24.5 to -39.3
		IV morphine vs IV paracetamol (15 to 30min): -15.7 to -23.6
	ED LOS	IV dexamethasone vs placebo; -15.3min (-18.4 to -12.2)
		IV morphine vs IV morphine/promethazine; -78min (-140 to -16); LoE moderate

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	✓	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	X	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	Some authors supported by public research grants. No industry funding.
Conflict of interest	None (reported).

Potential threats to validity

Chance	None?
Selection bias	Electronic searches, citation reference lists, no language restrictions. No mention of publication bias assessment.
Measurement bias	Missing data managed by contacting authors for extra information, or by Cochrane handbook methods. Quality assessments done using PEDrO scale (majority low RoB), and GRADE overall evidence methods (limited domains?).
Analysis bias	All trial outcomes reframed to 0-100 scales, and no statement/standardization of MCID (minimal clinically important difference) for pain intensity. Overall GRADE quality of evidence for primary/secondary outcomes was low/moderate. No definition of clinically important ED LOS reduction.
Confounding	Possible lack of generalizability of results of direct head-2-head comparisons of medications that not be readily available worldwide.

Administrative details

Key words	Emergency department, interventions, low back pain
Appraisers	Upadhye S,
Reference(s)	Oliveira CB, Amorim HE, Coombs DM, Richards B, Reedyk M, Maher CG, Machada GC. Emergency department interventions for adults with low back pain: a systematic review of randomised controlled trials. Emerg Med J 2021; 38: 59-68. doi:10.1136/emermed-2020-209588

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the efficacy of methoxyflurane (MTxF) in the treatment of emergency trauma pain?

BEEM Bottom Line

Why is this study important? Inhalational analgesia using methoxyflurane (MTxF) has been recommended for moderate/severe trauma pain in Europe and Australasia. It is considered a fast-acting effective analgesia alternative to standard treatments.

Which, if any, threats to validity are most likely to have an impact on the results and how? Effect estimates showed statistical significance favouring MTxF at certain time points, but not necessarily clinically important effects. Lack of standardized analgesia comparisons may distort/attenuate the measured benefits of MTxF. No cost data provided for MTxF vs. standard analgesia.

How do the key results compare with the current evidence? These results attenuate the conclusions of industry-sponsored trials/reviews that may over-embellish analgesic efficacy.

How should this study impact the care of ED patients? Inhaled MTxF may be a useful analgesic strategy for prehospital/ED trauma care, but more research is needed to prove clinically important benefit, and cost comparisons.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Liu H, Fu X, Ren YF, *et al*. Does Inhaled Methoxyflurane Implement Fast and Efficient Pain Management in Trauma Patients? A Systematic Review and Meta-Analysis. Pain Ther 2021; 10: 651-674. DOI: 10.1007/s40122-021-00258-9
Design	Systematic review and meta-analysis of randomized controlled trials.
Population	*Included:* RCTs with trauma pain randomized to receiving methoxyflurane (MTxF) inhalation vs placebo/standard analgesia Rx in ED or prehospital settings. *Excluded*: Protocol papers, missing data on outcomes.
Intervention	Inhaled MTxF (3ml in all included studies).
Comparison	Placebo/standard analgesic treatment (varied between trials).
Outcomes	*Primary:* Change in baseline pain scores during first 30minutes of treatment (5min intervals). *Secondary:* Time to first pain relief, proportion of patients experiencing pain relief, rescue analgesia rates, treatment satisfaction (patients/investigators), MTxF Tx-emergency adverse events (TEAE's during ED visit, 14day follow-up).

Key Results

9 studies = 1806 patients.

Sig.	*Outcome*	*N/Studies*	*Outcome Measure (95% CI)*	*I^2*
NSS	Primary 25min	2 studies	WMD -0.36 (-0.85 to 0.13)	3%
	30min	2 studies	WMD -0.39 (-0.97 to 0.19)	0%
SS	Primary 5min	6 studies	WMD -0.93 (-1.14 to -0.71)	28%
	10min	6 studies	WMD -1.11 (-1.56 to -0.66)	65%
	15min	6 studies	WMD -1.23 (-1.99 to -0.47)	85%
	20min	6 studies	WMD -1.12 (-1.75 to –0.49)	75%
	Time to pain relief	6 studies	-5.29min (-6.97 to -3.82) favouring MTxF	100%
	Overall pain relief	6 studies	RR 1.41 (1.17 to 1.70) favouring MTxF	85%
	Need for rescue analgesia	7 studies	RR 0.32 (0.21 to 0.49) favouring MTxF	38%
	Analgesia satisfaction	4-8 studies	Patients RR 1.31 (1.07-1.60, 7 studies, I^2 86%), MD RR 1.50 (1.29-1.74, 6 studies, I^2 58%) nurses RR 1.89 (1.37-2.62, 3 studies, I^2 80%) all favouring MTxF	
	Total TEAEs	7 studies	RR 3.09 (1.72-5.57) against MTxF	87%

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	X	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	Provincial Development Grant from Traditional Chinese Medicine – Key Discipline of TCM. Journal Rapid Service fee paid by authors.
Conflict of interest	None (declared).

Potential threats to validity

Chance	None?
Selection bias	Thorough search of all electronic databases, trial registries, gray literature, conference proceedings, reference lists. Contacted authors as needed. No language restrictions. Unable to measure publication bias (too few studies to do a funnel plot analysis).
Measurement bias	Minimum clinically important difference (MCID) for pain scale improvements clearly defined (1.5cm on 10cm VAS scale). Quality assessment of RCTs done with Cochrane risk of bias (RoB) tool; 4 DB-RCTs low RoB, 5 open label trials high RoB. Overall quality of evidence was low/very low for most outcomes.
Analysis bias	Fixed effects analyses for low heterogeneity outcomes (I2 <50%), and random effects if >50%. Sensitivity/subgroup analyses performed for sources of high heterogeneity; found mostly due to open label designs (higher RoB). A priori sensitivity analysis to exclude studies with high RoB, and post hoc analysis to exclude 1 study (PenASAP). No differences in effect estimates found after planned sensitivity analyses. Subgroup analyses found attenuation of benefits based on control group interventions, reducing the benefit of MTxF at 15 and 20min.
Confounding	No costing data provided for MTxF vs. standardized analgesia.

Administrative details

Key words	Acute trauma analgesia, inhaled methoxyflurane.
Appraisers	Upadhye S,
Reference(s)	Liu H, Fu X, Ren YF, Tan SY, Xiang SR, Zheng C, You FM, Shi W, Li LJ. Does Inhaled Methoxyflurane Implement Fast and Efficient Pain Management in Trauma Patients? A Systematic Review and Meta-Analysis. Pain Ther 2021; 10: 651-674. DOI: 10.1007/s40122-021-00258-9 Fabbri A, Borobia AM, Ricard-Hibon A, Coffey F, Caumont-Prim A, Montestruc F, Soldi A, Lugilde ST, Dickerson S. Low-Dose Methoxyflurane versus Standard of Care Analgesics for Emergency Trauma Pain: A Systematic Review and Meta-Analysis of Pooled Data. J Pain Res 2021; 14: 93-105. doi: 10.2147/JPR.S292521

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the benefit of therapeutic hypothermia (TH) in improving neurologic outcomes in cardiac arrest survivors?

BEEM Bottom Line

Why is this study important? Improving neurological outcomes in cardiac arrest survivors is a critical goal, and early therapeutic hypothermia (TH) may be helpful to preserve brain function. Recent trials show conflicting results on TH benefits.

Which, if any, threats to validity are most likely to have an impact on the results and how? A limited electronic search may have missed important articles/abstracts/information that may influence final effect estimates. Absent reporting of quality assessments of included trials may leave readers uncertain about the trustworthiness of individual trials and summaries presented here. Heterogeneity in TH intervention delivery likely led to different magnitudes of effect.

How do the key results compare with the current evidence? These results are congruent with prior reviews, and includes an updated RCT (HYPERION).

How should this study impact the care of ED patients? The pooled studies are heterogeneous, and the pooled TH effect estimate suggests a small potential benefit of providing TH to cardiac arrest survivors, especially those who had an initial shockable rhythm.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Rout A, Singh S, Sarkar S, *et al*. Meta-analysis of the Usefulness of Therapeutic Hypothermia After Cardiac Arrest. Am J Cardiol 2020; Oct 15;133:48-53. doi: 10.1016/j.amjcard.2020.07.038.
Design	Systematic review and meta-analysis of randomized controlled trials.
Population	*Included:* RCTs of adults surviving in- or out-of hospital cardiac arrest (IHCA, OHCA) treated with TH. *Excluded*: Nonrandomized studies, in-hospital vs pre-hospital comparisons of TH initiation only.
Intervention	Therapeutic hypothermia, and reporting of one outcome of interest. Duration of cooling 24hr, with target temp range 32-34°C.
Comparison	Usual care, with maintenance of body temp ≥36°C.
Outcomes	*Primary:* Neurological outcome (based on Cerebral performance category scores) at 14-180days, or hospital discharge. *Secondary:* Mortality

Key Results

8 RCTs included; 2026 pts in TH arm, 1001 in controls. Mean age 64yo, 72% males. 40% nonshockable rhythm at initial presentation.

Sig.	*Outcome*	*Studies*	*Measure NNT (95% CI)*	*I^2*
NSS	Mortality reduction	7 studies (1167 deaths in 1972 pts)	RR 0.94 (0.85-1.03)	28%
SS	Poor neurological outcome (overall)	8 studies	RR 0.87 (0.77-0.98) favouring HT	64%
	Poor neuro outcome (initial shockable rhythm)	4 studies	RR 0.81 (0.67-0.99) favouring HT	49%
	Mortality (initial shockable rhythm)	4 studies	RR 0.85 (0.73-0.99) favouring HT	72%

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	X	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	?	?✓X	?✓X
7. The quality of the primary studies is high.	?	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	None (reported).
Conflict of interest	None (declared).

Potential threats to validity

Chance	Some differences in the TH intervention arms of different studies (techniques, duration of cooling, time to initiate TH, etc.) may have impacted the final trial outcomes.
Selection bias	Search limited to electronic databases only. No publication bias analysis reported.
Measurement bias	No reporting of quality assessments tools used (nor results) to analyze included trials. One comment in discussion that half of included trials had low risk of bias, but no details on what tools used and individual study scores.
Analysis bias	Random effects analyses for high heterogeneity pooled studies.
Confounding	Inclusion/exclusion of a single large negative trial (TTM) can influence the pooled effect estimate considerably (ie. excluded = pooled estimate significantly positive towards TH, included = weaker positive effect, almost nonsignificant).

Administrative details

Key words	Cardiac arrest, neurological outcome, therapeutic hypothermia.
Appraisers	Upadhye S,
Reference(s)	Rout A, Singh S, Sarkar S, Munawar I, Garg A, D'Adamo CR, Tantry US, Dharmadhikari A, Gurbel PA. Meta-analysis of the Usefulness of Therapeutic Hypothermia After Cardiac Arrest. Am J Cardiol 2020; Oct 15;133:48-53. doi: 10.1016/j.amjcard.2020.07.038.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the benefit of using tranexamic acid (TXA) in acute brain injury?

BEEM Bottom Line

Why is this study important? Tranexamic acid (TXA) is commonly used in various acute ED bleeding situations (eg. epistaxis, post-partum hemorrhage, etc.), so it's use has been explored for acute traumatic brain injury (TBI).

Which, if any, threats to validity are most likely to have an impact on the results and how? Different studies used varied outcome definitions, and are incongruent with large recent CRASH-3 trial. The Optimal Information Size (OIS) for sufficient trials to inform the primary all-cause mortality outcome was not reached.

How do the key results compare with the current evidence? This meta-analysis tries to homogenize outcomes of past studies and recent CRASH-3 trial. Analysis of all-cause vs head-injury mortality showed no likely useful benefit of TXA for acute TBI.

How should this study impact the care of ED patients? The pooled results of this meta-analysis state that TXA is likely of no clinically important benefit in treating acute TBI.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Al Lawati K, Sharif S, Al Maqbali S, *et al*. Efficacy and safety of tranexamic acid in acute traumatic brain injury: a systematic review and meta-analysis of randomized controlled trials. Intens Care Med 2021; 47(1):14-27. doi: 10.1007/s00134-020-06279-w.
Design	Systematic review and meta-analysis of randomized controlled trials.
Population	*Included:* Adolescents/adults (≥ 15 years) with any intracranial TBI hemorrhage and received TXA (any dose). *Excluded*: Enter text here, separated by semicolons.
Intervention	TXA administered within 8hrs (max 24hrs). Similar dosing in all included trials (1g loading dose, then 1g over 8hrs).
Comparison	Placebo.
Outcomes	*Primary:* Mortality, disability (Glasgow Outcome Scale/Extended [GOS/GOS-E] or Disability Rating Scale [GRS]), hematoma expansion on subsequent neuroimaging, need for neurosurgical interventions, hospital/ICU length of stay. *Secondary:* Adverse events (PE, DVT, stroke seizure). Longest reported follow-up time point for studies reporting multiple timepoint outcomes. Planned subgroup analyses based on trial quality, excluding CRASH-3 trial and adolescents.

Key Results

9 studies = 14747 patients. Mean age of included patients 35-55yrs.

Sig.	*Outcome*	*Outcome Measure (95%CI); Level of evidence*	I^2
NSS	Mortality	RR 0.95 (0.88-1.02); Risk Difference 1%, Mod certainty	0
	Disability	DRS Mean Diff (-0.18 points; -0.43 to 0.08); Mod certainty	0
		GOS/GOS-E <4 (RR 0.9, 0.69-1.17); Very low certainty	58
	Hematoma size	RR 0.77 (0.58-1.03); Risk Diff 3.6% (6.6% decrease to 0.5% increase). Low certainty. Volume Diff -2.46ml (-6.46ml to 1.55ml) Mod evidence	
	Hospital LOS	MD 0.19 days (-1.11 to 1.49d); Low certainty	
	ICU LOS	MD 1.33days (-0.99 to 3.65d); Very low certainty	
	Need for NeuroSx	RR 1.11 (0.89-1.39); Risk Diff 1.7% increase, Low certainty	
	Adverse events	RR 0.97 (0.85-1.11); Risk Diff 0%, Mod certainty	
		**No difference on planned post hoc sensitivity analyses	

CI = confidence interval; I^2 = inconsistency index (measure of statistical heterogeneity); *N* = number of patients; n = sample size; N/A = not applicable; NNT = number needed to treat; NSS = not statistically significant; *p* = probability; RR = relative risk (because this is a ratio, if the value of the range includes 1, there is no difference); Sig. = significance; SS = statistically significant.

P-values express the probability of observing differences that are as or more extreme than the observed differences when no true differences exist between the tested quantities. These are usually compared against an arbitrary cutoff value such as 0.05 (5%). We encourage readers to instead rely on effect sizes and confidence intervals for clinical decision-making, which communicate magnitude and precision of observed differences.

*Because NNT (and NNH) refer to people the estimates have been rounded off to the next highest whole number. If the value '∞' is included in the CI, then there is no difference in outcomes between the intervention and control groups.

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	✓	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	?✓X	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	✓	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	✓	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding	None declared.
Conflict of interest	None reported.

Potential threats to validity

Chance	Optimal Information Size (OIS) not reached for mortality (as per TSA analysis).
Selection bias	Thorough unrestricted search. Unable to complete publication bias (<10 trials).
Measurement bias	QA assessments with Cochrane Risk of Bias (RoB) tool; Low (2 studies), probably low (1), probably high (4), high (2).
Analysis bias	Random effects meta-analysis for high heterogeneity studies.
Confounding	Inclusion of CRASH-3 trial mortality outcomes (related to head-injury, not all-cause) was purposefully sub-analyzed to avoid confusion. Small improvements in hematoma size are not likely to be clinically relevant. Not enough data to examine role of TXA in TBI patients using OACs/antiplatelet agents.

Administrative details

Key words	Acute brain injury, tranexamic acid.
Appraisers	Upadhye S,
Reference(s)	Al Lawati K, Sharif S, Al Maqbali S, Al Rimawi H, Petrosiniak A, Belley-Cote EP, Sharma SV, Morgenstern J, Fernando SM, Owen JJ, Zeller M, Quinlan D, Alhazzani W, Rochwerg B. Efficacy and safety of tranexamic acid in acute traumatic brain injury: a systematic review and meta-analysis of randomized controlled trials. Intens Care Med 2021; 47(1):14-27. doi: 10.1007/s00134-020-06279-w.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Can functional bracing replace traditional plaster casting for non-operative ankle fracture care?

BEEM Bottom Line

Why is this study important? Plaster casts for ankle fractures hamper physical activity for prolonged time periods, and have significant impact on patient quality of life, sleep, and independence. Removable functional bracing can improve these outcomes without compromising healing.

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. This large multi-centre trial met its sample size requirements, had balanced comparison groups and accounted for missing patients competently.

How do the key results compare with the current evidence? This large RCT reaffirms prior smaller studies showing no differences between traditional casting vs functional bracing (including 1 large non-inferiority trial).

How should this study impact the care of ED patients? It is reasonable to offer removable functional bracing for closed ankle fractures, with appropriate orthopedic follow-up/cooperation.

Study Summary

Article	Kearney RS, McKeown R, Parsons H, *et al*, on behalf of the AIR trial collaborators. Use of cast immobilisation versus removable brace in adults with an ankle fracture: multicentre randomised controlled trial. BMJ 2021;374:n1506 http://dx.doi.org/10.1136/bmj.n1506
Design	Pragmatic multicentre RCT (superiority design) at 20 UK NHS trauma units; registration ISRCTN15537280
Population	*Included:* Adults >18yo with a closed ankle fracture; included both operative and non-operative patients. *Excluded:* No immobilization needed (treating physician decision), known metastatic fracture, complex intra-articular injury (eg. Pilon), wound complications that contra-indicate bracing, pre-existing neuropathic joint disease, previously enrolled, unable to meet trial follow-up processes, or required close contact casting.
Intervention	Removable functional bracing (minimum 3 weeks); braces not standardized across all study sites. Ankle exercises as soon as pain allowed (10 repetitions TID).
Comparison	Traditional plaster casting (minimum 3 weeks). Ankle exercises after cast removed.
Outcomes	*Primary:* Olerud Molander ankle (OMA) score at 16 weeks; composite of 9 different ankle functional domains, 0-100pt scale. MCID 10pts previously validated. *Secondary:* Manchester-Oxford foot questionnaire, disability rating index, resource use, quality of life (on EQ-5D-5L scale), and complications at 6, 10 and 16 weeks. Complications = DVT/PE, pain, swelling, foot numbness, wound infections, fracture healing.
Key Results	669 patients recruited (334 plaster cast, 335 removable brace). Mean age 46yo, 57% female. 502pts completed the trial (75%). Operative mgt in 54% recruited patients. No statistically significant difference between OMA scores at 16 weeks; mean Diff 1.8pts (-2.0 to 5.6) favours bracing. No differences in OMA scores at other time points, nor any significant differences in any secondary outcomes at any time point. No differences in outcomes for subgroup analyses based on age or non/operative care.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	X	X
6. All groups were treated equally except for the intervention.	?	?
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	X	X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = J. Owen

Funding and conflicts of interest

Funding Funding via the UK National Institute for Health Research, for research fellowship lead author. No industry supports.

Conflict of interest None; various authors do work for different govt health policy agencies.

Potential threats to viability

Chance No mention of consecutive vs convenience sampling; difficult to manage in 20 separate units? Sample size calculated for 20% lost to follow-up, and 25% actually missing (not evenly balanced; more missing in cast group).

Selection bias Both groups demographically well balanced at recruitment. Sampling from 20 different trauma units enhances generalizability.

Measurement bias Missing data imputed using various models (Rubens rules); no impact on primary outcome.

Analysis bias Intention to treat analysis specified. Preplanned sensitivity analysis for missing data and protocol adherence differences. Planned subgroup analyses based on non-operative vs operative, and age cutoff 50yrs (presumed higher risk of osteoporotic fractures in age>50).

Confounding Operative patients randomized after post-operative backslab and routine wound checks, and enrolled 2 weeks post-op if no concerns, whereas non-operative patients enrolled/randomized immediately.
Blinding of participants and clinicians not possible.
Patients started ankle range exercises ASAP after cast removed, or when pain allowed in removable brace group. Other rehab inputs permitted based on local practices (eg. choice of weight-bearing, duration of immobilization, offer of physiotherapy services).

Administrative details

Key words ankle fracture, cast immobiliization, functional removable bracing

Appraisers S. Upadhye, J. Owen

Reference(s)

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Julian J. Owen, MD FRCPC
Assistant Clinical Professor, Emergency Medicine/Critical Care/Trauma, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Is milrinone superior to dobutamine in the treatment of cardiogenic shock?

BEEM Bottom Line

Why is this study important? It is unclear which agent is superior in treatment of cardiogenic shock. This trial compared two inotropes (milrinone vs dobutamine) to assess superiority of either agent for a variety of efficacy and safety outcomes.

What, if any, threats to validity are most likely to have an impact on the results and how? The primary composite outcome calculated sample size based on a presumed large treatment difference (none detected), so may have been under-powered to determine smaller treatment differences. Most patients did not have formal invasive hemodynamic evaluation (pulmonary artery catheter) to guide management.

How do the key results compare with the current evidence? This pragmatic trial adds to the sparse body of evidence around use of inotropes in cardiogenic shock. There is no clear-cut "winner" in previous/current work. Selection of an inotrope should continue to be tailored based on one's experience/comfort with the agent and hemodynamic goals with attention to known side effects.

How should this study impact the care of ED patients? Patients presenting to the ED with cardiogenic shock are uncommon. The SCAI classification may be used to classify such patients and norepinephrine remains the first line vasopressor in cardiogenic shock. For selected patients requiring inotropic support, either milrinone or dobutamine may be initiated.

Study Summary

Article	Mathew R, Di Santo P, Jung RG, et al. Milrinone as Compared with Dobutamine in the Treatment of Cardiogenic Shock. NEJM 2021; 385(6):516-525. doi: 10.1056/NEJMoa2026845.
Design	Randomized controlled trial (superiority); single-site (Ottawa hospital)
Population	*Included:* Adults ≥ 18yo admitted to ICU with ca and had one of the following indications for inotropic therapy: 1) A clinical diagnosis of cardiogenic shock and systolic blood pressure <90mmHg with end-organ dysfunction, 2) Clinical evidence of systemic and/or pulmonary congestion despite use of vasodilators and/or diuretics , 3) Acute coronary syndrome complicated by cardiogenic shock with hemodynamic reduction in cardiac index (<1.8L/min/m2 and left ventricular end-diastolic pressure >18mmHg) , 4) A clinically determined need to augment cardiac output in addition to ongoing vasopressor therapy, or 5) A treating team's clinical assessment that inotropic therapy is required for developing cardiogenic shock without current evidence of hypoperfusion. *Excluded:* 1) presented with an out-of-hospital cardiac arrest; 2) pregnant; 3) had milrinone or dobutamine initiated prior to randomization; 4) treating physician was of the opinion that the patient was not eligible for the study; 5) patient was participating in another interventional trial; 6) inability to obtain written informed consent from the patient or substitute decision maker
Intervention	Milrinone infusion (std dosing scale for stage 1-5)
Comparison	Dobutamine infusion (std dosing scale for stage 1-5)
Outcomes	*Primary:* Composite of in-hospital death from any cause, resuscitated cardiac arrest, receipt of a cardiac transplant or mechanical circulatory support, nonfatal AMI, TIA or stroke diagnosed by a neurologist, or initiation of renal replacement therapy. *Secondary:* a) Efficacy = Total inotrope time, ICU LOS < or >7days, total days mech ventilation, change in cardiac index/PA pressure, presence of AKI, normalized serum lactate, arrhythmia requiring intervention. b) Safety = sustained hypotension, atrial arrhythmia, need for IV/po anti-arrhythmia Rx, ventricular arrhythmia, need for up-titration/additional vasopressor Rx

Pre-defined subgroup analyses of the primary outcome will be conducted according to the following subgroups: Age (<75 vs. ≥75 years old), gender, ventricular subgroup (LV vs. RV subgroup), etiology of ventricular dysfunction (ischemic vs. non-ischemic), severity of LV dysfunction (mild/moderate vs. severe), baseline renal dysfunction (mild/moderate vs. severe), and concomitant vasopressor use at time of randomization (yes vs. no).

Key Results

Mean age 69yrs (Mil) and 72yrs (Dob). Females 38% (Mil) and 35% (Dob). Ischemic cardiomyopathy 69% (Mil) and 65% (Dob). All-cause death 37% Mil vs 43% Dob

Primary Outcome Events: 47/96 (49%) in Mil, 52/96 (54%) in Dob; RR 0.90 (0.69-1.19, p=0.47). No heterogeneity in prespecified subgroups, no difference in time-to-event analyses or sensitivity analyses for primary composite outcome components or ICU LOS (RR 0.86, 0.72-1.04)

Secondary Outcomes: No differences for any efficacy or safety outcomes.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	?
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention.	?	?
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = J. Owen

Funding and conflicts of interest

Funding	Innovation Fund of the Alternative Funding Plan for the Academic Health Sciences Centres of Ontario (ClinicalTrials.gov number, NCT03207165)
Conflict of interest	None (disclosures on NEJM website)

Potential threats to viability

Chance	None; sample size met for superiority trial. Expected large Rx effect, so possibly under-powered to detect smaller differences (wide CI for primary outcome)?
Selection bias	No comment on consecutive sampling of patients. Groups essentially balanced at enrollment.
Measurement bias	None; all outcomes clinically measured in hospital ICU.
Analysis bias	Analysis as per ITT.
Confounding	Co-interventions during treatment period not reported in main report or supplemental materials. Absence of bolus dosing of milrinone (prior to infusion) may have attenuated any potential effect, although there may be higher risk of hypotension with bolus. Also, this trial is under-powered to detect any potential benefits of milrinone with primarily right ventricular dysfunction (NEJM correspondence).

Administrative details

Key words	Cardiogenic shock, dobutamine, milrinone
Appraisers	S. Upadhye, J. Owen
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Julian J. Owen, MD FRCPC
Assistant Clinical Professor, Emergency Medicine/Critical Care, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

Is CTA sufficient to rule out aerodigestive injury in hemodynamically stable penetrating neck trauma patients without hard signs?

BEEM Bottom Line

Why is this study important? Penetrating neck trauma (PNT) can be a diagnostic challenge in the ED given the significant airway, digestive tract, and vascular risks in each of the three zones of the neck. Since clinical evaluation alone is unreliable, multiple exploratory studies are needed to identify injuries. CT angiogram (CTA) has been shown to be accurate in assessing vascular injuries with PNT, but the evidence is unclear when it comes to airway/esophageal injuries when it comes to this imaging modality.

What, if any, threats to validity are most likely to have an impact on the results and how? There were a limited number of studies with potential selection, spectrum, incorporation and partial verification bias. High heterogeneity between studies that couldn't be accounted for without patient demographic data limits validity of pooling. There were also varied definitions of "hard vs soft" findings of ADI between studies may have affected testing practices, and subsequent test characteristics.

How do the key results compare with the current evidence? There is a general paucity of evidence on assessing PNT with different modalities, and few trials that examine airway, vascular and digestive tract injuries separately. Future large multicentre prospective trials regarding airway and digestive injuries are needed, with subgroup analyses for mechanism (stabbing, gunshots) pre-defined.

How should this study impact the care of ED patients? CTA for PNT can be a useful modality for screening airway and vascular injuries, but not necessarily esophageal penetration.

Study Summary

Article	Paladino L, Baron BJ, Shan G, Sinert R. Computed tomography angiography for aerodigestive injuries in penetrating neck trauma: A systematic review . Acad Emerg Med 2021; 28(10): 1160-1172. doi: 10.1111/acem.14298.
Design	Systematic review of diagnostic test studies. PROSPERO #: CRD42019133509
Population	*Included:* Patients with PNT that violated the platysma muscle (all neck zones), recruited from ED and undergoing CTA. *Excluded:* Narrative reviews, case reports, therapy studies.
Index Test	Computerized tomography angiography (CTA)
Reference Standard	Other diagnostic test (esophagogram, bronchoscopy), surgical intervention outcomes, or observation/clinical follow-up.
Diagnoses of Interest	Aerodigestive penetrating injury (ADI).

Key Results

7 articles included, 877 patients with PNT receiving CTA; 4 prospective, 3 retrospective. 5 studies involving all neck zones, 2 studies zone II only.
Average age 26-39yrs, predominantly male 48-91%. Stab wounds 51-86%, gunshots 14-49%.
Prevalence of ADI 13.4% overall (2.7% to 47%); 117 total ADI's, 26 esophageal. Most PNT's in zone II in 5 studies (22.5-43%), and zone III least affected (7.8-16%).
Missed injuries: esophageal 5, oropharyngeal 2, laryngotracheal 0.

Pooled results:
Sens 92% (85-97%; I^2=33.6%), Spec 88% (85-90%, I^2=93.8%), LR+ 12.2 (4.6-32.1, I^2=87.2%), LR- 0.14 (0.05-0.37, I^2=56.8%)

Bayesian analysis: With a 13.4% prevalence (ie. pre-test probability) and positive test LR+ 12.2 (4.6-32.1), the post-test probability of ADI ranges from 33-100%. With a negative test LR- 0.14), the post-test probability drops from 13.4% to 1%.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	?	X
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high.	?	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	?	X
9. The subgroups were stated a priori and appropriate.	N/A	X
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = R. Valani

Funding and conflicts of interest

Funding	Not reported
Conflict of interest	None (reported)

Potential threats to viability

Chance	Wide range of prevalence for included studies increases risk of spectrum bias. Evidence of selection bias of patients in individual studies.
Selection bias	*Specify comprehensive searches; publication bias*? Electronic searches, limited to human subjects, English language. Some manual bibliography searches. No mention of grey literature (abstracts, meetings).
Measurement bias	CT scanner technology ranged from 2001-2016; some impact of changing technology over time on diagnostic accuracy? Different reference standards among included studies, and some were not blinded to CTA results. This introduces elements of incorporation bias and partial verification bias.
Analysis bias	*Fixed/random effects? Heterogeneity mgt?* High heterogeneity amongst included studies analyzed using random effects model.
Confounding	*Enter independent factors affecting the outcome; clinicians to comment.* Non-standardized definitions of "hard vs soft" ADI's amongst included studies.

Administrative details

Key words	CT angiography, CT scans, esophageal injuries, penetrating neck trauma
Appraisers	S. Upadhye, R. Valani
Reference(s)	

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Rahim Valani, MD, MBA, LLM, M Med Ed
Associate Professor of Medicine, University of Toronto
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the benefit of using peripheral nerve blocks in ED patients with hip fracture?

BEEM Bottom Line

Why is this study important? Adult hip fracture is a common painful condition encountered in the ED. Having effective and safe alternatives for analgesia is important to optimize patient comfort. Peripheral nerve blockade (PNB) offers an attractive local effective, safe and opioid-sparing alternative to traditional ED parenteral analgesia strategies.

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. Use of fixed effects analyses for moderate/high heterogeneity pooled data may over-estimate benefits.

How do the key results compare with the current evidence? This review updates prior Cochrane reviews on the utility of PNB for acute hip fracture analgesia.

How should this study impact the care of ED patients? PNB for hip fracture is a safe and effective alternative for acute analgesia, allowing for less pain with early movement, lower chest infections, less opioid use and reduced confusional states.

Study Summary

Article	Guay J, Kopp S. Peripheral nerve blocks for hip fractures in adults. Cochrane Database of Systematic Reviews 2020, Issue 11. Art. No.: CD001159. DOI: 10.1002/14651858.CD001159.pub3.
Design	Systematic review and meta-analysis of randomized controlled trials.
Population	*Included:* Adults (≥ 18years) with acute hip fracture. *Excluded*: "Quasi" RCTs, cross-over trials. Many included studies excluded dementia patients.
Intervention	Peripheral nerve blockade (PNB) administered pre/intra/post-operatively.
Comparison	Sham injection.
Outcomes	*Primary:* Pain on movement 30min after block placement. Acute confusional states or AMI (0-30days). *Secondary:* Chest infections (0-30days), all-cause mortality (0-6mo), time to first mobilization after surgery, costs of analgesic regimens

Key Results

43 trials included (18 new): 1368 pts received PNB, 1352 sham blocks. Average age: 59-89yrs, avg ASA category 1-4, females 33-95%. 22 trials conducted a 3-in-1 femoral nerve block. 15 trials each used US-guided PNB or blind landmarking technique.

Sig.	*Outcome*	*Studies (pts)*	*Outcome Measure (95%CI)*
NSS	Mortality reduction (6mo)	11 (617)	RR 0.87 (0.47-1.60); low certainty evidence
	MI (30days)	1 (31)	Insufficient events detected; low certainty evidence
	Cost of analgesics	1 (75)	4 Euros difference (not economically significant); mod certainty evidence
SS	30min Pain on movement	11 (503)	SMD -1.05 (-1.25 to -0.86); equivalent to -2.5 on 0-10 Likert scale [High certainty evidence]. Benefit proportional to amount of local anesthetic used (p=0.0003).
	Reduced acute confusional states	13 (1072)	RR 0.67 (0.50-0.90); NNT=12 (7-47); high evidence certainty
	Reduced chest infections	3 (131)	RR 0.41 (0.19-0.89); NNT=7 (5-72); mod certainty of evidence
	Time to first mobilization	3 (208)	Mean Diff -10.80hrs (-12.83 to -8.77hrs); mod certainty of evidence

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	✓	✓
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	X

A1 = S. Upadhye A2 = C. Bedard

Funding and conflicts of interest

Funding	None.
Conflict of interest	None.

Potential threats to validity

Chance	Optimal information size was met for primary outcome. Certainty of evidence was downgraded for imprecision for only MI, mortality, and cost.
Selection bias	While a sufficient search was conducted, some publication bias was evident for different outcomes based on funnel plot analyses.
Measurement bias	The authors show that the primary outcome is improved by 2.5pts on 0-10 Likert scale, but do not identify/justify the minimal important clinical difference for pain scales used (usually 13mm on 100mm scale in general pain literature).
Analysis bias	Use of fixed effects models due to concern for small study effect, however, this effect was only detected in one analysis and most remaining meta-analyses had evidence of some heterogeneity beyond chance. May under-estimate the impact of error in pooling data.
Confounding	Blinding of patients/treating physicians likely impossible. It is feasible, however, to blind outcome assessors and data analysts.

Administrative details

Key words	Hip fracture, peripheral nerve blockade.
Appraisers	Upadhye S, Bedard C.
Reference(s)	Guay_J, Kopp_S. Peripheral nerve blocks for hip fractures in adults. Cochrane Database of Systematic Reviews 2020, Issue 11. Art. No.: CD001159. DOI: 10.1002/14651858.CD001159.pub3.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact, McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Chloe Bedard, PhD
Postdoctoral Fellow , School of Public Health Sciences University of Waterloo
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What topical medications are most effective for corneal abrasions?

BEEM Bottom Line

Why is this study important? Corneal abrasions are the most common ED eye-complaints, and cause significant pain/morbidity. Finding an efficient analgesic strategy that is safe is important to manage these self-limited conditions.

What, if any, threats to validity are most likely to have an impact on the results and how? The various meta-analyzed outcomes (n=15) are based on GRADE very low/low/moderate evidence. Heterogeneity of outcomes was high, but stable to sensitivity analysis based on analytic models (random vs fixed effects). Imprecision and risk of bias in the few available studies limits certainty around the estimates of effects.

How do the key results compare with the current evidence? This evidence expands prior reviews (Calder 2005) that NSAIDs are an effective and safe first choice for corneal abrasion analgesia. There is insufficient evidence to support/refute use of topical anesthetics, cycloplegics, steroids or bandage contact lens. Patching is not helpful, and possibly harmful (reconfirmed).

How should this study impact the care of ED patients? Patients with uncomplicated corneal abrasions can be effectively and safely managed with a short course (<72hrs) of topical NSAIDs.

Study Summary

Article	Yu CW, Kirubarajan A, Yau M, Armstrong D, Johnson DE. Topical pain control for corneal abrasions: A systematic review and meta-analysis. Acad Emerg Med 2021; (8):890-908. doi: 10.1111/acem.14222
Design	SR/MA of prospective trials on managing uncomplicated corneal abrasions.
Population	*Included: Traumatic uncomplicated corneal abrasions* *Excluded: Nontraumatic or spontaneous abrasions*
Intervention	Topical NSAIDs, anesthetics, steroids, cycloplegics, eye patching, bandage contact lens (BCL)
Comparison	Antibiotic ointments, artificial tears, oral analgesics
Outcomes	*Primary: Percentage of corneal abrasions healed at 24, 48, and 72 hours, as well as pain control at 24 and 48 hours. Healing was defined as no epithelial defects or only punctate defects on slit-lamp Examination with fluorescein. Pain control measured by 10pt scales.* *Secondary: Use of oral analgesia (weighted mean number of tablets), and incidence of complications (e.g., ulcers, keratitis, recurrent corneal erosion [RCE], corneal melt, perforation).*
Key Results	33 studies included (31 RCTs, 2 cohorts); 4167 pts. Patients 75.1% male, weighted mean age 36.9yrs.

Intervention Summary (effect estimate [95% CI], level of evidence certainty)

Outcome	NSAIDs	Anesthetics	Patching	BCL	Cycloplegics
Healing	64.6% at 24hrs, 93.6% at 48hrs, 100% at 72hrs. (26 studies, mean 48hrs). No difference vs controls.	No difference at 24hrs (1 study), 48hrs (3 studies, RR 0.94 [0.83-1.06 (low)]. No studies 72hrs.	(10 studies) Full healing 61% at 24hrs, 85% at 48hrs, 95% at 72hrs. No sig difference vs controls at any time.	No studies	No studies
Pain Reduction	SMD -0.69pts [-0.98 to -0.14, mod] at 24hrs; SMD -0.56 [-1.02 to -0.10, low] at 48hrs (31 studies, median 24hrs)	Reduced pain between 24-48hrs (2 studies). No diff beyond 48hrs. (1 study)	No difference SMD -0.07 [-0.53 to 0.39] (low).	No difference (1 study)	No studies
Oral Analgesia Use	Reduced; RR 0.47, [0.33-0.66 (mod)]	Mixed results (2 studies no diff, 1 study some reduction)	No difference RR 1.01 (0.78-1.09, low)	No difference (1 study)	No difference (2 studies)
Complications	No difference: RR 0.67, [0.13-3.41 (low)]	No diff 4 studies (RR 0.72 [0.20-2.54], very low)	Trend of harm with patching RR 2.44 (0.33-17.71, low)	No complications (3 studies)	No complications

Patching vs BCL: No difference in 24hr healing (4 studies; RR 1.18 [0.75-1.84], low). Unclear difference at 48hrs (2 studies). No difference pain scores 24hrs.

Topical NSAIDS + BCL vs BCL alone: Reduced pain (24hrs, 1 study).

Cycloplegics vs patching: Faster healing ($p=0.049$), less pain 24hrs ($p=0.009$) favouring cycloplegics.

Topical NSAIDs vs cycloplegia: Reduce pain ($p<0.05$), lower oral analgesia ($p<0.01$) favouring NSAIDs.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	X	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	X

A1 = S. Upadhye A2 = C. Bedard

Funding and conflicts of interest

Funding	None reported.
Conflict of interest	None (reported). Review registered with PROSPERO with ID CRD42020201288

Potential threats to viability

Chance	While unlikely that chance lead to spurious effects, imprecision due to a lack of total events (too few studies) has lowered the certainty of evidence.
Selection bias	The search strategy appears sufficient; however, funnel plots could not be completed due to an insufficient number of trials.
Measurement bias	Use of subjective pain scales with undefined minimally clinically important differences (MCID) introduces uncertainty of the validity and clinical meaning of pain outcomes. Self-reporting of complications in included studies likely resulting in detection bias, especially considering the lack of blinding in most studies. Risk of bias: RCTs = Cochrane RoB tool, Observational = MINORS criteria. Quality of evidence rated using GRADE; overall very low/low/moderate for 15 meta-analyzed outcomes. Limited studies with high risk of bias and small sample sizes (imprecision).
Analysis bias	Appropriate use of random effect analysis. However, high heterogeneity existed for various outcomes (57-66%) and was not explained by subgroup analyses (few exceptions). Some supplementary meta-analyses pooled both observational and randomized trials which is not recommended.
Confounding	Variable reporting of different outcomes (particularly pain and complications) in included studies. Risk of selection and attrition bias likely has influenced the results. Heterogeneity in abrasion mechanisms, size and use of adjunct meds.

Administrative details

Key words	corneal abrasions, emergency department, pain control
Appraisers	S. Upadhye, C. Bedard
Reference(s)	Calder L, Balasubramanian S, Fergusson D. Topical nonsteroidal anti-inflammatory drugs for corneal abrasions: meta-analysis of randomized trials. Acad Emerg Med 2005, 12(5): 467-73. doi: 10.1197/j.aem.2004.10.026.

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Chloe Bedard, PhD
Postdoctoral Fellow, School of Public Health Sciences University of Waterloo
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What is the effectiveness of topical tetracaine in the treatment of corneal abrasions?

BEEM Bottom Line

Why is this study important? There is controversy over the historic efficacy & safety of topical tetracaine for ED corneal abrasion analgesia, although this has been recently challenged.

Which, if any, threats to validity are most likely to have an impact on the results and how? This is a single center study that had some relevant co-analgesic interventions that could have been confounding (opioid use), but likely wasn't.

How do the key results compare with the current evidence? Current results are congruent with recent trials supporting the safe use of tetracaine for corneal abrasions for 24hrs.

How should this study impact the care of ED patients? For uncomplicated corneal abrasions, topical tetracaine is an efficacious and safe analgesic strategy for 24hrs.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article Shipman S, Painter K, Keuchel M, Bogie C. Short-Term Topical Tetracaine is Highly Efficacious for the Treatment of Pain Caused by Corneal Abrasions: A Double-Blind Randomized Clinical Trial. Ann Emerg Med. 2021;77:338-344. https://doi.org/10.1016/j.annemergmed.2020.08.036

Design Enter text here. State true design not what the investigators call it.

Population *Included:* Adults (≥ 18 and ≤ 80 years) with an uncomplicated corneal abrasion.
Excluded: Contact lens wearer, prior corneal surgery/transplanted in affected eye, >36hrs after injury, retained/contaminated foreign bodies present, co-existing ocular infection, pregnancy, penetrating eye injury, immunosuppression, allergy to study medication, unable to attend follow-up, unable to speak/read English or Spanish, or injury requiring urgent ED ophthalmology consultation (lacerations, ulcers, vision loss).

Intervention 1 vial of tetracaine 0.5% in a single 2ml bottle.

Comparison 4 vials of balanced artificial tears solution.

Outcomes *Primary:* Numeric Rating Scale score (0-10cm) at initial ED follow-up visit (24hrs after initial visit, and 48hrs).
Secondary: Breakthrough opioid use, adverse events.

Key Results *N* = 118 patients (59 each arm).

Sig.	*Outcome*	*Intervention*	*Control*	*ARR (95% CI)*	*NNT (95% CI)*
SS	Primary	Median score (n=56) 1 (IQR 1-2); 6pt diff from baseline	Median score (n=55) 8 (7-8); 0pt difference from baseline		
	Opioid tabs used	1	7		
	Adverse events (%)	2 (3.6)	6 (11)		

****NO DIFFERENCE:** Residual abrasion on slit lamp exam at 24hrs (18% Int vs 11% Ctrl).

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The patients were recruited consecutively.	✓	X	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	?✓X	?✓X
3. The allocation sequence was adequately concealed.	✓	?✓X	?✓X
4. The patients in all groups were similar with respect to prognostic factors.	✓	?✓X	?✓X
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	?✓X	?✓X
6. All groups were treated equally except for the intervention.	✓	?✓X	?✓X
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	X	?✓X	?✓X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	?✓X	?✓X
9. All patient-important outcomes were considered.	✓	?✓X	?✓X
10. The effect size of the primary outcome is clinically significant.	✓	?✓X	?✓X

A1 = S. Upadhye A2 = A3 = ITT = intention to treat.

Funding and conflicts of interest

Funding	Study was funded in part by a grant from the Foundation of Osteopathic Emergency Medicine Young Investigator's Award.
Conflict of interest	None (reported).

Potential threats to validity

Chance	None or enter text here. Type I & II errors? "Blinded" opaque envelopes had 1 vial of tetracaine (Int) vs. 4 vials of balanced artificial tears (placebo); loss of blinding amongst treating staff?
Selection bias	None. Consecutive sampling 24hrs a day by all ED staff.
Measurement bias	NRS minimal clinical important difference (MCID) was 1.5cm (SD 2.5cm); justification for this?
Analysis bias	Calculated need for 60pts per arm, recruited 59pts/arm. ITT analysis; 3/59 LFTU in Int arm (5%), 4/59 LTFU in Ctrl arm (6%). Majority of patients did not attend 1wk f/u appt with ophthalmology (<20% each arm). Study under-powered for safety outcomes. Raw data for group outcomes not provided to calculate ARR/NNT.
Confounding	Patients were also treated with antibiotic drops in both groups for same 24hr period. They also all received a prescription for hydrocodone/acetaminophen #12 (1-2 tabs q6h prn) for breakthrough pain.

Administrative details

Key words	Corneal abrasions, emergency department, tetracaine.
Appraisers	Upadhye S,
Reference(s)	Shipman S, Painter K, Keuchel M, Bogie C. Short-Term Topical Tetracaine is Highly Efficacious for the Treatment of Pain Caused by Corneal Abrasions: A Double-Blind Randomized Clinical Trial. Ann Emerg Med. 2021;77:338-344. https://doi.org/10.1016/j.annemergmed.2020.08.036

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

Research Question

What are the complications risk with use of peripheral IV vasopressors?

BEEM Bottom Line

Why is this study important? Rapid vasopressor (VP) infusion is important in time-dependent critical care scenarios (eg. septic shock). Using peripheral intravenous (IV) catheters can achieve such treatment faster than central venous line placement/ confirmation.

Which, if any, threats to validity are most likely to have an impact on the results and how? Varied study designs with high heterogeneity makes outcome data pooling unreliable (even with more conservative random effects analysis). Lack of weight-based dosing limits comparisons/generalizability of results.

How do the key results compare with the current evidence? These results show congruence with past trials, especially those using larger peripheral IV catheters in ED settings.

How should this study impact the care of ED patients? Use of peripheral IV catheters for vasopressor infusion is faster, effective and safe.

Suneel Upadhye, MD MSc FRCPC
Associate Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)

AUTHOR 2 Enter name and credentials here
Enter professional positions held here
No conflicts of interest/Identify conflicts (ICMJE)

Study Summary

Article	Tran QK, Mester G, Bzhilyanskaya V,*et al*. Complications of vasopressor infusion through peripheral venous catheters: A systematic review and meta-analysis. Am J Emerg Med 2020; 38: 2434-2443. https://doi.org/10.1016/j.ajem.2020.09.047
Design	Systematic review and meta-analysis of trials using peripheral IV vasopressor (VP) infusions.
Population	*Included:* All trials (prospective RCTs, observational studies, retrospective studies) with adults (≥ 18 years) receiving VPs. *Excluded*: Case reports.
Intervention	All trials (prospective RCTs, observational studies, retrospective studies) using peripheral IV VP infusions.
Comparison	N/A.
Outcomes	*Primary:* Any VP-related complication at longest time of VP infusion. *"Minor" complications = extravasation, infiltration, cellulitis, thrombophlebitis. "Major" complications = limb ischemia, tissue necrosis, deep venous thrombosis.* *Secondary:* Treatments for complications = amputations, debridements, hot/cold compresses, analgesia, observation, local phentolamine infiltration.

Key Results

9 studies, 1835 patients (1 RCT). Mean age 63yrs, 48% female. Two studies set in ED (275pts). Most common catheter size 18-20G. Most common VP: norepinephrine (NE; 65%), epinephrine (Epi; 12%), phenylephrine (PhEpi; 12%). Mean infusion time 9.7-49hrs.

Outcome	*Event rates*		*I^2*
Primary	122 total (7%); 96% minor, 4% major (peripheral thrombosis). 72% minor infiltration, 21% minor erythema.	Pooled proportion all complications 0.086 (95%CI 0.031-0.21). Larger catheters (18-20G) associated with lower complications. ED IV VP complications 5% (2 studies, I^2 0%; 95%CI 3-8%). Significantly lower rates of complications in studies using explicit safety guidelines (2 studies).	96%
Secondary	None; no treatments reported?		

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	X	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	X	?✓X	?✓X
3. The search for studies was unbiased and reproducible.	?	?✓X	?✓X
4. The selection of studies was unbiased and reproducible.	✓	?✓X	?✓X
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	?✓X	?✓X
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	?✓X	?✓X
7. The quality of the primary studies is high.	X	?✓X	?✓X
8. The methods used to combine the included primary studies were reported and valid.	✓	?✓X	?✓X
9. The outcomes are clinically relevant.	✓	?✓X	?✓X
10. The statistical heterogeneity of the primary outcome is low (< 25%).	X	?✓X	?✓X

A1 = S. Upadhye A2 = A3 =

Funding and conflicts of interest

Funding None (reported).

Conflict of interest None (reported).

Potential threats to validity

Chance None? Only 1 prospective RCT included; remainder of studies were heterogeneous designs.

Selection bias None or enter text here (incomplete search, publication bias, etc.). Limited search to few electronic databases, and selected article reference lists. No extended searches (gray literature), excluded non-English language studies.

Measurement bias None or enter text here (e.g., missing details on study selection; missing results of quality assessments). Quality assessments Cochrane Risk of Bias (RCTs) and Newcastle-Ottawa scale (observational studies). All included studies rated as Moderate quality (inter-rater agreement Kappa scores 70%). Only 1 study reported objective measurements of complications.

Analysis bias None or enter text here (e.g., fixed vs. random effects, combined results of studies of different design). Pre-defined subgroup analyses (study design, clinical settings ED vs ICU, shock states, sample size, and presence of explicit safety guidelines). Random effects analyses for highly heterogeneous studies; majority of heterogeneity due to study designs with different patient populations (97%).

Confounding None or enter text here (clinicians to comment). Insufficient information to determine risk factors for complications. Lack of weight-based dosing limits inter-study comparisons/generalizability of results.

Administrative details

Key words Complications, peripheral intravenous vasopressors

Appraisers Upadhye S,

Reference(s) Tran QK, Mester G, Bzhilyanskaya V, Afridi LZ, Andhavarapu S, Alam Z, Widjaja A, Andersen B, Matta Ann, Pourmand A. Complications of vasopressor infusion through peripheral venous catheters: A systematic review and meta-analysis. Am J Emerg Med 2020; 38: 2434-2443. https://doi.org/10.1016/j.ajem.2020.09.047

Clinical Appraisal faculty

Suneel Upadhye, MD MSc FRCPC
Assoc. Professor, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University
No conflicts of interest/Identify conflicts (ICMJE)