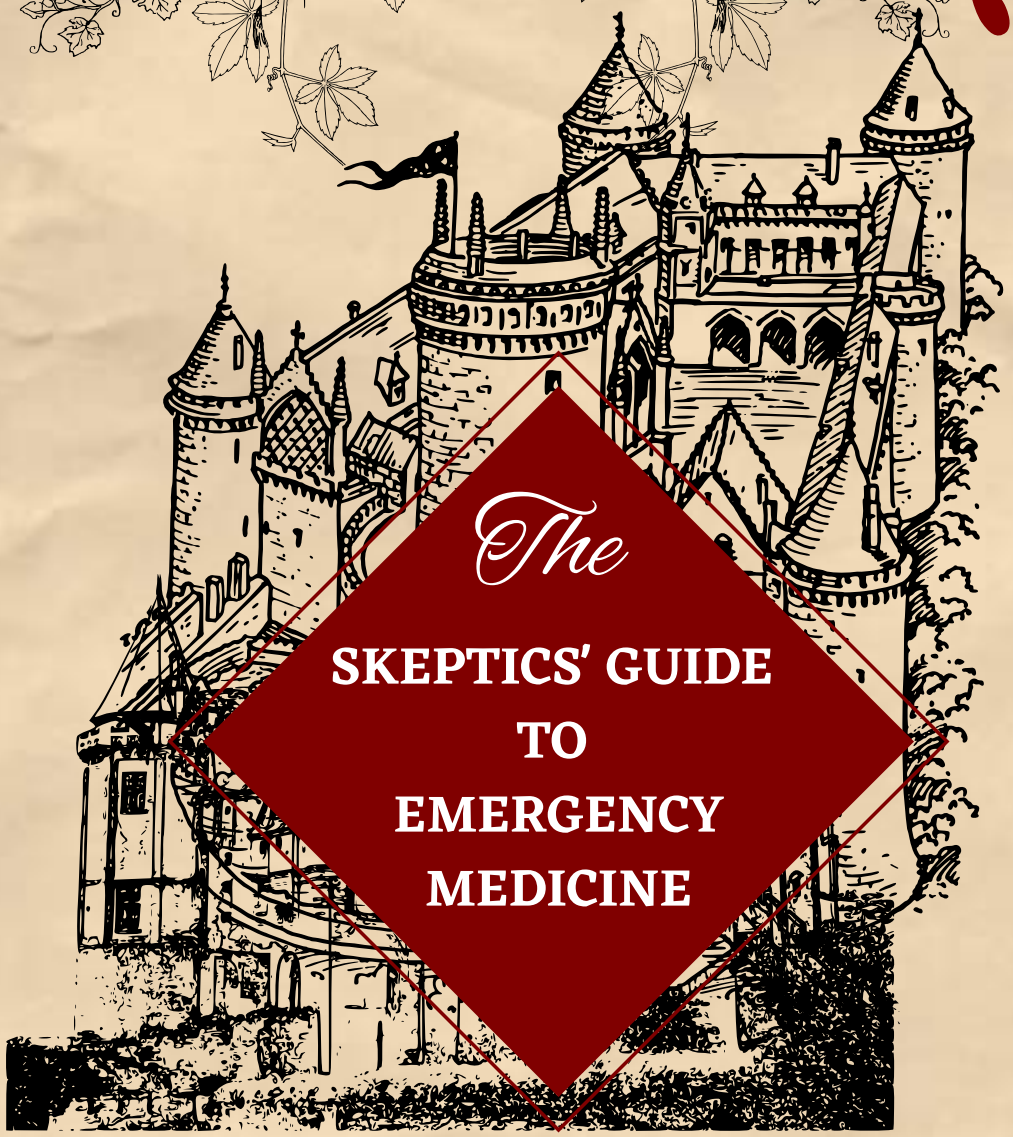
Season 10



The SKEPTICS' GUIDE TO EMERGENCY MEDICINE

Written by: Dr. W.K. Milne
Foreword by: Dr. Kirsty Challen
Designed by: Dr. Tayler Young

Foreword:

Skeptico evidentium!

Harry Potter arrived in our consciousness in 1997 as an unsupported orphan venturing into the magical world for the first time, facing the ever-present but initially under-appreciated threat of Voldemort with Ron and Hermione. The Skeptics Guide to Emergency Medicine was a few years behind, emerging into the #FOAMEd-o-sphere in 2012, but as Harry and his world developed through the books, so has the SGEM.

This 10th Edition arrives as advocates of Evidence-Based Medicine continue to tackle the forces of misinformation and pseudoscience. Like Voldemort rising slowly back to power, many in the Ministry of Magic office of academic medicine failed to spot or believe the level of influence social media would have in the world of 2023. Ken Milne was an early adopter of using social media to narrow the knowledge translation gap and reduce the time it takes for quality research to percolate into clinical practice.

This isn't always easy; as Dumbledore says in the Goblet of Fire "there will be a time when we must choose between what is easy and what is right". As clinicians it might sometimes seem easier to adopt the line of least resistance; blindly and unthinkingly to follow the "rules" of specialty guidelines or the preferences of consultants. But things are not always what they seem; many initially promising treatments fail to translate to benefit in the longer term and it can be tricky to know which is the Scabbers (apparently benign and well-received, eventually found to be treacherous and deadly) and which is the Snape (initially unpleasant but at his core hugely valuable).

As Harry's group of friends and allies grew wider through the books, so Ken has grown the SGEM faculty; the rotating cast of the SGEM-HOP has been joined by Dennis Ren leading SGEM-PEDS and an ever-increasing number of guest skeptics from many backgrounds (no exclusion of the mudbloods here) ensuring a clinician- and patient-relevant gaze is cast on the medical literature. The structured critical appraisal provides readers and listeners with a Marauder's Map to see through the complexity and (sometimes) obfuscation of published articles and reach their own, sometimes surprising, conclusions.

Foreword:

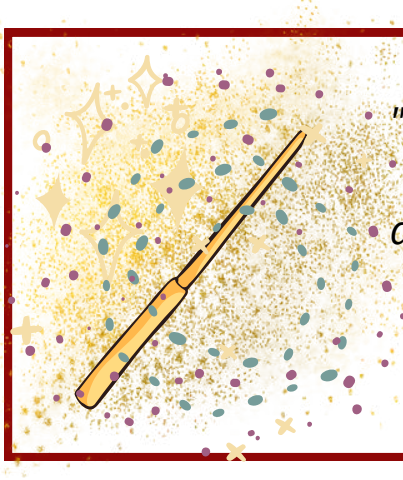
Like Voldemort (or Harry) some things never seem to die; this 10th edition features the perennial topics of where, if anywhere, thrombolytic agents should feature in the management of ischemic stroke, plus whether the choice of crystalloid for resuscitation really matters at all. New topics with wider relevance also appear, including the strength of the overall evidence base in Emergency Medicine and Orthopedics, and the persistent gender gap in EM remuneration.

Even Ron Weasley recognises “when in doubt, go to the library”. Emergency clinicians are well advised “when in doubt, listen to or read the SGEM”. You too can be a skeptic, Harry!

Introduction:

Welcome to the Skeptics' Guide to Emergency Medicine (TheSGEM). Meet 'em, greet 'em, treat 'em and street 'em. The goal of the SGEM has always been to cut the knowledge translation (KT) window down from over ten years to less than one year. It does this by using social media to provide you with high quality, clinically relevant, critically appraised, evidence based information. The SGEM wants you to have the best evidence so you can provide your patients with the best care.

Much of the SGEM content is a result of the Best Evidence in Emergency Medicine (BEEM) process. The BEEM process is a reliable and validated method of selecting relevant emergency medicine articles.
BEEM is evidence-based medicine worth spreading. You can get the BEEM critical appraisal tools as part of the Free Open Access to Meducation movement. FOAMed – Medical education for anyone, anywhere, anytime



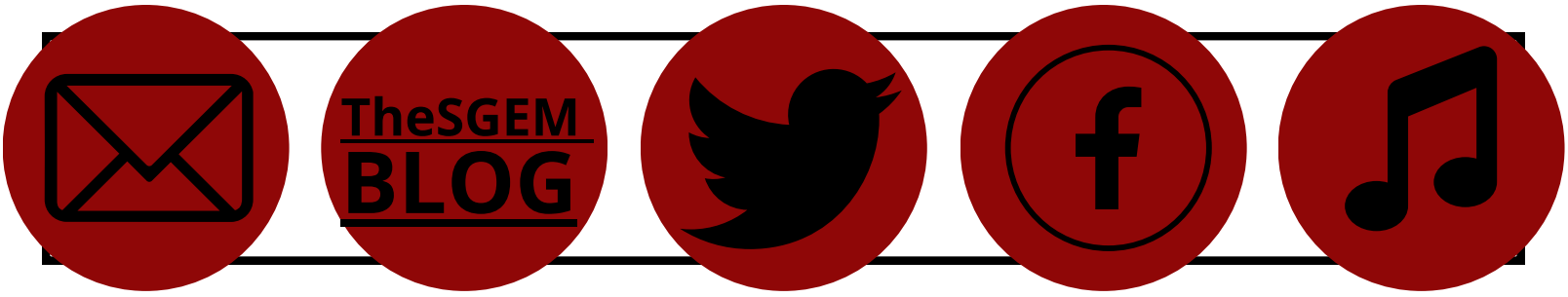
"FOAM should not be seen as a teaching philosophy or strategy, but rather as a globally accessible crowd-sourced educational adjunct providing inline (contextual) and offline (asynchronous) content to augment traditional education principles."
https://litfl.com/foam-free-open-access-medical-education/

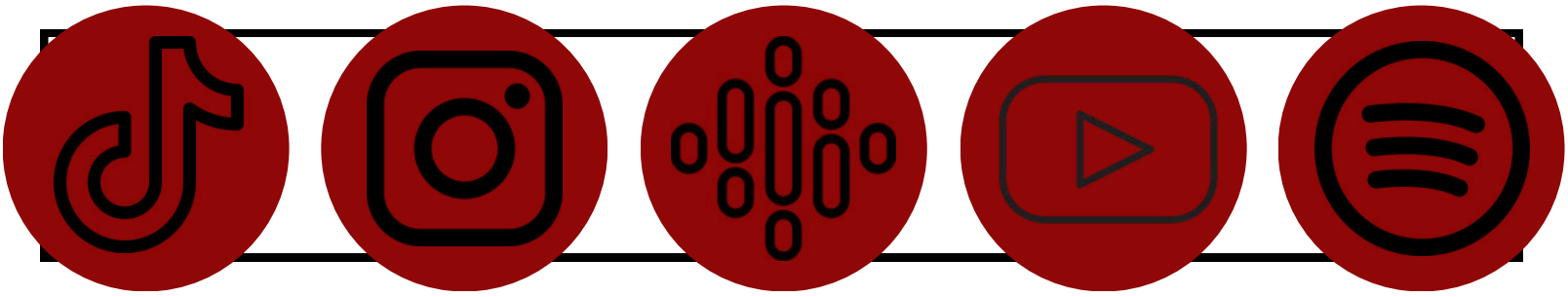
The SGEM consists of a weekly podcast and blog. It also has a Facebook page, active Twitter feed, and YouTube channel.

So stop practicing medicine from ten years ago and start practising medicine based on the best evidence. Listen to the podcast and turn your car into a classroom. And always remember:

BE SKEPTICAL OF ANYTHING YOU LEARN, EVEN IF YOU LEARNED IT FROM THE SKEPTICS' GUIDE TO EMERGENCY MEDICINE

To Access the SGEM:





Disclaimer

The Skeptics' Guide to Emergency Medicine (SGEM) is produced in Canada and is intended for medical students, residents, physicians, physician assistants, nurse practitioners, paramedics, pharmacists, and anyone else caring for emergency patients. The goal of The Skeptics' Guide to Emergency Medicine (SGEM) program is to provide followers with the best evidence so they can provide their patients with the best care.

The provider of this educational material may discuss commercial products and/or devices as well as the approved/investigative use of commercial products/devices.

The provider of this educational material report that they do not have significant relationship that create, or may be perceived as creating, a conflict relating to this educational activity.

The SGEM makes a reasonable effort to supply accurate information but does not assume any liability for errors or omissions. Because of the nature of the program and its format, it is not recommended that they serve as the sole basis for patient evaluation and treatment.

345

CHECKING IN, CHECKING OUT FOR NON-OPERATIVE TREATMENT OF APPENDICITIS

Clinical Question:

Is a course of oral, outpatient antibiotic treatment non-inferior to a course of initial inpatient, IV antibiotics followed by completion of oral, outpatient antibiotics?

Bottom Line:

The claim of non-inferiority of outpatient oral antibiotics compared to inpatient IV antibiotics followed by outpatient oral antibiotics in healthy adult patients with NOTA is not supported with this data

Guest:

Dr. Rob Leeper is an assistant professor of surgery at Western University and the London Health Sciences Center. His practice is in trauma, emergency general surgery, and critical care with an academic interest in ultrasound and medical simulation.

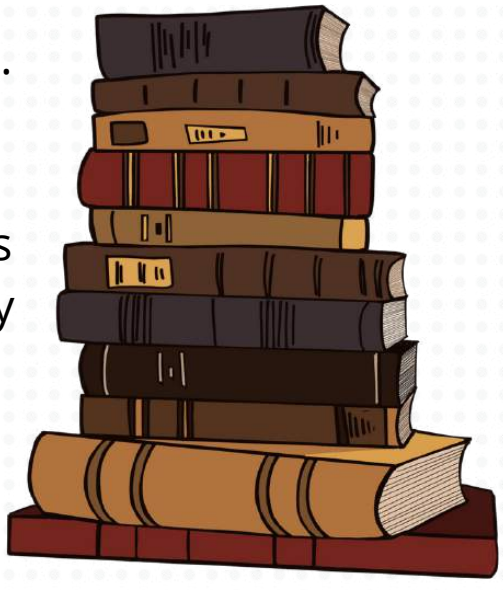
Case Overview:

A 23-year-old man with CT confirmed uncomplicated appendicitis, mild abdominal pain, stable clinical signs, and essentially normal laboratory investigations has just concluded his bedside consultation with the on-call general surgery team. The patient and surgeons have had an evidence-informed discussion and have arrived at a mutually agreed upon decision to proceed with non-operative treatment of his appendicitis. The patient is recommended to undergo admission to hospital for serial observation and intravenous antibiotics. The patient asks; “gosh doc, if this disease is so mild why can’t I just go home and take antibiotics by mouth?”.

Background:

The appendix is a structure about as long as your pinkie finger that hangs off the beginning of the colon, in the right lower quadrant of your abdomen. There are lots of theories about subtle functions of the appendix, but its most prominent role is to become inflamed or infected in approximately 7% of people.

Usually appendicitis occurs because the lumen, or inside, of the appendix is obstructed by something. Often that is a piece of stool called a fecalith, but other times it can be lymph tissue or another process we may never actually identify. This causes the pressure in the appendix to increase eventually obstructing venous outflow and then arterial inflow.



We used to assume that this was an ordered progression that always leads to appendiceal rupture in a stepwise fashion, but we now think that there is more of a spectrum of severity based on individual anatomic and other factors. While the presentation of appendicitis can vary from patient to patient, as our emergency medicine colleagues know well, most patients are not diffusely peritonitic or systemically unwell.

Before we had things like surgery or antibiotics, appendicitis carried up to a 50% case fatality rate. Luckily now, with these treatments the mortality rate is almost zero. For the last 135 years we have treated appendicitis with an appendectomy, which is now almost always performed in laparoscopic fashion.

A laparoscopic appendectomy involves a general anesthetic, making three small incisions between 1 and 2 cm in length; and the operation usually takes somewhere between 30 to 60 minutes. Most patients go home the same day or the next morning, either with a short course of antibiotics or with none after surgery.

Most patients who have this surgery are back to work and their usual routine at around the two-week mark. The chance of requiring additional procedures is quite low unless we find that the appendix has already perforated. It is a good, and generally very safe operation, with a high rate of patient satisfaction.

Omar et al published a study in 2008 showing just how safe laparoscopic appendectomies have become. They found in over 230,000 UK patients the death rate was less than half compared to the open procedure (0.64% vs 0.29%; $p<0.001$).

Nonoperative treatment of appendicitis (NOTA) was first described in the 1940s and moved into the public consciousness when Patrick Roy was treated with antibiotics alone during the 1994 Stanley Cup playoffs. In 2014, tennis star Rafael Nadal was diagnosed with acute appendicitis. He was participating in the Shanghai Masters Tennis Tournament at the time. Nadal opted to be treated with antibiotics and had his appendix removed via laparoscopic one month later.

There have been several randomized trials like the APPAC trial and the CODA trial demonstrating that, in general, nonoperative management is safe, but that 25-60% of patients would go on to require an appendectomy during follow-up, which was usually around one year. The recent Eastern Association for the Surgery of Trauma (EAST) guidelines from 2019 on appendicitis could not provide a recommendation on the use of NOTA as first line treatment. Despite this, we know from database studies that appendectomy remains far more common in North America, with nonoperative management reserved for remote areas or extenuating circumstances.

We have covered adult uncomplicated NOTA a couple of times on the SGEM. The first time was on SGEM#115 and we reviewed two SRMAs on the topic that came to opposite conclusions. The other time we looked at this issue was with Dr. Leeper on SGEM#256. We reviewed an observational study on NOTA.

In that observational study by Sceats et al in JAMA 2019, all the patients were admitted to hospital for their antibiotic therapy or surgery. The study we are going to be looking at today compared outpatient vs. inpatient NOTA with antibiotics.

Reference: Sippola et al. Effect of Oral Moxifloxacin vs Intravenous Ertapenem Plus Oral Levofloxacin for Treatment of Uncomplicated Acute Appendicitis. The APPAC II Randomized Clinical Trial. JAMA 2021

P

Population: Nonoperative treatment of appendicitis (NOTA) was first described in the 1940s and moved into the public consciousness when Patrick Roy was treated with antibiotics alone during the 1994 Stanley Cup playoffs. In 2014, tennis star Rafael Nadal was diagnosed with acute appendicitis. He was participating in the Shanghai Masters Tennis Tournament at the time. Nadal opted to be treated with antibiotics and had his appendix removed via laparoscopic one month later.

- **Exclusions:** They excluded those outside the age range, allergy to contrast media or iodine, allergy on contraindication to antibiotic therapy, kidney insufficiency or elevated serum creatinine level, type 2 diabetes, and use of metformin medication, severe systemic illness (eg, malignancy, medical condition requiring immunosuppressant medication), pregnancy or lactation.

I

Intervention: Oral antibiotics for seven days (moxifloxacin 400mg daily)

C

Comparison: Intravenous IV antibiotics for two days (ertapenem sodium 1 g once daily) followed by oral antibiotics for 5 days (levofloxacin 500 mg a day plus metronidazole 500 mg three times daily)

- **Primary Outcome:** Success at one-year. This was defined as resolution of acute appendicitis resulting in discharge from the hospital without the need for surgical intervention and no recurrent appendicitis during the 1-year follow-up.
- **Secondary Outcomes:** Postintervention adverse events related to antibiotics or appendectomy, abdominal symptoms, duration of hospital stay, pain, and length of sick leave.

Authors' Conclusions

"Among adults with uncomplicated acute appendicitis, treatment with 7 days of oral moxifloxacin compared with 2 days of intravenous ertapenem followed by 5 days of levofloxacin and metronidazole resulted in treatment success rates greater than 65% in both groups, but failed to demonstrate noninferiority for treatment success of oral antibiotics compared with intravenous followed by oral antibiotics."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [ ] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [ ] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [ ] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.

Results

Key Results:
They randomized 599 patients, mean age was 36 years, and 44% were female.

- **Primary Outcome:** The treatment success rate at one year
  - 70.2% outpatient oral vs 73.8% inpatient IV followed by outpatient oral
  - −3.6% difference (1-sided 95% CI, −9.7% to ¥) p = 0.26
- **Secondary Outcomes:** There were no statistical differences in any of the secondary outcomes measured.

Time to Talk Nerdy:

1. Exclusions – They excluded pregnant and breastfeeding patients. This is a common exclusion and contributes to the lack of knowledge about how best to treat women (Women and Health Research IOM 1999). If there were concerns regarding lactation, potential participants could have been asked about bottle feeding temporarily during the study period.

2. Participation Rate – There were 1,036 patients eligible to be included in the trial. 433 declined to participate immediately (42%) and 16 more withdrew their consent after randomization. This means that 57% of patients agreed to NOTA. When using a script to explain the pros and cons of NOTA to patients, Minecci et al showed a real-life uptake of about 35% for NOTA in pediatric patients. What then was the discussion by the Finnish surgeons in the trial with patients about primary operative therapy? It reads as though this isn't even offered anymore and that is both a) wrong and b) strongly colors my impression of the external validity of this trial.

3. Non-Inferiority Margin – This was set by the research team at 6% based on the APPAC trial. What would patients consider non-inferior? Perhaps now that we have a global pandemic patients would be more motivated to be treated as an outpatient and accept higher rate of failure if they could increase their chance of avoiding COVID. If the margin was set at 10% then they authors could have claimed non-inferiority.

4. Outcomes – It is hard to understand that there was no difference in hospital length of stay. It was 28.9 hours for outpatient management and 29.9 hours for inpatient management. How is this possible when one group had to stay for two days of IV antibiotic therapy and the other was supposedly sent home with oral antibiotics?

Time to Talk Nerdy:

They also did not consider quality of life in their analysis. More than one-third of patients treated with NOTA would need to return to hospital within one year in both groups to have an appendectomy. They did not consider cost either. They asserts that analysis of the APPAC trial showed costs to be decreased NOTA but I wonder about the external validity of this result given database research done in North American centers.

5. External Validity – This multicentered trial was done in Finland. It is unsure how acceptable this approach would be to patients in other countries like Canada, USA, UK, rest of Europe and Australia.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors conclusions

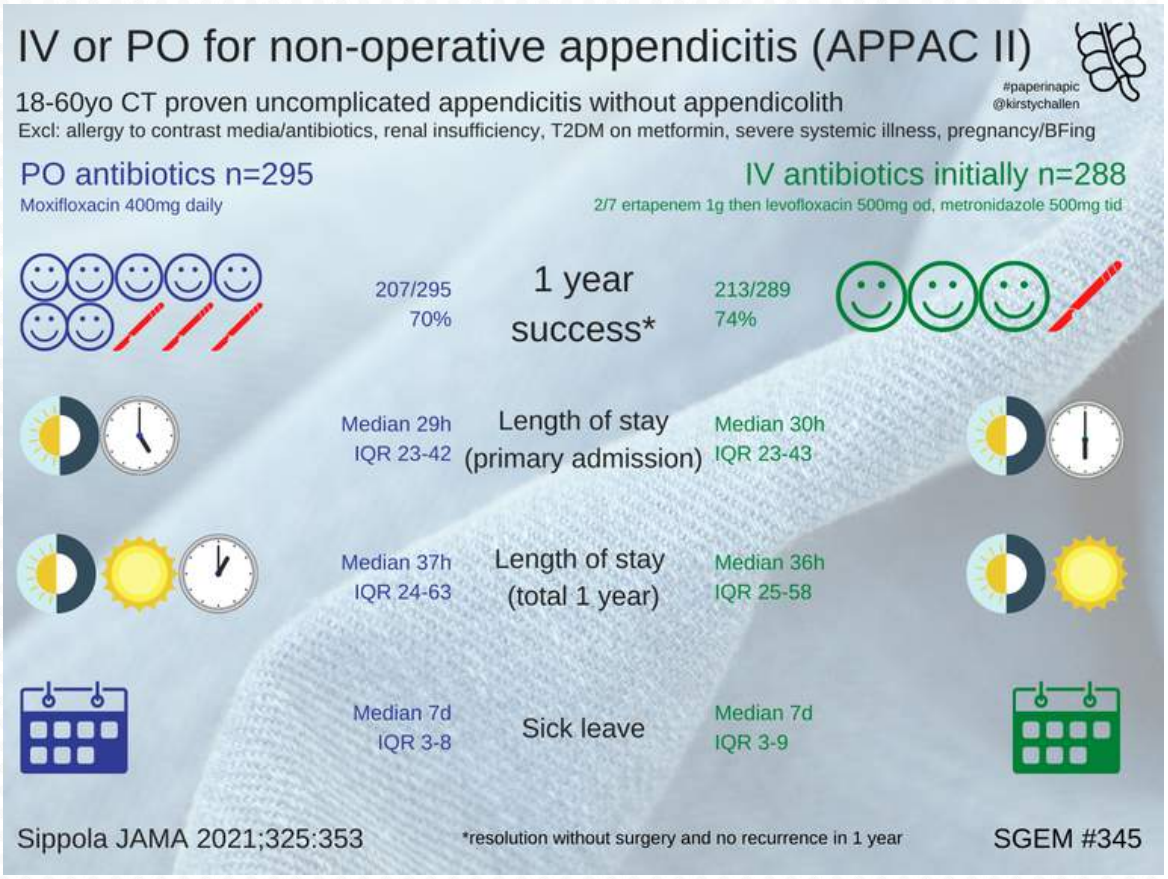
Clinical Application: This trial gives more clarity to the discussions that we all need to have with patients about treatment options, requirements, and expectations surrounding uncomplicated acute appendicitis. I'm still going to offer healthy young patients without appendicolith or signs of complicated appendicitis either an outpatient appendectomy (surgery and home four hours post op) versus admission for IV antibiotics and serial observations. In accordance with previously published literature, the majority still opt for an appendectomy.

What Do I Tell My Patient? I know you want to go home and just take pills. Unfortunately, evidence suggests this is not as good as being admitted to hospital on IV antibiotics. It will only be for 24-48 hours and them you can go home on pill antibiotics. He agrees to stay but wonders if he just should have had his appendix out and gotten this over with.

Case Resolution: The patient is told that outpatient, oral antibiotics alone has not been shown to be non-inferior to inpatient IV antibiotics. He decides to be admitted to hospital for his antibiotic treatment.

What would be your preference if you were diagnosed with acute uncomplicated appendicitis?
NOTA=Non-Operative Treatment of Appendicitis
Abx=Antibiotics
@rob_leeper @ewwalser @westernuSurgery
thesgem.com/2021/09/sgem34...

Open Appendectomy	3.3%
Laparoscopic Appendectomy	**76.8%**
NOTA: Inpatient IV Abx	11.7%
NOTA: Outpatient Oral Abx	8.1%



346

SEPSIS – YOU WERE ALWAYS ON MY MIND

Clinical Question:

What proportions of patients meeting sepsis criteria were actually diagnosed with sepsis, and how many non-septic patients had risk factors for harm from aggressive fluid administration?

Bottom Line:

Many people meeting sepsis criteria will not have sepsis and that exposes them to potential harm from protocolize treatments.

Guest:

Dr. Jess Monas is a Consultant in the Department of Emergency Medicine at the Mayo Clinic Hospital, Phoenix, Arizona. She is also an Assistant Professor, Department of Emergency Medicine Mayo Clinic Alix School of Medicine in Scottsdale, Arizona. Jess also does the ultra summaries for EMRAP.

Case Overview:

A 60-year-old man presents to the emergency department with a non-productive cough and increasing shortness of breath. He has a history of chronic obstructive pulmonary disease (COPD), hypertension (HTN), congestive heart failure (CHF), and benign prostatic hypertrophy (BPH). He's afebrile. He has a heart rate of 93 beats per minute, a blood pressure of 145/90 mm Hg, respiratory rate of 24 breaths per minute, and an oxygen saturation of 92% on room air.

Initial labs come back with a slightly decreased platelet count (149) and a minimally elevated creatinine (1.21 mg/dl or 107 umol/L). He triggers a sepsis alert, and you get a pop-up suggesting IV antibiotics and 30cc/kg of IV fluids. So, you ask yourself, is this guy really septic and should we bypass those fluids?

Background:

We have covered sepsis many times on the SGEM since 2012. This has included the three large RCTs published in 2014-15 comparing early goal-directed therapy (EGDT) to usual care. All three showed no statistical difference between the two treatments for their primary outcome (SGEM#69, SGEM#92 and SGEM#113).

There was also SGEM#174 which said don't believe the hype around a Vitamin C Cocktail that was being promoted as a cure for sepsis and SGEM#207 which showed prehospital administration of IV antibiotics did improve time to get them in patients with suspected sepsis, but did not improve all-cause mortality.

The SGEM was part of a group of clinicians who were concerned about the updated 2018 Surviving Sepsis Campaign (SSC) guidelines.

Specifically, the fluid, antibiotics, and pressor requirements within the first hour of being triaged in the emergency department.

Despite the lack of high-quality evidence to support these sepsis bundles, many hospitals incorporated them into their electronic medical record (EMR). They created these sepsis alerts with the intention of identifying septic patients, so they can be treated accordingly. Most physicians agree that antibiotics should be given early in septic patients. However, the jury is still out for other interventions with potential for harm, particularly, the infusion of 30cc/kg of IV fluids.

Worldwide sepsis contributes to the death of 5.3 million hospitalized people annually. It is the leading cause of death in the intensive care unit (ICU) in the US and the most expensive diagnosis. Since 2015, the Centers for Medicare & Medicaid Services (CMS) have indexed the quality of hospital care for sepsis to the SEP-1 core measure. Interventions, particularly early antibiotics, have been associated with improved mortality.

Diagnosing sepsis can be challenging. To adequately capture patients, specificity has been sacrificed for better sensitivity. We care more about catching all the true positives and worry less if a few true negatives get mixed up in there. Using vital signs and lab abnormalities certainly captures more patients, but it also identifies those without an infection. Patients with cirrhosis, toxicities, those on dialysis. It is possible that some of these patients can be at risk for harm from one of these interventions.

Reference: Litell et al. Most emergency department patients meeting sepsis criteria are not diagnosed with sepsis at discharge. AEM 2021.

P

Population: These were adult ED patients presenting to a tertiary academic medical center who met criteria for Sepsis-3 or Sepsis-3 plus shock. Sepsis-3 was defined as patients with a SOFA score ≥ 2 (Sequential Organ Failure Assessment score) and a suspected infection (which they counted if patients were given IV antibiotics within 24 hours of admission). Sepsis-3 plus shock was defined as Sepsis-3 with an initial lactate level > 2 and any systolic blood pressure < 90.

- **Excluded:** Trauma patients and those with missing ICD-9 codes. This is because prophylactic antibiotics often administered in traumatic or orthopaedic injuries.

I

Intervention: N/A

C

Comparison: They compared those with a sepsis diagnosis at discharge to those without a sepsis diagnosis at discharge.

O

- **Primary Outcome:** The primary outcome was proportion of ED patients with suspected sepsis based on consensus criteria who were not diagnosed with sepsis at discharge. Basically, they were initially flagged as potentially septic, but didn't turn out to be.
- **Secondary Outcomes:** Proportion of non-septic patients at risk of harm from the administration of a rapid weight based IV fluid bolus. The risk factors

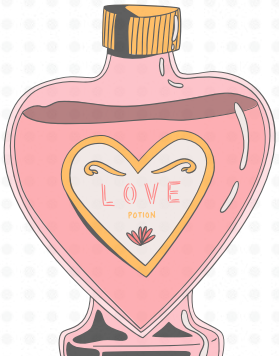
- included congestive heart failure, cirrhosis, dialysis-dependent renal failure, and morbid obesity. They also looked at mortality for Sepsis-3 and Sepsis-3 plus patients.
- Type of Study: Retrospective observational cohort design.

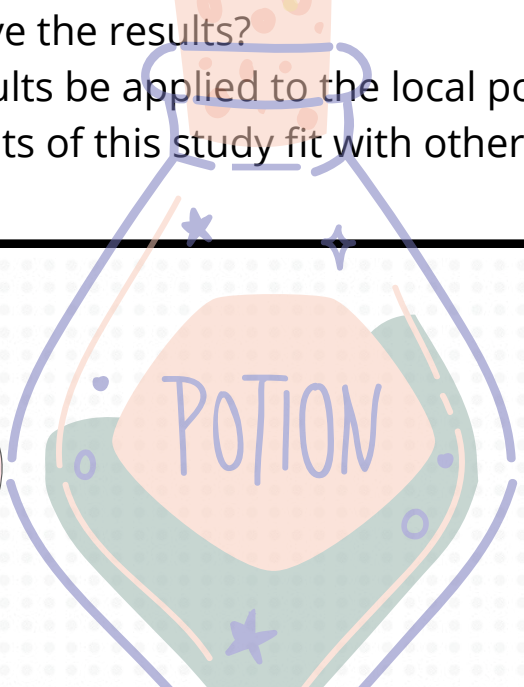
Authors' Conclusions

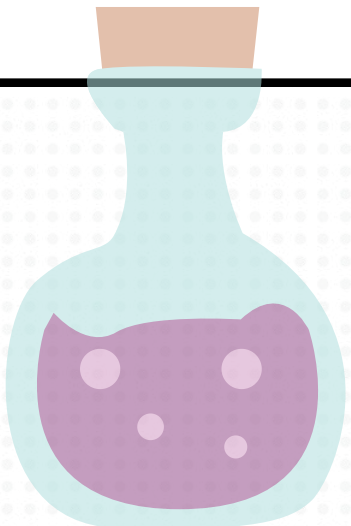
"Among adults with uncomplicated acute appendicitis, treatment with 7 days of oral moxifloxacin compared with 2 days of intravenous ertapenem followed by 5 days of levofloxacin and metronidazole resulted in treatment success rates greater than 65% in both groups, but failed to demonstrate noninferiority for treatment success of oral antibiotics compared with intravenous followed by oral antibiotics."

Quality Checklist for Observational Study

- ☑ 1. Did the study address a clearly focused issue?
- ☒ 2. Did the authors use an appropriate method to answer their question?
- ☑ 3. Was the cohort recruited in an acceptable way?
- ☑ 4. Was the exposure accurately measured to minimize bias?
- ☒ 5. Was the outcome accurately measured to minimize bias?
- ☒ 6. Have the authors identified all-important confounding factors?
- ☑ 7. Was the follow up of subjects complete enough?
- ? 8. How precise are the results? Fairly precise given the small sample size
- ☑ 9. Do you believe the results?
- ? 10. Can the results be applied to the local population?
- ☑ 11. Do the results of this study fit with other available evidence?







Results

Key Results:

- **Primary Outcome:** The proportion of ED patients with suspected sepsis based on consensus criteria who were not diagnosed with sepsis at discharge
- 75% of patients meeting Sepsis-3 criteria did not receive an explicit diagnosis of sepsis at discharge and about half (52%) did not receive an implicit diagnosis.
- 52% of patients meeting Sepsis-3 plus shock criteria did not receive an explicit diagnosis of sepsis at discharge and 38% did not receive an implicit diagnosis

- **Secondary Outcome:**
- Proportion of non-septic patients at risk of harm from the protocolized administration of a rapid weight-based crystalloid bolus.
- About 40% of patients meeting Sepsis-3 criteria and 30% of patients meeting Sepsis-3 plus shock, were not diagnosed with sepsis at discharge, but did have at least one risk factor for harm from large-volume fluid resuscitation.
- About 30% treated for suspected sepsis, had no infectious etiology found. The most common non-infectious diagnoses were overdose, inhalation pneumonitis, acute respiratory failure (asthma, COPD, CHF), DKA and acute renal failure
- 9% mortality in Sepsis-3 patients and 16% in Sepsis-3 plus shock patients

Time to Talk Nerdy:

1) Retrospective Study Design: The authors used a retrospective method to collect data. The study was not originally designed to answer the question being asked. This retrospective methodology may have both overestimated the patients that would have been considered septic by assuming a normal baseline and underestimated the patients by assuming normal values when data was missing. Sepsis-3 states that the SOFA score should be an increase in organ dysfunction, meaning a change ≥ 2 from baseline. It appears that the study assumed a normal baseline and assigned sepsis label if SOFA ≥ 2. This leads to uncertainty and greater difficulty in interpreting the data.

2) Diagnosis of Sepsis: How accurate was the diagnosis of sepsis? ICD-10 codes are used for SEP-1 core measures in reporting to CMS. However, this hospital used ICD-9 codes as the reference standard for the final diagnosis. This could have led to misattribution bias. It would have been less likely to occur using explicit codes rather than implicit codes which are comparatively more ambiguous.

3) SOFA Score: The SOFA score has good but not great ability to predict outcomes from sepsis in various populations. (Ferreira 2001, Arts 2005, Jones 2009, Cárdenas-Turanzas 2012, and Miller 2021). Sepsis-3 states that the SOFA score should be an increase in organ dysfunction, meaning a change ≥ 2 from baseline. They assumed a normal baseline which could overestimate the prevalence of sepsis. If data was missing, they assumed normal values and that would underestimate the number of patients with sepsis.

Time to Talk Nerdy:

4) Single Center: This was a single center study which can limit the external validity of their findings. It would depend on how sick the patients were in this study at baseline compared to local populations. In order to generalize to your demographic, it would be helpful to know what the baseline SOFA score is of this population. This paper assumed that patients had no organ dysfunction at baseline, however they also note that many had underlying comorbid conditions, which is contradictory.

5) Harms: The harms were theoretical based on risk factors for fluid resuscitations. They did not collect actual harm of any patients in this study.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We feel their conclusions are reasonable.

Clinical Application: This article is a reminder that there is a balance between the potential benefits and potential harms of any treatment. If you cast the net too wide you will increase your sensitivity (the true positives) but this can be at the cost of specificity (the true negatives). Treating people without disease can lead to an increase in harms. When the evidence is not great for benefit, such as the 30 cc/kg bolus for every sepsis alert, we would be wise to take a moment and use our clinical judgment before relying solely on an algorithm.

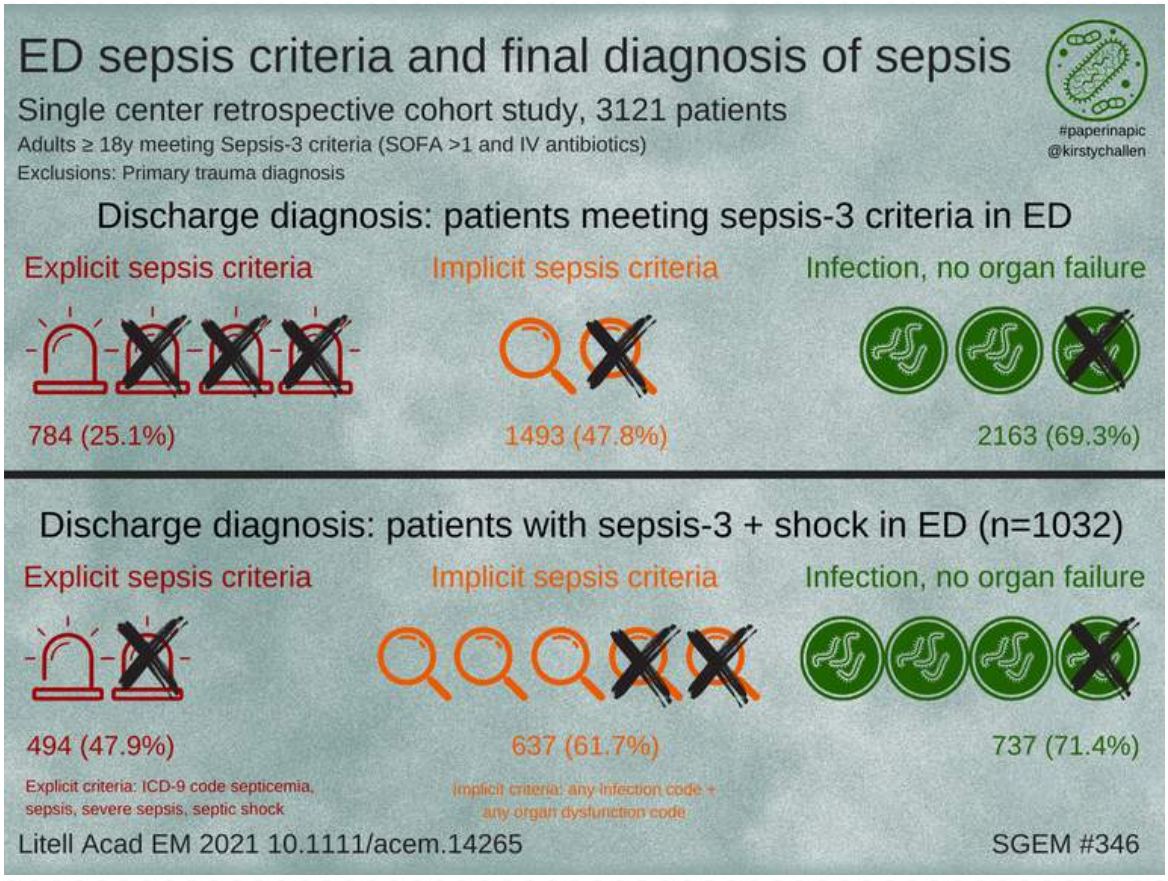
What Do I Tell My Patient? I think your cough and shortness of breath is due to fluid backing up on your lungs. Our hospital has a system to try and identify patients that might have a severe infection called sepsis. The protocol is to give you a large amount of fluid through your IV. My clinical judgment is this is not a lung infection. Giving you extra fluid could actually make things worse. The cardiologists agree. We will admit you to the hospital and work on getting the fluid off your lungs to make you feel better.

Case Resolution: You do a bedside lung ultrasound, and you see B-lines. So, you sign the order for antibiotics but hold off on the IV fluids based on the patient's sufficient blood pressure and what you just saw on the ultrasound. It turns out, his cough and shortness of breath is due to a CHF exacerbation and not sepsis. He's admitted to cardiology, they give him diuretics, and he is discharged home a few days later.

What percent of patients meeting sepsis-3 criteria were discharged with an explicit diagnosis of sepsis?
thesgem.com/2021/09/sgem34... @JAMA_current @srrezaie @KirstyChallen

90%	3.5%
75%	3.5%
50%	28.4%
25%	**64.5%**

141 votes · Final results



347

IT DON'T MATTER TO ME – BALANCED SOLUTION OR SALINE

Clinical Question:

Does administration of a balanced solution (plasma-lyte 148) during intensive care unit (ICU) stay, compared with saline solution, result in improved 90-day survival in critically ill patients?

Bottom Line:

In adult ICU patients at risk for kidney injury, administering modest volumes of plasmalyte 148 versus normal saline, at fast or slow infusion rates, did not influence 90-day mortality.

Guest:

Dr. Aaron Skolnik is an Assistant Professor of Emergency Medicine at the Mayo Clinic Alix School of Medicine and Consultant in the Department of Critical Care Medicine at Mayo Clinic Arizona. Board certified in Emergency Medicine, Medical Toxicology, Addiction Medicine, Internal Medicine-Critical Care, and Neurocritical Care, Aaron practices full time as a multidisciplinary intensivist. He is the Medical Director of Respiratory Care for Mayo Clinic Arizona and serves proudly as the medical student clerkship director for critical care medicine.

Case Overview:

A 66-year-old woman is brought in by EMS from home with lethargy and hypotension. Chest x-ray is clear, labs are remarkable for a leukocytosis of 16,000 with left shift; exam is notable for left flank pain and costovertebral tenderness. Straight catheter urinalysis is grossly cloudy, and pyuria is present on microscopy. Blood pressure is 85/50 mm Hg. You wonder which intravenous (IV) fluid should you order?

Background:

In ten seasons of the SGEM we have not covered the issue of which IV solution is the best in critical ill patients. That includes both trauma patients and septic patients. The controversy has been long standing with the standard joke being that there is nothing “normal” about normal saline. Saline is a hypertonic acidotic fluid.

Many critically ill patients receive intravenous crystalloids for volume expansion as part of their resuscitation. Some bench work, observational studies, and now two large, unblinded, cluster-randomized single-center trials (SMART and SALT-ED) suggested a benefit to using balanced crystalloids (i.e. Lactated Ringer’s or Plasmalyte 148) over 0.9% saline.

In the two large trials, this benefit was seen as a reduction in a composite outcome of major adverse kidney events within 30 days (MAKE-30). In the non-blinded SMART trial, there was no statistical difference in the individual components of the composite outcome (in-hospital death before

30 days, new renal replacement therapy or in creatinine >200% of baseline).

The SALT-ED trial was also a single-centre unblinded trial, but the primary outcome was hospital free days. They reported no statistical difference between the two groups. Their secondary composite outcome of death, new renal-replacement therapy, or final serum creatinine >200% of baseline, was statistically better with balanced crystalloid vs saline. However, there was not a statistical difference in any of the individual components of the composite outcome.

The BaSICS trial attempts to answer whether balanced solutions are superior to saline using a large, double-blind, factorial, multi-center randomized trial.

Reference: Zampieri et al. Effect of Intravenous Fluid Treatment With a Balanced Solution vs 0.9% Saline Solution on Mortality in Critically Ill Patients: The BaSICS Randomized Clinical Trial. JAMA 2021

P

Population: Adult patients admitted the ICU for more than 24 hours, needing at least one fluid expansion and with at least one risk factor for acute kidney injury (age over 65, hypotension, sepsis, required mechanical ventilation or non-invasive ventilation, oliguria or increased serum creatinine level, cirrhosis or acute liver failure)

- **Exclusions:** Required or expected to require renal replacement therapy within 6 hours of admission, severe electrolyte disturbances (sodium < 120 mmol/L or > 160 mmol/L), death considered imminent within 24 hours, suspected or confirmed brain death, palliative or comfort care only or patients previously enrolled in the trial. During the study, hyperkalemia (K+ > 5.5 mEq/L) was removed as an exclusion criteria, after the second interim

I

Intervention: Plasmalyte 148 solution at either slow (333 mL/hr) or fast (999 mL/hr) infusion rate.

C

Comparison: 0.9% sodium chloride solution at either slow (333 mL/hr) or fast (999 mL/hr) infusion rate.

- **Primary Outcome:** 90-day survival
- **Secondary Outcomes:** Need for renal replacement therapy up to 90 days after enrollment, occurrence of acute kidney injury, for patients without acute kidney injury at enrollment, SOFA score and, number of days not requiring mechanical ventilation within 28 days
- Trial Design: Double-blind, factorial, randomized clinical trial conducted at 75 ICUs in Brazil.

Authors' Conclusions

"Among critically ill patients requiring fluid challenges, use of a balanced solution compared with 0.9% saline solution did not significantly reduce 90-day mortality. The findings do not support the use of this balanced solution."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [?] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [?] 11. The treatment effect was large enough and precise enough to be clinically significant.

Results

Key Results:

- A total of 10,520 patients were randomized and available for analysis. The mean age was 62 years, 44% were female, 48% admitted after elective surgery, 68% had received crystalloid bolus before ICU admission (45% getting > 1 litre), 60% were hypotensive or getting vasopressors, 44% required mechanical ventilation and median volume of fluid was 1.5 litres during the first day of enrollment.
- **Secondary Outcomes:**
  - There were 19 secondary outcomes evaluated. Of those, two met the threshold for statistical significance with both reporting harm with the balanced solution. Specifically, SOFA score at day 7 (absolute difference 0.27 [0.08-0.45]) and neurological SOFA score > 2 at day 7 (32.1% vs 26.0% for the saline solution group; odds ratio, 1.40 [95% CI, 1.18-1.66]).

Time to Talk Nerdy:

1) External Validity: This study was conducted in 75 ICUs in Brazil. Half of the patients were admitted after elective surgery and 44% were on mechanical ventilation. The median APACHE II score was 12 and the median SOFA score was 4. Are these the same patients you see in your ICU?

2) Fluids: Almost half of patients had received more than 1 litre of IV fluids prior to enrollment. More of the patients received balanced solution compared to saline solution. This could have impacted the results.

The total volume of crystalloids received by patients in the trial was small. The median volume of fluid was 1.5 litres during the first day of enrollment. During the first three days after enrollment the accumulated median fluid administered (including study fluid and non-study fluid) was 4.1 L (SD, 2.9 L) and the median study fluid administered during the same period was 2.9 L (SD, 2.4 L).

3) Power Calculation. The sample size was calculated based on an estimated 90-day mortality of 35% in the saline group. Actual mortality was lower (around 27%) in both groups. The authors say that this may have resulted in a lower power to observe a clinically important difference.

Power calculation is mainly dependent on two things: the effect size, and the sample size. The effect size is the delta, the difference between intervention and the control or comparison group. The sample size is the number of participants in the cohort.

Time to Talk Nerdy:

You will read papers that say the study was underpowered to find a difference. I've probably said this before and been in error. Once you have run the experiment the results are as reported. An assumption was made a priori as to effect size. You no longer have an assumption for the magnitude of effect. Now you have a data set with the "actual" effect size in that population. This is probed for analyzed for statistical significance with the appropriate tools. No more assumptions on effect size needs to be made and what you see is what you get.

4) Secondary Outcomes or Subgroup Analyses: They found two of 19 secondary outcomes that were statistically significant. Both showed increased harm with balanced solution compared to saline The authors say: "all of the subgroup and secondary outcome analyses should be considered as only hypothesis-generating".

The authors are correct that it is hypothesis generating. We should not over-interpret secondary outcomes or subgroups. We have seen in other trials where these statistical differences are highlighted (CRASH-3) because of the potential positive patient impact. I think this could be an example of intervention bias (Foy and Filippone 2013). I doubt we will see people advocating for "normal" saline in the ICU for these secondary outcomes

5) Industry Involvement: Baxter supported this large trial by providing the fluids. There were some financial conflicts of interest declared with some of the authors. However, Baxter did not have a role in the design and conduct of the study.
Funding and fCOIs are just additional data points that need to be considered. They occur on a spectrum from no industry involvement to being designed, conducted, analysed, and written by employees of a company. None of that makes the information incorrect but our

Time to Talk Nerdy:

skepticism should be proportional to the degree of industry involvement.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We would have modified the conclusion to: "Among adult patients admitted the ICU for more than 24 hours, needing at least one fluid expansion and with at least one risk factor for acute kidney injury use of a balanced solution compared with 0.9% saline solution did not significantly reduce 90-day mortality. The findings do not support the use of this balanced solution in this cohort of patients."

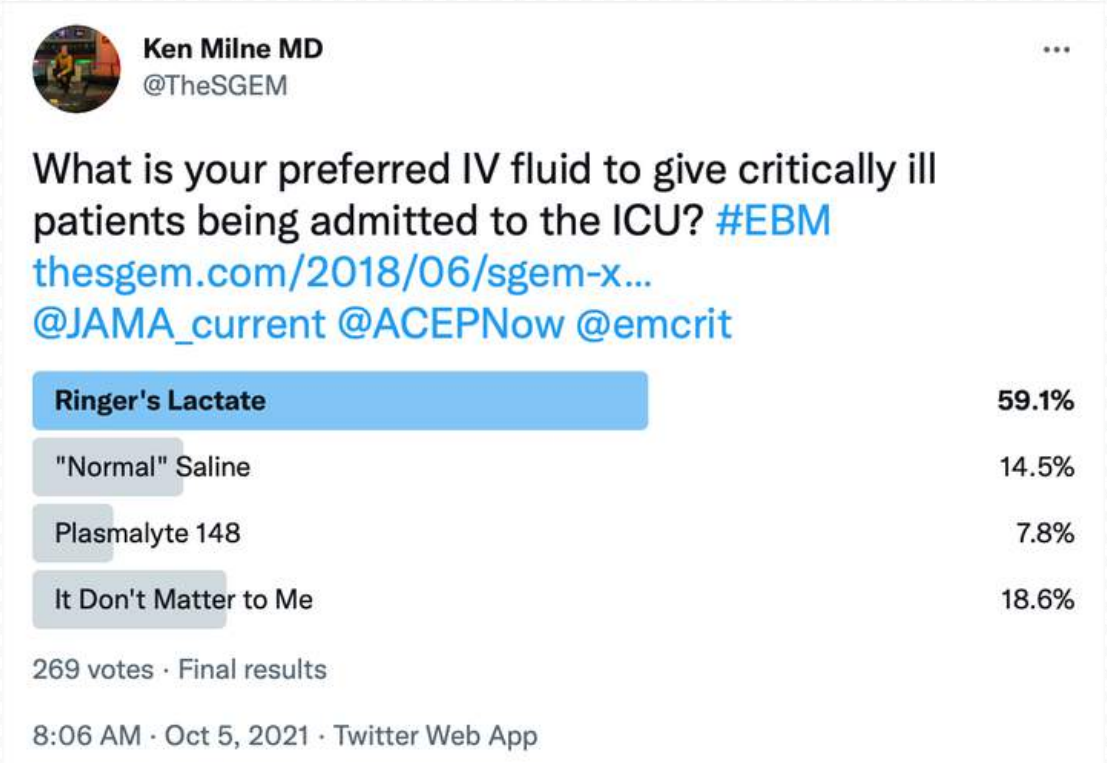
Clinical Application: When resuscitating critically ill patients in the emergency department, the type of crystalloid and rapidity of infusion do not likely influence 90-day mortality, at least at low total volumes administered.

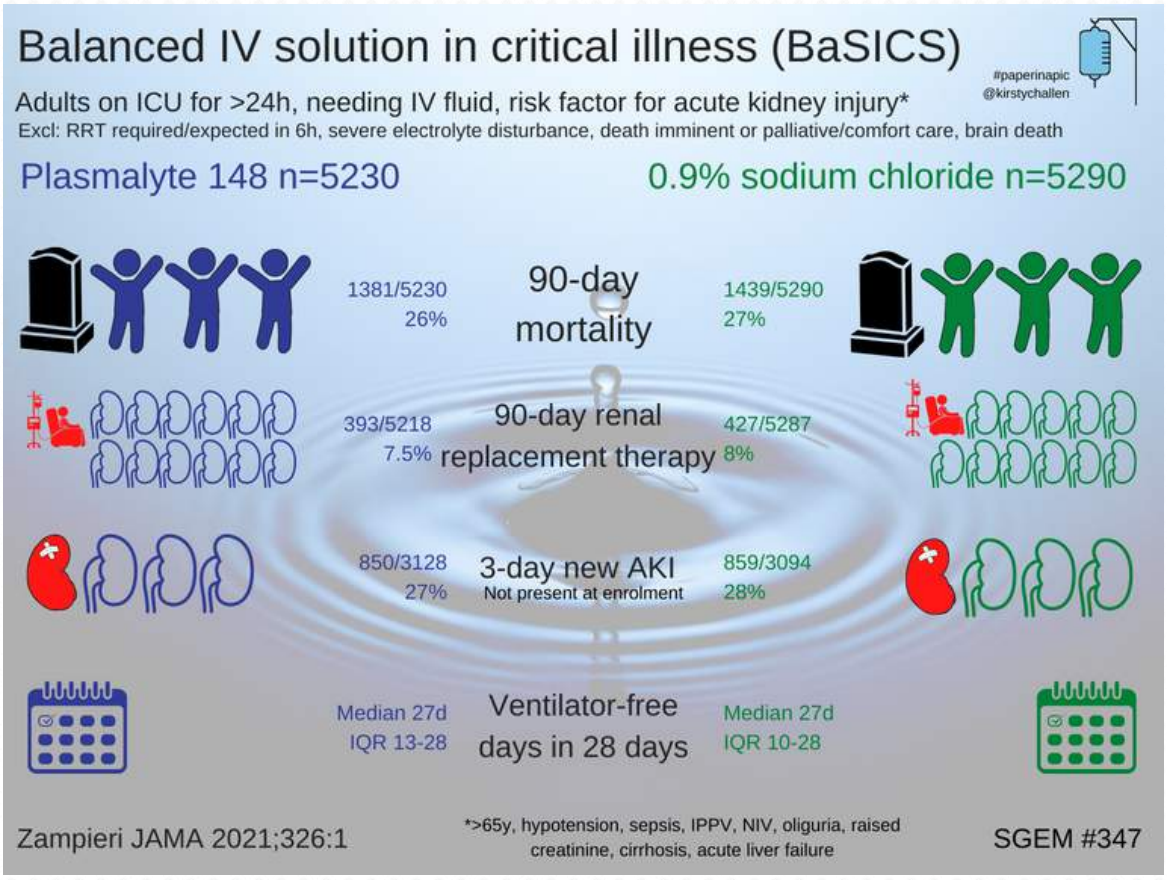
What Do I Tell My Patient? You have a severe urine infection. We are going to give you some IV antibiotics to treat the infection. Your blood pressure is low and that can be dangerous. We are going to also give you some IV fluids to bring your blood pressure up. You will be admitted to the intensive care unit where than can continue the treatment and watch you closely.

Case Resolution: You only have ready access to 0.9% saline in your emergency department. You administer a total of one liter before the patient is transferred to the ICU.

Other FOAMed:

- First10EM: The Basics Trial Normal Saline has Been Fine All Along
- EMCrit: BaSICS Trial





348

TAKE THE LONG MED HOME – FOR CELLULITIS

Clinical Question:

Does the use of a clinical pathway, including a dose of intravenous Dalbavancin, in emergency department patients with skin and soft tissue infections reduce hospitalizations?

Bottom Line:

In hospital systems with access to IV Dalbavancin and the ability to establish expedited telephone and in-person follow up, this clinical pathway is associated with a decrease in hospitalizations for patients with moderately severe cellulitis.

Guest:

Dr. Lauren Westafer an Assistant Professor in the Department of Emergency Medicine at the University of Massachusetts Medical School – Baystate. She is the cofounder of FOAMcast and a pulmonary embolism and implementation science researcher. Dr. Westafer serves as the Social Media Editor and research methodology editor for Annals of Emergency Medicine. Lauren also recently won the SAEM FOAMed Excellence in Education Award.

Case Overview:

A 46-year-old male with a history of diabetes controlled on metformin presents with erythema and warmth to his right lower leg measuring 27 cm by 10 cm for the past four days. The patient is neurovascularly intact and there is no evidence of deep vein thrombosis (DVT) on ultrasound. He has no fever, and his white blood cell count is 12,500.

Background:

Emergency department visits for skin and soft tissue infections (SSTI) are common and increasing [1]. These types of infections include cellulitis and abscesses. The SGEM has a couple of episodes on the treatment of cellulitis with antibiotics (SGEM#131 and SGEM#209).

The treatment of abscesses has been covered a few more times on the SGEM (SGEM#13, SGEM#156, SGEM#164 and SGEM#311). The latest episode looked at the loop technique to drain uncomplicated abscesses. The result was no statistical difference in failure rates between the loop and standard packing. Our conclusion was to consider using the loop technique on your next uncomplicated abscess.

Most patients can be managed as outpatients. However, the average length of stay for inpatient care is one week and costs close to $5 billion dollars a year in the USA [2]. The mortality rate for hospitalized patients with SSTI is <0.05% [3, 4].

The only reason for in-patient management in 40% of patients was to provide parenteral antibiotics [5]. This has led to greater interest in long-acting parenteral antibiotics as a possible alternative to admission.

Reference: Talan et al. Pathway with single-dose long-acting intravenous antibiotic reduces emergency department hospitalizations of patients with skin infections. AEM October 2021

P

Population: Patients ≥18 years old with abscess, cellulitis, or wound infection believed or confirmed to be due to gram-positive bacteria and an area of infection of at least 75 cm2.

- **Excluded:** Unstable comorbidity (e.g. severe sepsis), immunosuppression, injection drug use and fever, pregnancy, breastfeeding, bilateral lower extremity involvement, severe neurologic disorder, allergy to glycopeptide antibiotics, suspected gram negative infection or infection likely to need more intensive care or broad spectrum antibiotics, suspected osteomyelitis, septic arthritis, or endocarditis.

I

Intervention: Clinical pathway included a single dose of intravenous (IV) dalbavancin

- 1500 mg (creatinine clearance ≥30 mL/min) or 1,125 mg for creatinine clearance <30 mL/min not on dialysis
- Telephone follow up call 24 hours after the visit and a follow up appointment 48-72 hours after discharge

C

Comparison: Usual care pre-implementation of the new clinical pathway

- **Primary Outcome:** Hospitalization rate at the time of initial care in the population that received at least one antibiotic dose
- **Secondary Outcomes:** Hospitalizations through 44 days, health resource utilization (length of stay, level of care, major surgical interventions, ICU admissions), adverse events, and patient-related outcomes (satisfaction, work productivity, and quality of life surveys at 14 days)

- **Trial Design:** Before-and-after observational study at eleven US academic affiliated emergency departments (EDs).

This is an SGEMHOP episode which means we have the lead author on the show. Dr. Talan is considered an authority in acute infections that result in severe morbidity and death. He is currently on the faculty of the Department of Emergency Medicine, and Department of Medicine, Division of Infectious Diseases at UCLA Medical Center. Dr. Talan also serves on the editorial board of the Annals of Emergency Medicine.

Authors' Conclusions

““mplementation of an ED SSTI clinical pathway for patient selection and follow-up that included use of a single-dose, long-acting IV antibiotic was associated with a significant reduction in hospitalization rate for stable patients with moderately severe infections.”

Quality Checklist for Observational Study

- ☑ 1. Did the study address a clearly focused issue?
- ☑ 2. Did the authors use an appropriate method to answer their question?
- ☑ 3. Was the cohort recruited in an acceptable way?
- ☑ 4. Was the exposure accurately measured to minimize bias?
- ☑ 5. Was the outcome accurately measured to minimize bias?
- ☐ 6. Have the authors identified all-important confounding factors?
- ☑ 7. Was the follow up of subjects complete enough?
- ☐ 8. How precise are the results? Fairly precise given the small sample size
- ☑ 9. Do you believe the results?
- ☐ 10. Can the results be applied to the local population?
- ☑ 11. Do the results of this study fit with other available evidence?

Fairly Precise

Results

Key Results:

- Over 3,000 patients were screen in the before and in the after phase of this study. Only 5% were eligible for inclusion. The median age of participants was in the late 40's, two-thirds were male, and over 80% had cellulitis.

- **Primary Outcome:** Hospitalization rate at the time of initial care
  - 38.5% usual care vs 17.6% new pathway
  - Absolute Difference 20.8% (95% CI; 10.4% to 31.2%)
- **Secondary Outcome:**
  - Hospitalizations through 44 days: Absolute Difference 16.1% (95% CI; 4.9% to 27.4%)
  - Length of Stay: 3.0 days (IQR 2.0 to 5.0) vs 2.0 days (IQR 1.0 to 4.0)
  - Infection-Related Surgery: 0.6% vs. 3.3%
  - ICU Admissions: 1.9% vs 0.7%
  - Mild, Moderate and Severe AE: Were all more common in the new pathway group
  - Deaths: None
  - Patient-Related Outcomes; These were detailed in the supplemental material

Time to Talk Nerdy:

We asked David five nerdy questions about his study. Listen to the SGEM podcast to hear his responses.

1. Inclusion/Exclusion – The patient flow diagram, Figure 1, does not list reasons for exclusion, so it's difficult to know why patients weren't included and if they are different than those who were excluded. Do you have any data on the characteristics of the excluded patients, and could this have led to some selection bias?

2. Study Design – Your team used a before/after study design to investigate the association between a new clinical pathway and hospitalization for patients with SSTI. One drawback to this type of design is the possible contamination of treatment effect by confounders such as other system or local factors. For example, it's not clear how much the protocol to ensure close outpatient follow up or education contributed to the lower hospitalization rates.

3. Hawthorne Effect – In this study, clinicians in the intervention period knew they were being studied. It is possible that some portion of the treatment effect was the result of the clinicians being aware that their management of skin and soft tissue infections was being evaluated and that discharge was encouraged.

4. Impact – The pathway demonstrated an absolute difference of 21% for the primary outcome of hospitalizations. As mentioned earlier, only 5% of those screened for eligibility were enrolled. That means most patients who present with SSTI the data does not directly apply to their management. Does this not limit the impact of this intervention significantly?

Time to Talk Nerdy:

5. External validity – This study was conducted in 11 academic affiliated EDs in the US. The US has a much different healthcare system than other countries like Canada, UK and Australia. Do you think this data can be applied outside the US?
The academic world is also different than community EDs. The clinical pathway included telephone follow up and an outpatient follow up visit within 48-72 hours. This may not be feasible in many community practice environments or certain patient populations.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: It all depends. This medication costs ~$5,000 for 1,500mg. It is unclear if this would be a cost effective strategy. There could also be a concern with indication creep leading to increased antibiotic resistance.

What Do I Tell My Patient? You have a severe urine infection. We are going to give you some IV antibiotics to treat the infection. Your blood pressure is low and that can be dangerous. We are going to also give you some IV fluids to bring your blood pressure up. You will be admitted to the intensive care unit where than can continue the treatment and watch you closely.

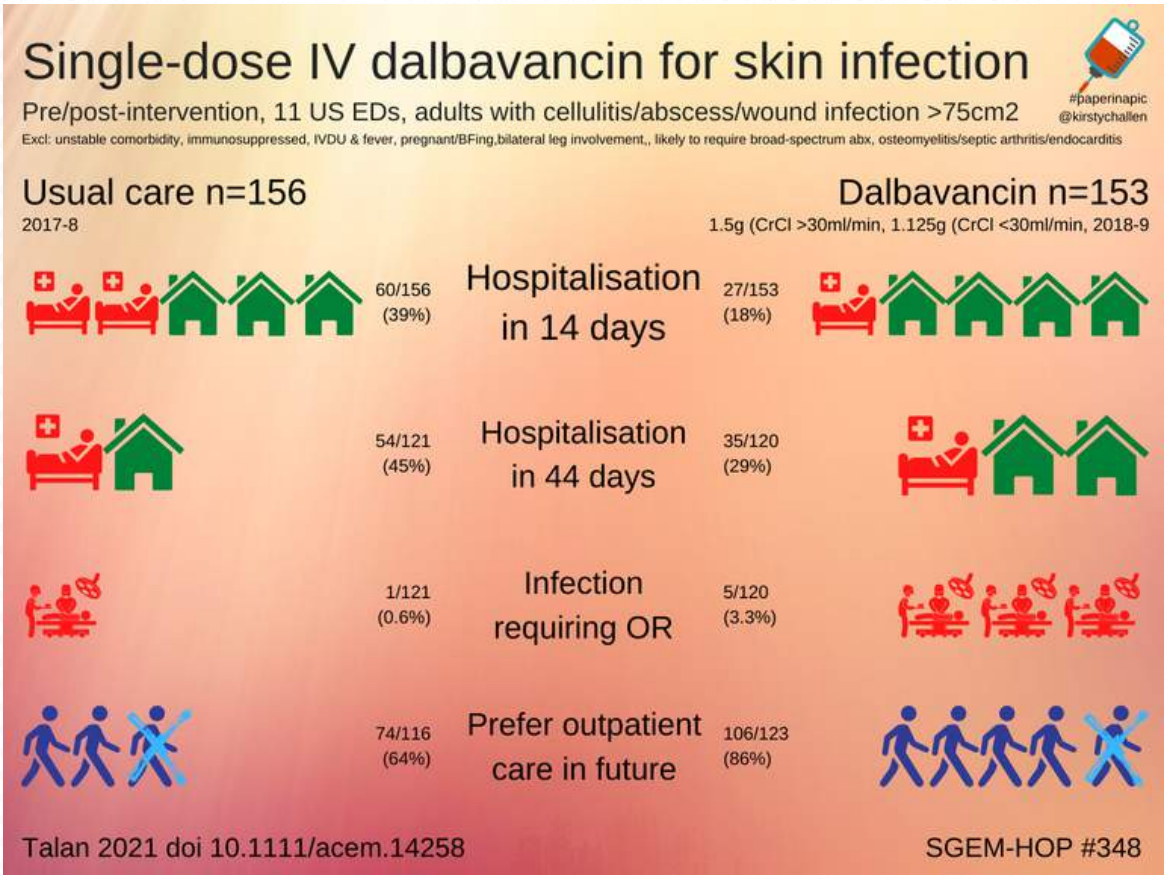
Case Resolution: You offer the man the new long-acting single-dose IV antibiotic and outpatient management. He is happy to not need to be admitted to hospital and is discharged home with follow-up instructions.

Would a single-dose long-acting IV antibiotic pathway to reduces hospitalization in patients with skin and soft tissue infections have a net benefit at your ED? #SGEMHOP thesgem.com/2021/10/sgem34... @AcademicEmerMed @LWestafer @SAEMonline

Yes	**68.5%**
No	31.5%

54 votes · Final results

9:23 AM · Oct 26, 2021 · Twitter Web App



349

TAKE THE LONG MED HOME – FOR CELLULITIS

Clinical Question:

What is the best strategy for treating patients with an acute large vessel occlusion stroke, direct to mechanical thrombectomy or a bridging approach with TPA followed by mechanical thrombectomy?

Bottom Line:

Currently there is insufficient evidence to know what the best strategy for patients with large vessel occusions is, direct to mechanical thrombectomy or bridging with TPA.

Guest:

Dr. Michal Krawczyk is in his fifth year of neurology residency at Western University in London, Ontario, Canada. He is interested in acute neurological illness, including cerebrovascular disease and epilepsy. Next year he will be beginning a Neurohospitalist fellowship at the University of Texas at Houston.

Case Overview:

A 70-year-old male with a past medical history of hypertension and peripheral artery disease, last seen normal 1.5 hours ago, presenting with acute onset of aphasia and right sided face and arm weakness. He has a National Institute of Health Stroke Scale (NIHSS) score of 7. At 1am a CT angiogram is obtained that demonstrated a left M2 occlusion, and an Alberta Stroke Program Early CT Score (ASPECTS) of 10. Given the recent publications of trials assessing if mechanical thrombectomy alone is non-inferior to a bridging approach with tPA in addition to mechanical thrombectomy, you wonder whether these trials apply to your patient and what is the best course of action.

Background:

There are two treatments for acute ischemic stroke, systemic tPA and mechanical thrombectomy (MT). We have covered some studies looking at both treatment modalities on the SGEM.

- SGEM#29: Stroke Me, Stroke Me
- SGEM#70: The Secret of NINDS (Thrombolysis for Acute Stroke)
- SGEM#85: Won't Get Fooled Again (tPA for AIS)
- SGEM#137: A Foggy Day – Endovascular Treatment for Acute Ischemic Stroke
- SGEM#292: With or Without You – Endovascular Treatment with or without tPA for Large Vessel Occlusions
- SGEM#297: tPA Advocates Be Like – Never Gonna Give You Up
- SGEM#333: Do you Gotta Be Starting Something – Like tPA before EVT?

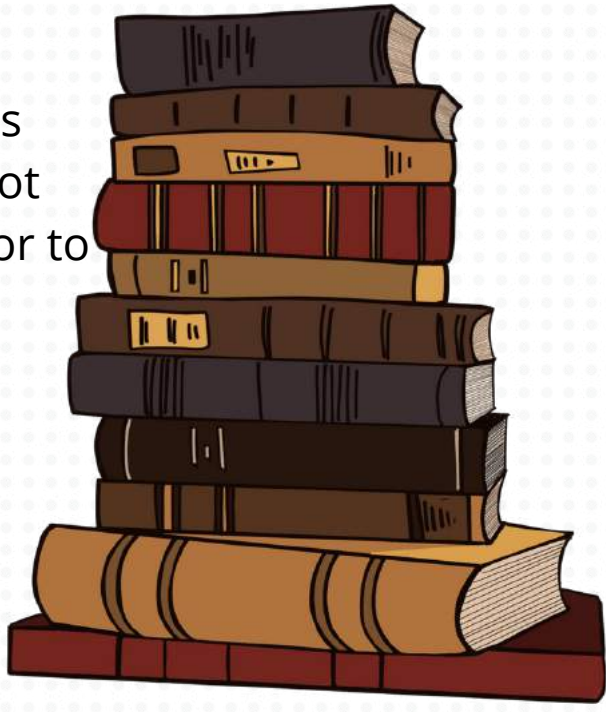
Background:

Mechanical thrombectomy is indicated only for patients with large vessel occlusions (LVOs) on imaging. There were a few earlier studies on MT that failed to demonstrate superiority, but it was the study MR CLEAN published in NEJM 2015 that really changed practice. It was a multicenter, randomized, unblinded trial treating 500 patients with an anterior circulation LVO within six hours of symptom onset. The primary outcome was mRS 0-2 at 90 days and it showed an absolute difference of 14% favoring MT. This gives a NNT of 7.

Six RCTs have been published since MR CLEAN. All supported MT and all were stopped early (SWIFT PRIME, EXTEND-IA, REVASCAT, ESCAPE, DAWN, and DEFUSE).

For patients with LVOs it is unclear whether there is any additional benefit with administering tPA before thrombectomy, also known as a bridging approach, in contrast to skipping tPA and directly proceeding with MT.

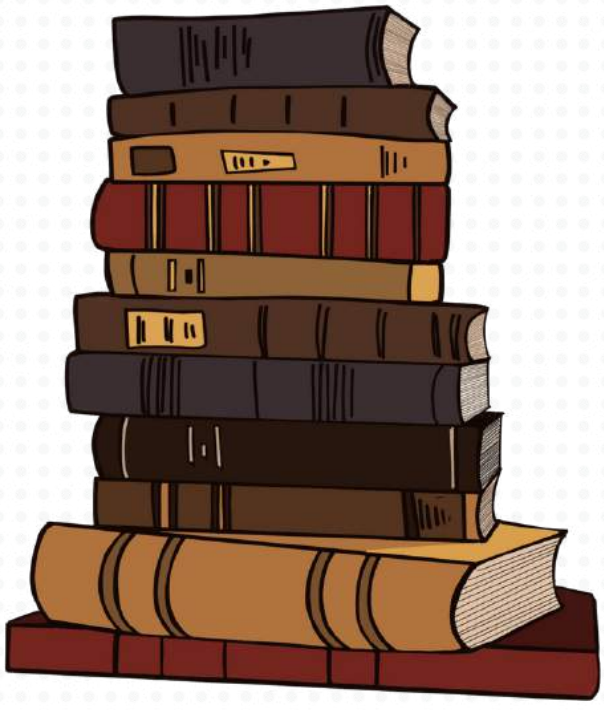
There are several theoretical advantages of a bridging approach. These potential advantages include thrombus debulking allowing easier clot retrieval, distal emboli lysis, recanalization prior to MT, and it may be beneficial in cases of unsuccessful MT. Conversely, a direct to MT approach may lead to fewer intracerebral hemorrhages (ICH) and quicker initiation of endovascular thrombectomy.



Background:

Recently, three randomized control non-inferior trials on this topic have been published, two from China (DIRECT-MT, and DEVT) and one from Japan (SKIP). Two trials demonstrated non-inferiority while one trial failed to show that direct MT was non-inferior.

Reference: Katsanos et al. Utility of Intravenous Alteplase Prior to Endovascular Stroke Treatment: A Systematic Review and Meta-analysis of RCTs. Neurology 2021



P

Population: Randomized controlled trials of patients with acute large vessel occlusion stroke qualifying for MT

- **Exclusions:** Observational studies and non-randomized trials

I

Intervention: MIT alone

C

Comparison: MT bridged with tPA

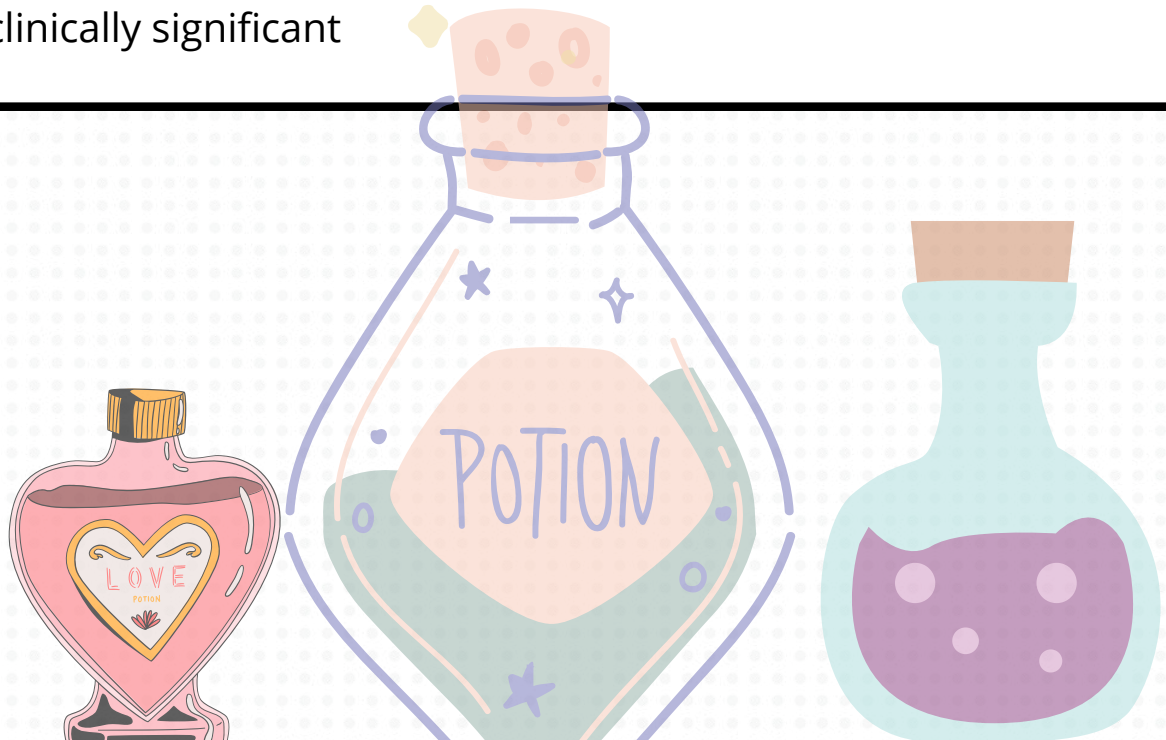
- **Primary Outcome:** mRS score 0-2 at three months
- **Secondary Outcomes:** mRS 0-1 and ordinal shift at three months, successful recanalization before MT, successful recanalization after MT, randomization to puncture time, symptomatic intracranial hemorrhage (sICH), any ICH and all-cause mortality

Authors' Conclusions

"We detected no differences in functional outcomes of IV thrombolysis–eligible patients with an acute LVO receiving dEVT compared to BT. Because uncertainty for most endpoints remainslarge and the available data are not able to exclude the possibility of overall benefit or harm, further RCTs are needed."

Quality Checklist for Therapeutic Systematic Reviews

- [x] 1. The clinical question is sensible and answerable
- [x] 2. The search for studies was detailed and exhaustive
- [ ] 3. The primary studies were of high methodological quality
- [x] 4. The assessment of studies were reproducible
- [x] 5. The outcomes were clinically relevant
- [x] 6. There was low statistical heterogeneity for the primary outcomes
- [ ] 7. The treatment effected was large enough and precise enough to be clinically significant



Results

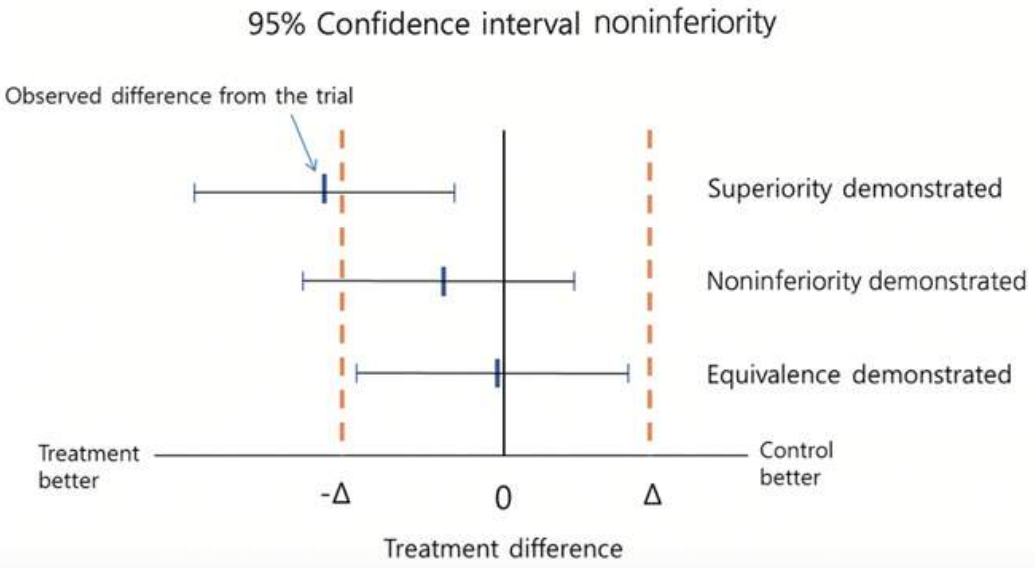
Key Results:

- The three RCTs included a total of 1,092 patients. Median age was in the early 70's and 42% were female.
- **Primary Outcome:** mRS score 0-2 at three months
  - OR 1.08 (95% CI 0.85 to 1.38) and adjusted OR 1.11 (95% CI 0.76 to 1.63)
- **Secondary Outcome:**
  - mRS score 0-1 at three months OR 1.10 (95% CI 0.84 to 1.43) and adjusted OR 1.16 (95% CI 0.84 to 1.61)
  - Successful recanalization before EVT: OR 0.37 (0.18-0.77) Moderate certainty
  - Successful recanalization after EVT: OR 0.77 (0.54-1.08) Low certainty
  - sICH: OR 0.75 (0.45-1.25) Low certainty
  - Any ICH: OR 0.67 (0.49-0.92) Moderate certainty
  - All-cause mortality: OR 0.93 (0.68-1.29) Low certainty

Time to Talk Nerdy:

1. External Validity: All three trials were from Asia and as such may not be directly applicable to North American populations and healthcare systems. In one of the trials, they used 0.6mg/kg of tPA (SKIP) instead of the standard 0.9mg/kg. This could bias the trial to finding non-inferiority. In addition, these studies were all conducted at stroke centres with MT availability and do not address a drip and ship model of care.

2. Non-Inferiority Margins: All three studies included in the SRMA were non-inferiority trial designs. They were asking if direct to MT was non-inferior to the standard bridging with tPA before MT. Two out of three trials (DIRECT-MT and DEVT) the non-inferiority was met, but the non-inferiority margin was set at ≤10% absolute clinical effect in DEVT, and 20% effect size in odds ratio in DIRECT-MT. Even if non-inferiority is demonstrated, it does not mean there is no clinical benefit from a bridging approach if the non-inferiority margin is too large, which may represent a clinically important difference. Many argue that the non-inferiority claim should only be reserved when a less conservative margin of 5% is utilized. None of the trials met this less conservative margin.



Time to Talk Nerdy:

3. Performance Bias: We have discussed different forms of bias many times on the SGEM. This is the first time we have mentioned performance bias. This type of bias is defined by Cochrane Risk of Bias (RoB) Tool as the result of "systematic differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest."

As highlighted in this SRMA, there was a performance bias in the DIRECT-MT trial with 9.4% of patients in the bridging group not receiving MT, while only 5.2% in the direct group did not receive MT. This 4.2% difference may have resulted in worse outcomes in the bridging group, favoring direct MT and a finding of non-inferiority.

4. Selection Bias: This is a type of bias we have discussed many times on the SGEM. The Cochrane RoB Tool defines selection bias as the result of "systematic differences between baseline characteristics of the groups that are compared." Selection bias may affect the estimate of the per-protocol effect and/or the intention-to-treat effect. It depends on the definition that is used for the groups that are being compared.

In the DEVT trial, an exclusion criterion was "arterial tortuosity and/or other arterial disease that would prevent the device from reaching the target vessel." This exclusion criterion may effectively 'cherry-pick' patients, excluding those where thrombectomy would have been difficult, potentially resulting in less favorable outcome in the direct MT group. It is unclear how many patients were excluded from the DEVT trial for this reason. In the DIRECT-MT trial approximately 5.8% (38/654) of patients intended to undergo thrombectomy did not due to technical reasons, highlighting that even in specialized academic centers thrombectomy remains technically challenging.

Time to Talk Nerdy:

5. Timing of tPA: In the SKIP trial, 21% of patients in the bridging group had tPA started after groin puncture for MT. It is likely that in a significant proportion of these patients MT was completed even before the tPA infusion was finished. In the DIRECT-MT trial 87% of patients had a tPA infusion ongoing during MT, and 9% of patients in the bridging group did not receive the full dose of tPA. This could have biased the study towards finding non-inferiority for MT alone.

6. Subgroups: Certain subgroups that may benefit more from a bridging approach were underrepresented in the three trials. In the study design of the DEVT and SKIP trials they did not include patients with M2 occlusions. After final adjudication the percentage of M2 occlusions in the DEVT trail was 1.7%, SKIP 19%, and DIRECT-MT 10.1%. It is known that compared to M1/ICA occlusions, tPA is much more effective at lysing M2 clots. In the INTERRSeCT study, the odds ratio of recanalization with tPA of an ICA occlusion is 1, proximal M1 occlusion is 1.99, and M2 occlusion is 3.61 (1).

It is unclear which approach is better for M2 occlusions. The argument is that two out of the three trials did not include M2 occlusions based on their inclusion criteria, and as a result the amount of M2 occlusions overall was low. Therefore, it may be unwise to expect for patients with M2 occlusions as they were excluded from the majority of the trials we are discussing, and there is a rationale based on previous research to suggest that patients with M2 occlusions “may/may not” do better with a bridging approach (1).

In addition, recanalization would be a surrogate marker for good neurologic function. Just because blood flow is restored does not mean function will improve. This would be true if the damage was too great regardless of the time (futile recanalization). However,

recanalization is a variable strongly associated with better outcome (2), after all the entire point of thrombectomy is to pull out the clot, there is no conceivable benefit of thrombectomy without recanalization.

The benefits of tPA are strongly associated with earlier time to treatment (3), neither the DIRECT-MT or DEVT trial had any patients receiving tPA under two hours, the approximate median for both trials from symptom onset to tPA treatment was 3 hours. This is contrast to the HERMES meta-analysis (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials) the symptom onset to tPA treatment was 2.08 hours (interquartile range, 90-170) (4), approximately one hour shorter compared to DIRECT-MT or DEVT. A partial explanation is the less-than-ideal door-to-needle times of approximately 60 minutes in the DIRECT-MT and DEVT trials. The HERMES investigators demonstrated that a 1-hour delay in door-to-needle times is associated with 53% lower odds of functional independence in LVO patients treated with tPA (4). The unfavorable effect of such a delay may have led to an underestimation of the benefit of a bridging approach.

We need to be cautious not to over-interpret observational data. There are no RCT randomizing patients into early vs late treatment. There could be unmeasured confounders responsible for the association between faster times and better outcomes. Perhaps those teams that perform faster also do several other things better that are responsible for the observed improvement.

The concept of “time is brain” is initially based on animal studies (5-7). If the middle cerebral artery (MCA) is occluded in monkeys (5) or other animals (6), the duration of ischemia is directly related to volume of infarct up to a certain time point but not longer.

Time to Talk Nerdy:

These experiments formed the basis of our understanding of core and penumbra physiology and defined thresholds of cerebral ischemia (7).

Dr. Camilo Gomez coined the term "time is brain" back in 1993. He has since modified his position: "It is no longer reasonable to believe that the effect of time on the ischaemic process represents an absolute paradigm. It is increasingly evident that the volume of injured tissue within a given interval after the estimated time of onset shows considerable variability in large part due to the beneficial effect of a robust collateral circulation." (J Stroke Cerebrovasc Dis 2018)

We agree with Dr. Gomez that time to treatment is not an absolute paradigm, and there are other important variables such as collateral circulation that can perfuse the ischemic penumbra and slow core progression. Currently, at stroke onset we cannot predict which patients are slow or fast progressors. Even in patients that are slow progressors, over time the ischemic core grows. From DAWN and DEFUSE-3 we know that the limit is 24 hrs, but some argue that in a minority of slow progressors benefit from reperfusion can be up to 48 hrs (8).

Besides animal studies, advances in neuroimaging such as PET also demonstrated that time is a critical predictor of tissue fate (9) and allowed for the quantification of how much brain tissue is lost over time (10). Dr. Saver published an article in 2006 that quantified how much brain is lost over time and determined 1.9 million neurons are destroyed each minute (10).

1.9 million neurons sounds impressive, but we need to consider how many total neurons are in the brain. Our current best estimate is 86 billion (J Comp Neuro 2009).

Time to Talk Nerdy:

To put it another way, it would take over 750 hours or 31 days to lose all your neurons. No one is advocating for the loss of neurons but how many neurons must be lost and in what area of the brain to be clinically significant?

In the same study by Dr. Saver, it was estimated that each hour without recanalization the ischemic brain ages 3.6 years (10). Based on this scientific rationale, time to treatment is a critically important variable predicting outcome. This has been reported both in a pooled meta-analysis of RCTs on tPA (3) and MT (11, 12), not to mention multiple well designed observational studies (13, 14).

Again, we need to be careful not to over-interpret observational data. Pushing the system to go too fast can lead to increased potential harm. This has been reported in the STEMI literature in trying to reduce door-to-balloon time (Fanari et al 2015). We do not want to be too slow or to be too fast.

Acute ischemic stroke treatments needs to be provided in a safe manner. Some stroke centers have achieved excellent door-to-needle times of 20-25 minutes (15, 16) and they did not report any compromise of safety. The rate of thrombolyzed stroke mimic was low at 1.4% (15) and sICH post-thrombolysis was also low at 2.1% (16).

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions.

Case Resolution: Our case highlights the nuances of the application of these trials to individual care. There are many factors that may suggest a bridging approach is the preferred option.

First, the patient is presenting at 1.5 hours from stroke onset, and earlier time to treatment with tPA is strongly associated with better outcome (3). Neither the DIRECT-MT or DEVT trial randomized patients in this early time window.

It is true that there is a strong association, but tissue factors are probably more important than the clock. In terms of tissue viability, the patient has an ASEPCTS of 10, with no early ischemic changes, that is as good as it gets.

Second, the evaluation of this patient is occurring at 1am and not during standard working hours. All three trials had very quick work workflow with MT occurring after tPA in DEVT and DIRECT-MT trials in approximately 30 minutes, while SKIP trial in 8 minutes. If considerable delays to MT are expected, such as on call, or transfer from a community hospital, a bridging approach may be preferred.

Standard working hours for emergency medicine is 24/7/365. Patients can have acute ischemic stroke at any time of day. If there is a more effective/safer therapy, why should it be only offered during “banking hours”? Perhaps that means that the revascularization team needs to be available 24/7/365 in a timely fashion like we have with STEMI patients. We still do not know if a drip and ship model will have a patient oriented net benefit.

In many centers MT is available 24/7/365, but the reality is that, many of those centers the interventionalist and techs are at home and it takes time for everyone to arrive to the hospital and set up. Not to mention there is one interventionalist on call, rarely they may be busy with another case. These are the realities that we face and need to be cognizant of them when we are applying the results of trials with excellent workflow characteristics for mechanical thrombectomy.

Case Resolution: A study published in 2017 by Prasanna Venkatesan Eswaradass et al in CMAJ Open looked at eight Canadian provinces and estimated that 84.7%-99.8% have access to a current or proposed endovascular thrombectomy site within six hours by ground EMS.
Third, the patient has an M2 occlusion, which is more frequently recanalized with tPA compared with M1/ICA occlusions (1). Moreover, MT may be more challenging the more distal the clot.

Lastly, the patient has a history of peripheral artery disease, if severe may make it challenging to gain vascular access and may even preclude a transfemoral approach.

We cannot forget about the potential increase in harms. There is no doubt that the bridging approach using tPA increases the risk of sICH. The excess risk of sICH in all three included RCTs was just under 2%. However, it was not statistically significant and there was no increase in all-cause mortality.

The risk of sICH needs to be strongly considered before deciding on a bridging approach. There are many clinical (i.e., high NIHSS, uncontrolled hypertension, dual anti-platelet therapy), radiological (i.e., CT hypodensity), and laboratory (i.e., hyperglycemia, thrombocytopenia) risk factors for sICH (17).

There are many scoring tools used to predict sICH post-tPA that have not been applied clinically for two reasons. First, the scores have only moderate predictability, and second, the variables that predict sICH are also associated with benefit from tPA. For instance, high NIHSS is a consistent predictor of sICH, but patients with high NIHSS also benefit from tPA. I think with the publications of these trials, we have evidence that both approaches are not considerably different in terms of outcome. There may indeed be subgroups that benefit more from one approach versus another which remains to be seen. But overall, the outcome appears similar. Therefore, we really should consider a direct approach in patients with multiple risk factors for sICH. For instance, in a patient with high NIHSS, a large clot burden from a tandem occlusion, on DAPT, hypertensive, and hyperglycemic. In a patient like this, do we want to risk a sICH with tPA administration?

Clinical Resolution: The patient presented at the start of this SGEM episode had minimal risk factors for sICH. Therefore, the decision is made to go ahead and offer treatment with tPA, while you wait for the endovascular team.

Clinical Application: It would be premature for a general application of a direct MT approach, and more data is required. Importantly, as was mentioned by the authors, these trials are only applicable to a mothership model of stroke care.

Intervention bias is recognized as an issue in medicine (Foy and Filippone Yale J Biol Med 2013). They defined this type of bias as "bias on the part of physicians and the medical community to intervene, whether it is with drugs, diagnostic tests, non-invasive procedures, or surgeries, when not intervening would be a reasonable alternative." It is too bad we don't have more high-quality evidence to guide whether we should be using tPA as a bridging therapy for MT. This is not an unusual problem in medicine. There is a lack of high-quality evidence to help inform our care in emergency medicine and often need to rely upon our good clinical judgment (Parish et al AEM 2021).

We need to be guided by evidence and need to be careful in rushing too quickly applying RCTs to clinical care, when as we have been discussing there are major limitations in these studies.

It can take over ten years for high-quality, clinically relevant information to reach the patients' bedside (Morris et al J RSM 2011). However, new practices can be adapted too quickly as we have seen with targeted temperature management (TTM) for out-of-hospital cardiac arrest (OHCA) or TXA for epistaxis.

Clinical Application: It is unlikely that there will be a general application of a direct MT approach to all cases of LVOs. This prediction is based upon the results of two European trials, MR CLEAN-NO IV (ISC 2020) and SWIFT-DIRECT (ESOC 2021), which were presented, both failed to show that a direct MT approach was non-inferior to the standard of care. Therefore, there are now three out of five trials that failed to demonstrate non-inferiority. All the European trials failed to show non-inferiority, which highlights the limitation we addressed about the external validity of the trials conducted in Asia.

The fact that multiple trials are failing to show non-inferiority suggests some subgroups may be benefiting from a bridging approach. There is one other study pending called DIRECT-SAFE. Ultimately, a patient level meta-analysis of all studies may address which patients benefit from a direct MT versus bridging approach, likely necessitating an individualized treatment strategy.

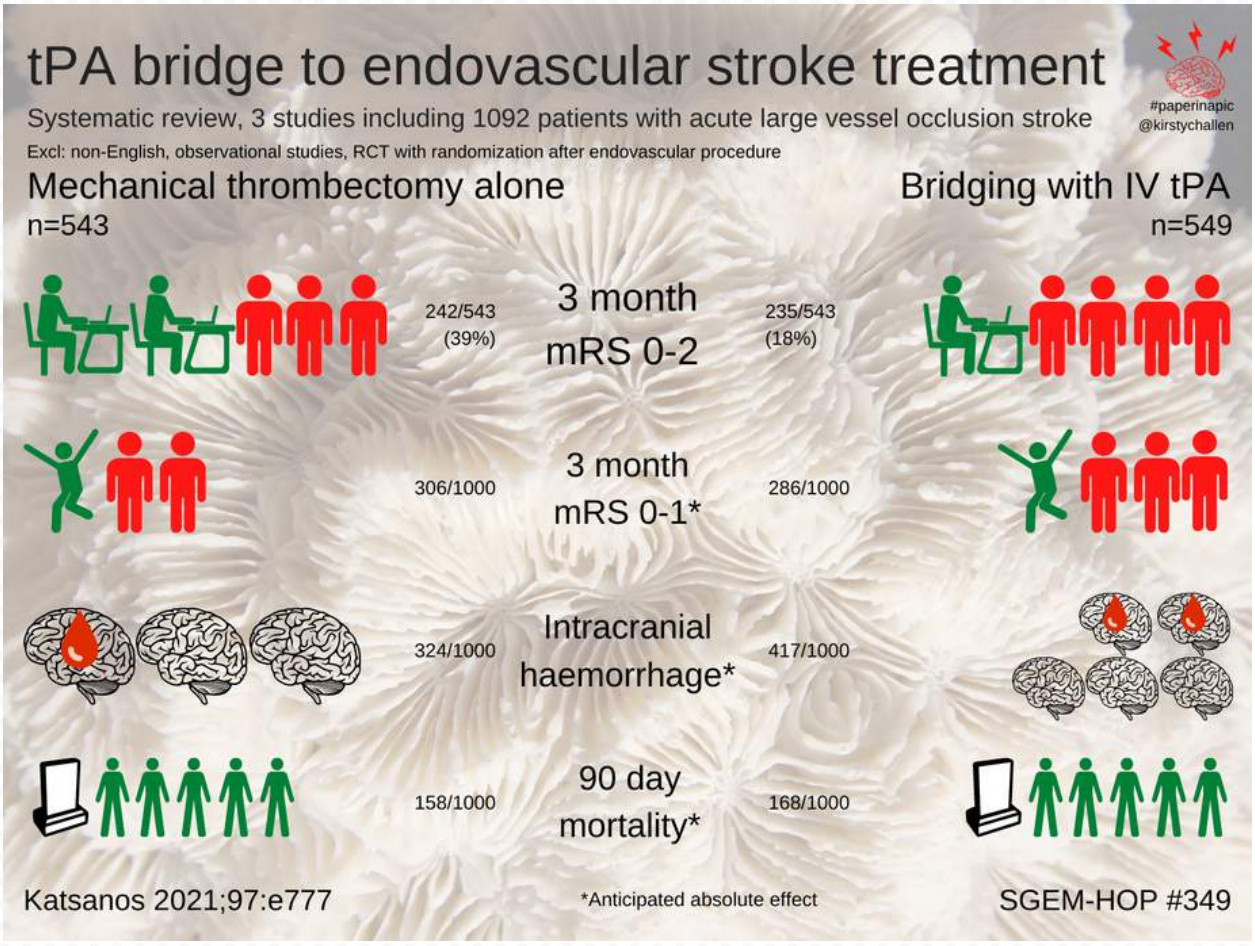
We will have to be skeptical of the SRMA and consider the quality of the included studies. Putting together several open label (non-blinded) trials may not get us any closer to the “truth” (best point estimate of an observed effect size).

Lastly, in the near future tenecteplase (TNK), which has greater fibrin selectivity, and the full dose is administered as a single bolus, may be adopted as the standard care. There is also suggestion that TNK may be more effective in lysing LVOs compared to tPA (18). In an RCT called EXTEND-TNK (2018) patients with LVOs prior to MT were randomized to either TNK or tPA. The primary outcome was vessel recanalization and secondary outcome was mRS. With an average time of thrombolytic administration of 42 min prior to MT, TNK was statistically associated with double the recanalization rate prior to MT (22% vs. 10%), and better clinical outcomes (18). If TNK does in fact replace tPA in the near future, the question will remain should we administer TNK prior to MT?

Clinical Application: We seem to be moving towards using TNK for acute ischemic stroke. The STEMI literature does not support TNK being superior to tPA for efficacy. The large ASSENT-2 trial (n=16,949) reported no difference in revascularization, equivalence for 30 mortality between TNK and tPA but less bleeding with TNK (19).

The previously mentioned EXTEND-IA TNK trial was a relatively small trial (n=202). The trial was partially funded by industry and multiple authors declared financial conflicts of interest. This does not make the data or conclusions wrong, but it should make us more skeptical. They had a composite primary outcome of reperfusion of greater than 50% of the involved ischemic territory or an absence of retrievable thrombus at the time of the initial angiographic assessment. Both are surrogate markers and not patient oriented outcomes. There were baseline differences between groups reported in their supplementary appendix (ex. atrial fibrillation, diabetes, and smoking). While the median score on ordinal analysis was statistically better with TNK none of the other three patient-oriented secondary outcomes were shown to be statistically different (early neurologic improvement, functional independence, or excellent outcome at 90 days).
is unlikely that there will be a general application of a direct MT approach to all cases of LVOs. This prediction is based upon the results of two European trials, MR CLEAN-NO IV (ISC 2020) and SWIFT-DIRECT (ESOC 2021), which were presented, both failed to show that a direct MT approach was non-inferior to the standard of care. Therefore, there are now three out of five trials that failed to demonstrate non-inferiority. All the European trials failed to show non-inferiority, which highlights the limitation we addressed about the external validity of the trials conducted in Asia.

What Do I Tell My Patient? Our patient is aphasic. If possible, a family member should be called to inform them that their loved one is having a stroke. Explaining that there is a blood clot in one of their vessels blocking blood from reaching part of their brain. This is causing them to have severe problems with language and weakness in their face and arm. There are two treatments currently available to treat his stroke. The first is a clot busting medication called tPA that has been shown to reduce risk of disability in three months, but there is also a risk of a serious complication of a brain bleed (2-7%) that could be life threatening. The second treatment is to give the clot busting drug and then try to retrieve the clot. The clot retrieval procedure where doctors put a tube inside a blood vessel in the leg. This is then threaded all the way up to the brain. The end of the tube has a special device to remove the clot. The usual practice is to give the combination therapy. The third option would be to go to directly try clot retrieval without using the clot busting drug. There is insufficient evidence to know what the best strategy is. What do you want to do?



Ken Milne MD
@TheSGEM

What treatment would you recommend for a patient with an acute large vessel occlusion stroke qualifying for mechanical thrombectomy (MT) presenting to your practice location?
thesgem.com/2021/11/sgem34... #EBM #FOAMed .
@4mmk36 .@First10EM .@broomedocs .
@KirstyChallen .@srrezaie

tPA alone	0.9%
tPA then MT	33.3%
Direct to MT	**45.8%**
It all depends	20%

330 votes · Final results

8:39 AM · Nov 9, 2021 · Twitter Web App

350

HOW DID I GET EPI ALONE? VASOPRESSIN AND METHYLPREDNISOLONE FOR IN-HOSPITAL CARDIAC ARRESTS

Clinical Question:

Does adding a combination of vasopressin and methylprednisolone increase the chance of achieving ROSC in cardiac arrest?

Bottom Line:

The routine use of vasopressin and steroids in addition to epinephrine cannot be recommended based on the available evidence in patients with in-hospital cardiac arrests.

Guest:

Dr. Neil Dasgupta is an emergency physician and ED intensivist from Long Island, NY, and currently an assistant clinical professor and Director of Emergency Critical Care at Nassau University Medical Center.

Case Overview:

A code blue is called for a 71-year-old male in-patient that is boarding in the emergency department (ED). He had been admitted the night before for a new diagnosis of rapid atrial fibrillation. He has a history of hypertension, dyslipidemia, and type-2 diabetes. His medications include a beta-blocker, statin, angiotensin converting enzyme inhibitor (ACE-I), metformin, ASA and direct oral anticoagulant (DOAC). You arrive and see that the Advanced Cardiac Life Support (ACLS) algorithm is being followed for adult cardiac arrest patients with pulseless electrical activity (PEA). Cardiopulmonary resuscitation (CPR) is in progress. The monitor shows a non-shockable rhythm. Epinephrine is provided and you quickly place an advanced airway. A second dose of epinephrine is given, and you start to think about reversible causes and your next steps for in-hospital cardiac arrests (IHCA).

Background:

We have looked an IHCA a couple of times on the SGEM. The first time we looked at this issue on (SGEM#50). This was also the first SGEM JC done where Dr. William Osler started the Journal Club initiative at McGill University.

We reviewed a randomized, double-blind, placebo-controlled, parallel-group trial done in three Greek tertiary hospitals. This trial (n=268) reported increased return of spontaneous circulation (ROSC) and increased survival to hospital discharge with good neurologic function with a vasopressin, steroids, and epinephrine (VSE) protocol compared to epinephrine alone. We felt this was interesting but would need to be validated/replicated before changing our IHCA protocols.

Background:

Corticosteroids have been suggested as a possible therapy in these cardiac arrest situations. A SRMA published in 2020 on the use of steroids after cardiac arrest reported an increase in ROSC and survival to discharge but was limited by the availability of adequately powered high-quality RCTs (Liu et al JIMR 2020).

We covered another SRMA that was published in 2021 looking at the same issue of whether the use of corticosteroids impact neurologic outcomes and mortality in patients with a cardiac arrest (SGEM#329)? These authors reported a statistical increase in good neurologic outcome and survival to hospital discharge with steroids but not survival at one year or longer. This study provided weak evidence in support of using corticosteroids for IHCA as part of a VSE protocol.

Answering clinical questions about cardiac arrest with clinical trials has always been fraught with difficulty. However, cardiac arrest is something we regularly treat in the emergency department, and we need more high-quality data to inform our care. Vasopressin had been included as a part of the American Heart Association (AHA) ACLS protocol for quite a while but was removed in favor of a vasopressor monotherapy strategy with epinephrine.

The tide now is shifting in resuscitation research to shift our focus from obtaining ROSC to measuring functionality and good neurologic outcomes. In the context of questioning epinephrine's role in ACLS after Paramedic2, we look at using the VSE protocol in cardiac arrest.

Reference: Andersen, et al: Effect of Vasopressin and Methylprednisolone vs Placebo on Return of Spontaneous Circulation in Patients With In-Hospital Cardiac Arrest. JAMA Sept 2021.

P

Population: Adult patients 18 years of age and older with an in-hospital cardiac arrest.

- **Excluded:** Out-of-hospital cardiac arrest (OHCA), valid do-not-resuscitate order, invasive mechanical circulatory support and known or suspected pregnancy at the time of the cardiac arrest.

I

Intervention: Vasopressin 20 IU and methylprednisolone 40 mg given as soon as possible after first dose of epinephrine, followed by vasopressin 20 IU after each epinephrine up to four doses.

C

Comparison: Placebo of normal saline

- **Primary Outcome:** ROSC defined as no further need of chest compressions for at least 20 minutes
- **Secondary Outcomes:** 30-day survival and 30-day survival with favorable neurologic outcome (defined as a Cerebral Performance Category of 1 or 2)
- **Trial Design:** Multicenter, single nation, multicenter, randomized, placebo-controlled, parallel group, double-blind, superiority trial

Authors' Conclusions

"Among patients with in-hospital cardiac arrest, administration of vasopressin and methylprednisolone, compared with placebo, significantly increased the likelihood of return of spontaneous circulation. However, there is uncertainty whether this treatment results in benefit or harm for long-term survival."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [x] 12. Was the study without any financial conflicts of interest.

Results

Key Results:

- They recruited and analyzed 501 patients with a mean age of 71 years, 64% were male and 2/3 were on a medical ward.

- **Primary Outcome:** ROSC
  - 42% intervention group vs 33% in control group. Absolute difference of 9.6% (95% CI, 1.1% to 18.0%). Risk ratio of 1.30 (95% CI, 1.03 to 1.63) p=0.03.

- **Secondary Outcomes:** No statistical difference between groups for both key secondary outcomes.
  - Survival at 30 days: 9.7% vs 12%. Absolute difference −2.0% (95% CI, −7.5% to 3.5%) with risk ratio, 0.83 (95% CI, 0.50-1.37); P = 0.48).
  - A favorable neurologic outcome at 30 days: 7.6% vs 7.6% with a risk ratio, 1.00 (95% CI, 0.55 to 1.83); P >0.99

Time to Talk Nerdy:

1. ED Patients: These are not ED patients, but they are often emergency physicians' responsibility. In many hospitals the only in-house physician at certain times is in the ED and will be responding to Code Blues. We need to be cautious not to over-interpret the data and directly apply it to patients who arrive in the ED and have an arrest. This data can help inform and guide our care, but it should not dictate our care.

These might be more like our patients than we think. Digging into the demographics of the included patients they seem like a surprisingly healthy cohort for IHCA. RRT (11% vs 8%), mechanical ventilation (8% vs 11%) and on pressor support (5% vs 9). Only 10% vs 7% of patients in the ICU, and 8% vs 14% in the ED. This may actually help us to better extract its applicability to the ED population and what gets brought in via EMS. It also may be a result of the inclusion/exclusion criteria set up.

2. Enrollment: This was surprisingly low. From 2,362 screened patients to 512 randomized, and 501 ultimately included for analysis. There were a lot of exclusions despite a liberal inclusion criteria and limited exclusion criteria. Large numbers of patients were excluded for not receiving epinephrine, ROSC prior to getting the drug, and a whole series of clinical team dependent factors (forgot about the study/early termination/physician preference/logistics). While the authors claim this did not have an impact on the outcome, it's hard to imagine it didn't have any impact on the included cohort or introduced some selection bias.

3. Patient-Oriented Outcome: The endpoint of ROSC is patient-centered, and a prerequisite for a good neurologic function. However, it is not a net benefit to save more people who have a poor quality of

life. This is what was demonstrated in the PARAMEDIC2 trial (SGEM#238). There was an increase in survivors with epinephrine for OHCA. Unfortunately, the increase was mainly for patients having severe neurologic impairment was more common among survivors in the epinephrine groups compared to the placebo group (31.0% vs. 17.8%).

4. Cerebral Performance Category (CPC) Score: Speaking of POO. The outcome measure for favorable neurologic outcome was the CPC score. Legend of EM, Dr. Ian Stiell from Ottawa published some data from the classic OPALS trail. They said that while the CPC can be an important outcome tool, it should not be considered a substitute for the Health Utilities Index (Annals EM 2009).

The inter and intra-rater reliability of the CPC score has also been questioned. A cohort study of patients with OHCA reported poor kappa values for classifying favorable vs unfavorable neurologic status at hospital discharge (Ajam et al Scan J Trauma Resusc Emerg Med 2001)

Another study looked about both OHCA and IHCA patients and the interrater reliability of the CPC score. They too found poor kappa values suggesting substantial variability in determining neurologic outcomes (Grossestreuer et al Resuscitation 2016). This could introduce some fuzziness around the CPC point estimate of effect size.

5. Time to Intervention: The time to administering the study drugs seemed to lag behind the administration of epinephrine. Mean time to epinephrine administration was five minutes for both groups, while study drug administration at eight vs nine minutes.

Time to Talk Nerdy:

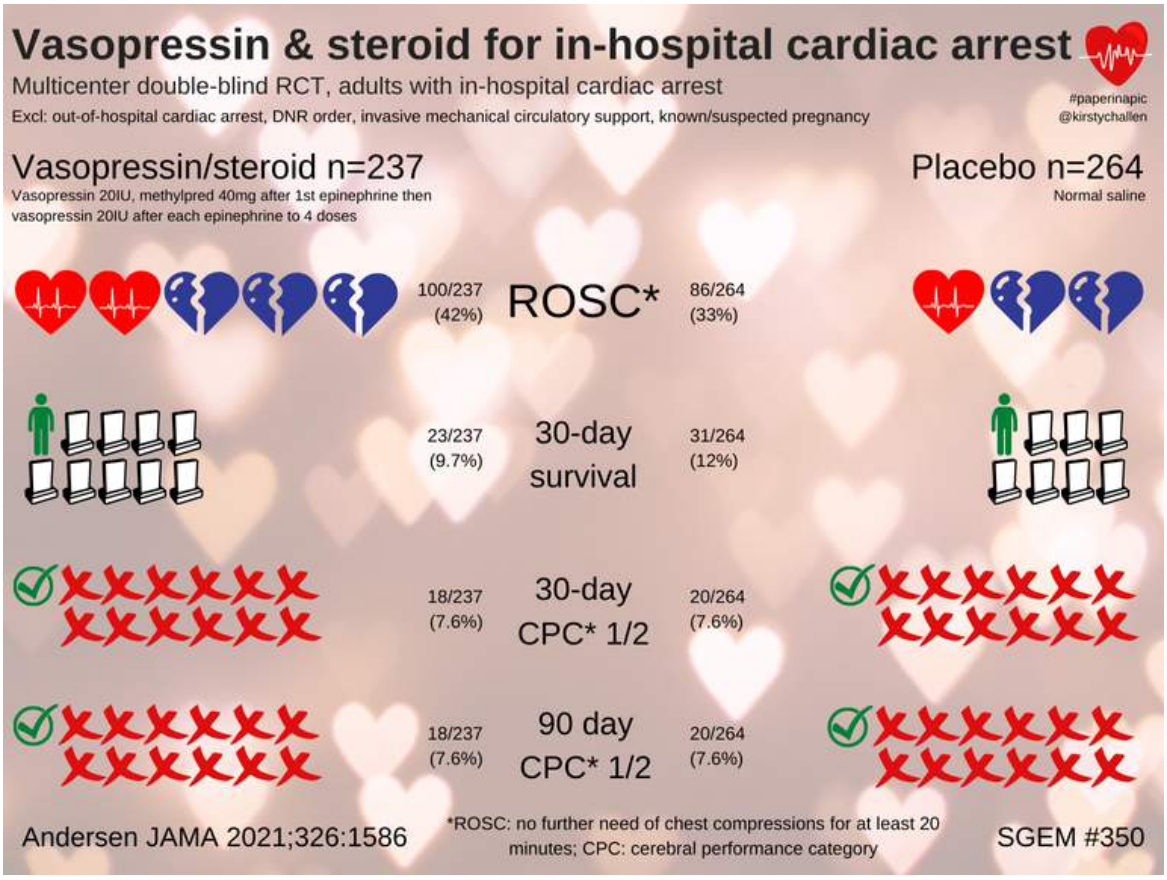
Based on the times presented in the paper and ACLS protocols, a subset patients may have received multiple doses of epinephrine prior to receiving the study combination. This is a clinically relevant difference between groups that is not accounted for, and may change our ability to measure a treatment effect.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: We still do not have high-quality, clinically relevant information to support the use of vasopressin, steroid, and epinephrine (VSE) protocol in patients with IHCA. That does not mean VSE should never be used and it will depend also on the clinicians' judgment. We are now left with a difficult choice, deciding on which drugs can help us resuscitate someone while preserving their quality of life, and more and more it seems these goals are at odds with each other.

What Do I Tell My Patient? Hopefully, you'll say "you probably don't remember me, and you might not believe me when I tell you this...but you had a cardiac arrest. It's very nice to be able to speak with you."

Case Resolution: Thinking about the causes of PEA arrest you obtain a stat glucometer reading and find out this man is hypoglycemic. An amp of D50 is given which aborts the arrest. Further blood work is obtained and reported showing he is also mildly acidotic and hyperkalemic. He is moved to a higher level of care in the hospital and the internist takes over his care to address his ongoing glucose, pH and electrolyte management.



Ken Milne MD @TheSG... · 1d

What treatment do you typically use for in-hospital cardiac arrests? @JAMA_current #EBM #FOAMed thesgem.com/2021/11/sgem35... @emcrit @stemlyns @ACEPNow @srrezaie

Epinephrine	**85%**
Epi + Vasopressin	7%
Epi + Vaso + Steroids	5%
Other (please specify)	3%

518 votes · Final results

5 8 11

351

HOW TO STOP GERIATRICS FROM FREE FALLIN'

Clinical Question:

In older patients presenting to ED with falls do risk stratification or fall prevention interventions influence patient-centered or operational outcomes?

Bottom Line:

Patients may (or may not) benefit from galls screening and interventions. There is inadequate evidence to support a specific tool or intervention across the board, but it is likely that multifactorial interventions are most effective.

Guest:

Dr. Kirsty Challen (@KirstyChallen) is a Consultant in Emergency Medicine and Emergency Medicine Research Lead at Lancashire Teaching Hospitals Trust (North West England). She is Chair of the Royal College of Emergency Medicine Women in Emergency Medicine group and involved with the RCEM Public Health and Informatics groups. Kirsty is also the creator of the wonderful infographics called #PaperinaPic.

Case Overview:

Mid-shift, you realise that the next patient you are about to see is the third in a row aged over 70 who has fallen at home, and that this is her third attendance for a fall in the last two months. You wonder if any emergency department (ED)-based interventions would help her and people like her be safe.

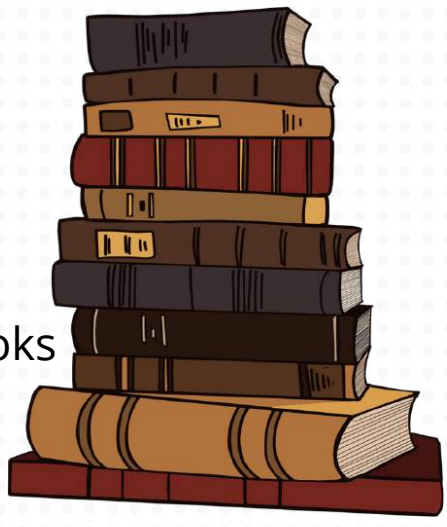
Background:

We looked at geriatric falls on an SGEM Xtra in 2015. Back then we found that at one academic site older adults attending ED with falls didn't receive guideline-based assessment, risk stratification or management.

In 2014 the SGEM looked at a systematic review by Dr. Chris Carpenter, which concluded that there wasn't a good tool to help us predict which ED patients are at risk of recurrent falls (SGEM #89).

Close to three million adults aged 65 and over visit American EDs annually after a fall [1]. Falling is the most common cause of traumatic injury resulting in older adults presenting to the ED [2]. Approximately 20% of falls result in injuries, and falls are the leading cause of traumatic mortality in this age group [3-5].

The SAEM Geriatric Emergency Medicine Task Force recognized fall prevention as a priority over 10 years ago. There is the Geriatric Emergency care Applied Research (GEAR) network, which is trying to improve the emergency care of older adults and those with dementia and other cognitive impairments. GEAR looks to identify research gaps in geriatric emergency care support research and evaluation of these areas.



Background:

GEAR 2.0 has recently been launched with funding opportunity in conjunction with EMF.

There are three other GEAR 1.0 manuscripts which have been published:

- Delirium Prevention, Detection, and Treatment in Emergency Medicine Settings AEM 2020
- Care Transitions and Social Needs AEM 2021
- Research Priorities for Elder Abuse Screening and Intervention J Elder Abuse Negl 2021

Reference: Hammouda et al. Moving the Needle on Fall Prevention: A Geriatric Emergency Care Applied Research (GEAR) Network Scoping Review and Consensus Statement. AEM November 2021

This publication presents two related but different scoping reviews so there are two PICOs.

PICO #1:

P

Population: Systematic search that found 32 studies of fall prevention interventions for patients aged 60 or over who presented to ED with a fall.

- **Exclusions:** Abstracts repeating data already included in full, not original research.

I

Intervention: Fall prevention interventions including multifactorial risk reduction, medication review, exercise training, models of care like Hospital-at-Home.

C

Comparison: Standard of Care.

Quality of care ED metrics, ED operational outcomes like length of stay, patient-centered outcomes like ED returns, further falls, fear of falling, functional decline, institutionalization.

PICO #2:

P

Population: Systematic search that found 17 studies of risk stratification and falls care plans in patients aged 60 or over in ED or pre-ED settings.

- **Exclusions:** As review 1.

I

Intervention: Risk stratification and falls care plan.

C

Comparison: No risk stratification and falls care plan.

O

ED referral (from pre-ED setting), quality of care ED metrics, ED operational outcomes, patient-centered outcomes.

This is an SGEMHOP episode which means we have the honour of having the lead author, Dr. Elizabeth (Liz) Goldberg, on the show. She is an Associate Professor of Emergency Medicine and Health Services, Policy and Practice at Brown University. Her specific areas of interest include improving care for older adults and public health interventions to enhance longevity and healthy aging.

Authors' Conclusions

"Harmonizing definitions, research methods, and outcomes is needed for direct comparison of studies. The need to identify ED-appropriate fall risk assessment tools and role of emergency medical services (EMS) personnel persists. Multifactorial interventions, especially involving exercise, are more efficacious in reducing recurrent falls, but more studies are needed to compare appropriate bundle combinations. GEAR prioritizes five research priorities: (1) EMS role in improving fall-related outcomes, (2) identifying optimal ED fall assessment tools, (3) clarifying patient-prioritized fall interventions and outcomes, (4) standardizing uniform fall ascertainment and measured outcomes, and (5) exploring ideal intervention components."

Quality Checklist for Scoping Systematic Reviews

- ☑ 1. Did they provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives?
- ☑ 2. Was a rationale for the review in the context of what is already known provided?
- ☑ 3. Was there an explicit statement of the questions and objectives being addressed with reference to their key elements?
- ☒ 4. Was their protocol pre-published and the study registered?
- ☑ 5. Characteristics of the sources of evidence used as eligibility criteria was specified?
- ☑ 6. All information sources in the search were described?
- ☑ 7. The presented the full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
- ☑ 8. The process for selecting sources of evidence (i.e., screening and eligibility) was included in the scoping review.
- ☑ 9. Methods of charting data from the included sources of evidence was described.
- ☑ 10. There was a list of all variables and definitions for which data were sought and any assumptions and simplifications made.

Quality Checklist for Scoping Systematic Review

- [x] 11. If done, a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate) was provided.
- [x] 12. The methods of handling and summarizing the data that were charted was described.
- [x] 13. Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.
- [x] 14. For each source of evidence, present characteristics for which data were charted and provide the citations.
- [x] 15. If done, present data on critical appraisal of included sources of evidence (see item 12).
- [x] 16. For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.
- [x] 17.The authors summarized and/or present the charting results as they relate to the review questions and objectives.
- [x] 18. The authors summarized the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.
- [x] 19. They discuseds the limitations of the scoping review process.
- [x] 20. The provided a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.
- [x] 21. The described sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.

Results

Key Results:

- 32 studies were included (3 meta-analyses and 23 RCTs) with a total of 571,071 patients to try to answer the first PICO question about falls prevention.

  Studies were from 11 countries, 1999-2019, with follow-up from 1 to 18 months. Interventions included falls risk assessment, physical rehabilitation sessions, preventive education, educational guidelines, follow-up with NP or PT, and alert devices. Most used recurrent falls as the outcome although anxiety over falls, functional ability and QALYs also featured.

- 17 studies were included (4 meta-analyses and 8 RCTs) with a total of at least 17,232 patients to address the second PICO question about risk stratification. Studies were from 9 countries, 2011-18, with follow-up from 6 to 12 months. 11 screening instruments were identified with interventions including educational, physical therapy, follow-up calls, discharge planning and home visits. Most used recurrent falls as the outcome.

1. EMS role in improving fall-related outcomes
2. Identifying optimal ED fall assessment tools
3. Clarifying patient-prioritized fall interventions and outcomes
4. Standardizing uniform fall ascertainment and measured outcomes
5. Exploring ideal intervention components

Time to Talk Nerdy:

We asked Liz five nerdy questions about her study. Listen to the SGEM podcast to hear her responses.

1. Question Selection: Your group original had three PICO questions (the third was about specific risk factors for falls e.g. polypharmacy). How and why did you decide to address the two that you did?

2. Consensus Conference: You held a consensus conference of your multidisciplinary group with the initial findings of the scoping review to generate and vote on research priorities. How do you manage an event like this to reduce the risk of one or two influential (or loud) people dominating discussions?

3. Disagreements: For your second PICO question, your reviewers disagreed with each other quite a lot about what should be included (Cohen's Kappa 0.12) – can you tell us a bit more about that and how you handled it?

4. Definitions: You talked in your discussion about how many definitions vary across research groups, even including what actually constitutes a "fall" – can you expand on that, and what do YOU consider to be a fall?

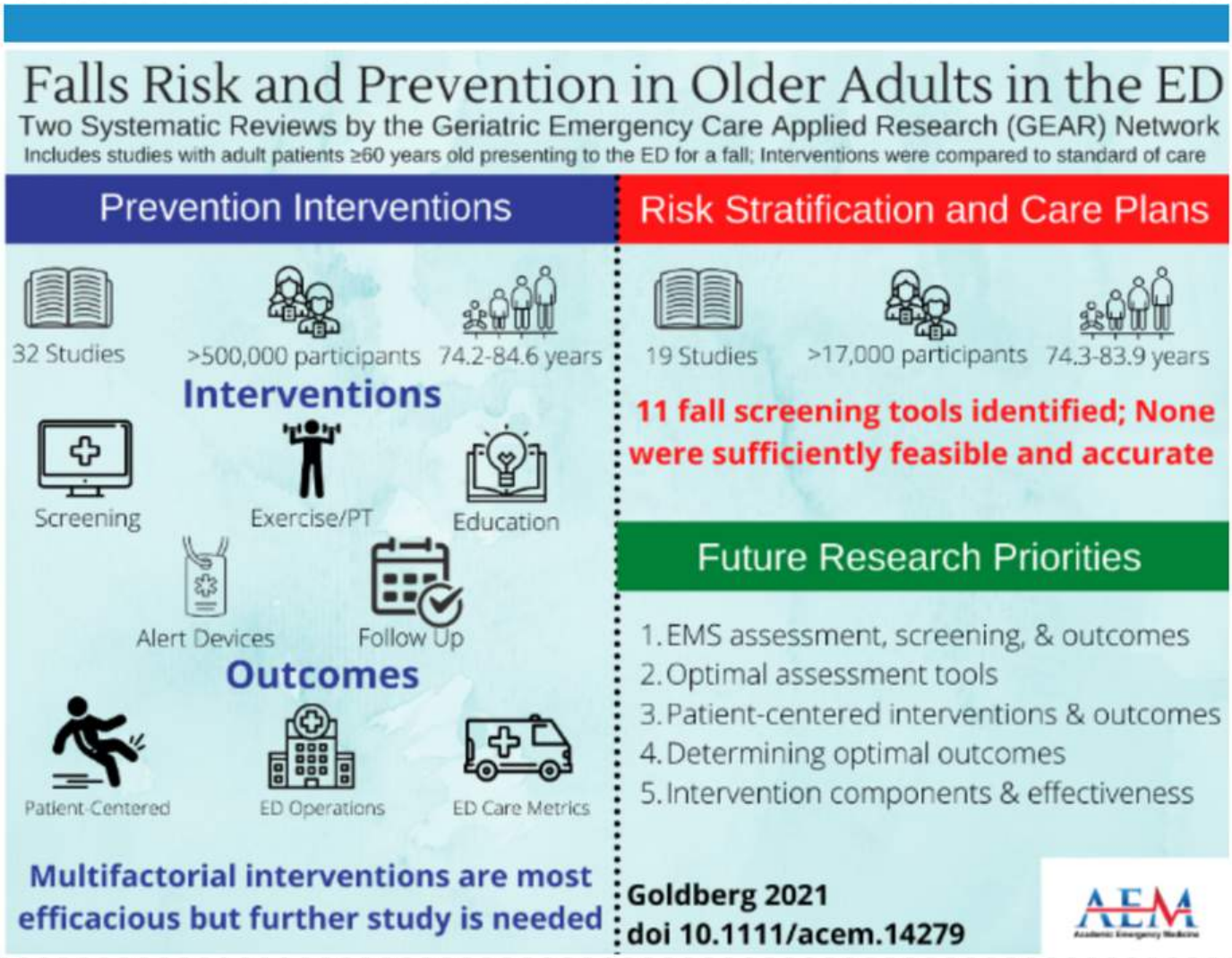
5. Patient Advocates: You had the review and the consensus recommendations reviewed and commented on by patient advocates before final write-up. What did the patient advocates change, and if you did it again would you include them earlier?

Comment on Authors' Conclusion Compared to SGEM Conclusion: The literature on falls in the older adult is difficult to synthesize due to differing definitions. There is plenty of room for good quality research on the identification of and interventions for older patients who fall.

Clinical Application: Many centers have falls screening or prevention program; encourage yours to get involved in the GEAR-Falls priority research areas (or the equivalent in your locality).

What Do I Tell My Patient? Previous falls are a predictor of future falls – we don't know the best way to support you to reduce this risk, but we think the most useful approach is looking at all those different factors that might contribute, so we have a team that can do this.

Case Resolution: You refer your patient to the Frailty outreach service, where she will undergo a comprehensive geriatric assessment.



@TheSGEM

Does your emergency department have a falls risk stratification protocol and/or falls prevention strategy? thesgem.com/2021/11/sgem35... #SGEMHOP @KirstyChallen @LizGoldbergMD @SAEMonline @AcademicEmerMed

No	35.6%
Yes	**47.7%**
I don't know?	16.8%

149 votes · Final results

352

AMENDMENT – ADDRESSING GENDER INEQUITIES IN ACADEMIC EMERGENCY MEDICINE

Clinical Question:

What can be done about gender inequty in Emergency Mediciine?

Bottom Line:

We acknowledge the significant gender inequities that currently exist in Emergency Medicinne, applaud the authors for their tremendous work, and hope that these efforts will eliminate gendeer inequities for the next generatiioni of doctors.

Guest:

Dr. Justin Morgenstern is an emergency physician and the creator of the #FOAMed project called First10EM.com

Case Overview:

At the completion of her 1-month elective in your rural emergency department (ED), you are discussing career plans with a medical student. She says that she is very interested in emergency medicine, but she isn't sure if it is the right choice for her. She has worked in five EDs so far, and a man has filled almost every leadership position. She also just got back from an emergency medicine conference, and more than 90% of the speakers were white males. She loves the clinical work in emergency medicine, but she is worried that these apparent gender inequities will limit her career opportunities.

Background:

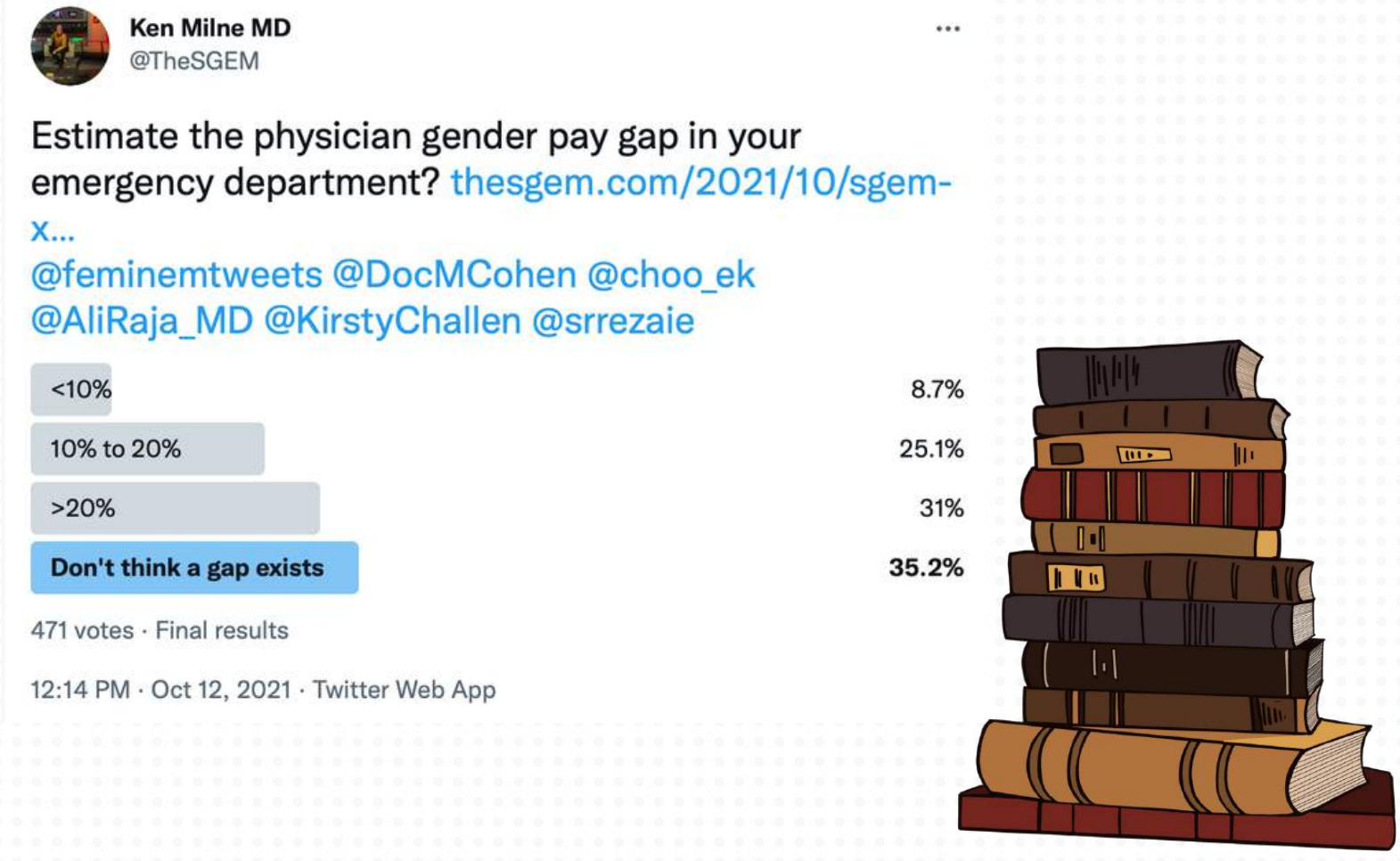
Gender equity is something we have spoken about often on the SGEM. Some listeners are happy we cover this topic while others have expressed concern. We recognize this can be an emotional issue. Our position is gender inequity exists in the house of medicine and it should be an issue everyone is interested in addressing. Here are some of the previous SGEM episodes that discussed gender equity:

- SGEM Xtra: From EBM to FBM – Gender Equity in the House of Medicine
- SGEM Xtra: Unbreak My Heart – Women and Cardiovascular Disease
- SGEM#248: She Works Hard for the Money – Time's Up in Healthcare
- SGEM Xtra: Money, Money, Money It's A Rich Man's World – In the House of Medicine
- SGEM Xtra: I'm in a FIX State of Mind

Background:

It is hard to believe some people deny the significant gender inequities that currently exist in medicine. Women are under-represented in leadership positions [1-3]. Women are less likely to be given senior academic promotions [4]. There are fewer women in editor positions in our academic journals [5]. Women receive less grant funding [6-7]. Women are paid less than men, even after accounting for potential confounders [2, 8-10].

Yet a recent twitter poll had more than 1/3 of respondents saying they did not think a physician gender pay gap existed in their emergency department. It is hard to move forward and address a problem when a significant portion of physicians do not even recognize that there is a problem.



Background:

The literature describes many factors that contribute to gender inequity. Institutional policies related to promotion or advancement may inherently disadvantage women and are likely exacerbated by implicit bias and stereotyping.

There are an insufficient number of women in current leadership positions, resulting in fewer mentors and role models for women earlier in their career. Policies around parental leave, emergency child-care, and breast-feeding support affect women disproportionately. Unfortunately, sexual harassment is also still widely documented in emergency medicine and has a major impact on career advancement and attrition [11-13].

The reasons for the gender gap are complex, and likely not completely understood. Existing gender balance within specialties, among other aspects of the "*hidden curriculum",* likely influence career decisions, with women trainees more likely to enter lower paying specialties. Current leadership positions are dominated by males, who may consciously or not be more supportive of other males for future promotions. Furthermore, there are numerous gender differences, both internal and external, that influence salary expectations and negotiations [14].

Female physicians are more likely to have female patients, and medical pay structures are often inherently biased. For example, in Ontario, where we both work, a biopsy of the penis pays almost 50% more than a biopsy of the vulva. Similarly, incision and drainage of a scrotal abscess pays twice as much as incision and drainage of a vulvar abscess [14].

Background:

There is data that suggests that practice patterns vary between women and men. Women in primary care are more likely to address multiple issues during a single appointment. They are more likely to provide emotional support and address psychosocial issues, and less likely to perform procedures. Although these are features most of us would want in a physician, unfortunately they result in lower remuneration in more medical payment models [14].

And of course, all of this occurs in the larger societal context in which women perform far more unpaid labour outside of medicine, resulting in much larger overall workloads, most of which is often overlooked. For a wonderful book on the topic, considering reading Invisible Women by Caroline Criado Perez.

Too often, women are blamed for the gender pay gap. It is true that women, on average, work fewer hours, and are more likely to work part time. However, this difference in work is not enough alone to explain the pay gap. For example, one study found that women earned 36% less than their male colleagues, despite only working three hours less per week [14].

It is also not true that women earn less because they are less efficient. Data from Ontario revealed that female surgeons earn 24% less per hour spent operating, despite completing procedures in the same amount of time as men. The difference seems to derive from women performing less lucrative procedures [15].

Background:

We clearly have a problem in medicine. There is no denying the current state of gender inequity. Solutions, while in some cases glaringly obvious, are probably rather complex. Solutions are unlikely to be “one size fits all”. The needs and desires of individual women will obviously be far more varied and far more complex than the “average woman”, and we should always be wary of unintended consequences when implementing social policy. However, those are not excuses. The data speaks for itself. More action is needed, and it is needed now.

The first step is to acknowledge the current problem widely and openly. This would be aided with transparent reporting on physicians’ payment, stratified by gender. It is worth noting that gender is not the only source of inequality in medicine, and this same data should be used to examine other factors such as race or disability.

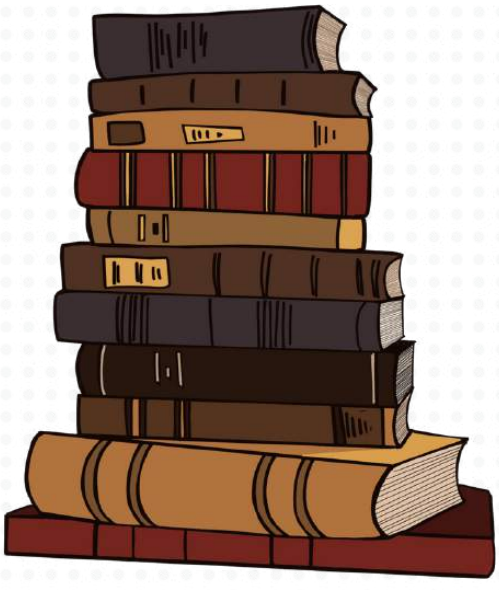
We need better training about bias in medicine, especially for those in leadership positions. We need to consider more egalitarian interview processes, where leadership are blinded to characteristics like gender or race. We need to consider the impacts of systemic discrimination and recognize that simply being fair in a single hiring decision is unlikely to be good enough, as it doesn’t account for the incredibly different paths that candidates took to reach the same point.

We need to fix the biased billing codes and referral patterns. We need better parental benefits, and systems to ensure career advancement can continue even when one is taking time to raise children.

Background:

So clearly there is a lot that needs to be done on this topic. But neither of us are experts on the topic, so I think we had better get into the meat of the episode and start talking to our guest who is an expert.

Reference: Lee et al. Addressing gender inequities: Creation of a multi-institutional consortium of women physicians in academic emergency medicine. AEM December 2021



There is no real PICO statement for this publication. We also normally do a quality check list to probe the publication for its validity. No such check list exists for this type of study seems to exist. it is still worth thinking critically about their methodology to consider the intrinsic and extrinsic validity of their discussion. When considering whether to develop a similar program, there are three major questions to consider:

1. **Does this program accomplish its intended goals?**
2. **Will the results here extrapolate to other settings?**
3. **What are the costs and alternative options?**

Methods: This article describes the creation of a multi-institutional consortium of women faculty in emergency medicine to promote career advancement and address issues of gender inequity. The consortium brought together female faculty from four hospitals associated with Harvard Medical School.

This is an SGEMHOP episode which means we have the lead author on the show, and we can hear about this program directly from the author. Dr. Lois Lee is a pediatric emergency medicine physician at Boston Children's Hospital and an Associate Professor of Pediatrics and Emergency Medicine at Harvard Medical School.

Neither Ken nor I have experienced these issues firsthand. Is there anything else you think is important to add to the background material we provided?

- *Thank you for continuing to highlight gender inequities in medicine and also for working to figure out some solutions to this complex problem. Although there are some things as an individual that can be done, many—if not most—of the solutions really need to be at the departmental leadership, institutional, and systemic level.*

What is the history behind this project and why did you think there was a need for this program?

- *Under our medical school there are five different institutions with separate emergency departments—four adult or general EDs and one pediatric specific. And it turns out over the last 5-10 years four of them had either formally or informally developed women faculty groups for career support. Then in 2018 several women from the different institutions came together and they formed the Harvard Medical School Women in EM Consortium. Although we all have academic affiliations under the same medical school, we otherwise had no formal connections through our EDs.*

Can you briefly describe the consortium and curriculum you developed?

- Site champions—at least two from each site
- Developed events based on informal needs assessment and literature reviews
- Developed systems for information sharing for important policy information among the hospitals
- Goals and priorities were developed using an interactive cycle: identify, learn, develop, and assess. This informed the activities we planned for the Consortium.

What was the conclusion from your paper?

- *“This consortium-building model could be used to enhance existing institutional career development structures for women and other physician communities in academic medicine with unique career advancement challenges.”*

- **Results:** In the 2020 academic year, you had a total of 80 female faculty (representing 37% of the total EM faculty) involved in this consortium. You ran multiple local career development events and organized a larger conference. Unfortunately, the COVID pandemic derailed in person events, but you managed to continue to host quarterly virtual events.

Can you tell us a little bit more about the challenges you faced during this process?

- **Challenges:**
  - Difficult to meet the individual needs of all participants across all career stages.
  - Scheduling is difficult in emergency medicine, with clinical responsibilities continuing 24 hours a day
  - Operating without a formal budget makes sustainability challenging.
  - Are there any key lessons you would pass along to other trying to replicate your success?
- **Advice**
  - For key domains: leadership, finances, communications, and curriculum development.
  - Formal leadership structure will improve sustainability and accountability.
  - A formal budget with ongoing funding is important for group sustainability.
  - Although smartphone texting groups allow for very easy group communication, suggest designating a specific communications director.

- Adopting a formal process for curriculum development based on a formal needs assessment of the faculty members, combined with the published literature, and setting a calendar of events to enhance attendance and relevance for group members.

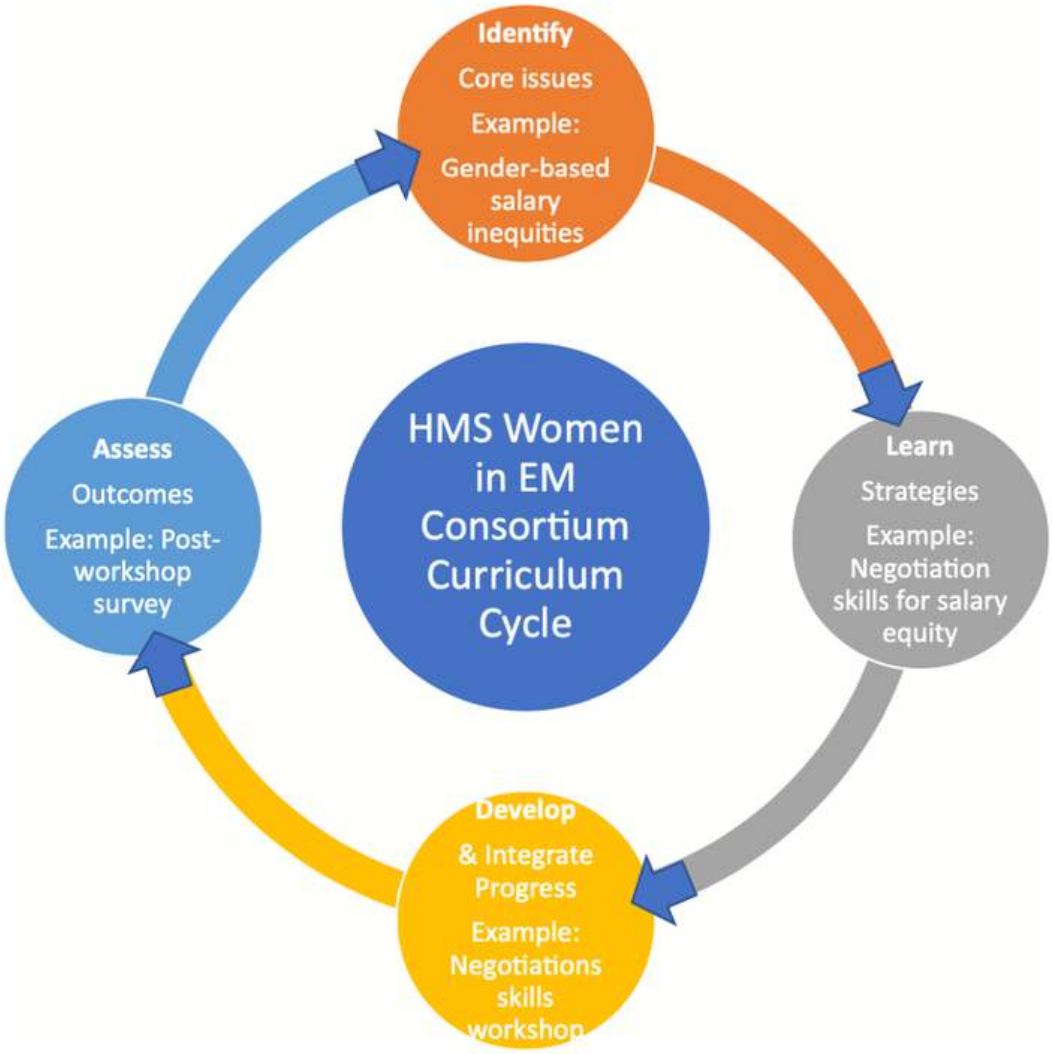


FIGURE 1 Consortium curriculum development model. An iterative cycle for the development, establishment, and curriculum planning for the Harvard Medical School Women in Emergency Medicine Consortium using the example of learning negotiations skills for salary equity; HMS (The Harvard Medical School)

Time to Talk Nerdy:

Part of the SGEMHOP critical appraisal process is to have at least five nerdy questions for the lead author. This helps us to better understand the publication.

1. Representativeness: We know that women are significantly under-represented in academic emergency medicine. This consortium brought together a group of women who hold academic positions at one of the most prestigious medical schools in the world. They are, by definition, outstanding. How well should we expect their experiences and solutions to extrapolate to women working in other settings?

- Although we are very fortunate to be working where we are, at the end of the day, working women have many—if not all—of the same challenges. How do you provide excellent clinical care, maintain or increase your academic productivity while caring for your family and loved ones—and yourself. From talking to women in academic medicine around the country, I think all of us have the same experiences. We all need support in academic productivity, networking and leadership skills as well as work-life integration. So I really do feel our solutions can be extrapolated to not only women in other settings—but other groups who may feel less empowered, including those who are Under-Represented in Medicine (UriM).

2. Trainees: This group chose to focus exclusively on faculty, rather than including trainees, for a variety of good reasons explained in the paper. I wonder how these lessons might translate to trainees, and perhaps more importantly, ways in which you think the needs to trainees might be different.

- Trainees have fewer academic demands and don't have the considerations for promotion and leadership, like faculty do.

- However, they also have much heavier clinical demands, which makes work life integration—already a challenge in EM—even greater. But they have different needs, including learning from role models, social supports, as well as learning career development and professionalism skills.

3. Differences Between Individual and Group Needs: In the paper, you mention that one challenge was meeting the professional and personal needs of all participating individuals. Even when groups have a very strong shared identify, that shared identity is likely always somewhat overwhelmed by the diversity of individuals who make up the group. I wonder if you can comment on the tension that might exist between a shared group identity and individual identities when approaching career advancement in medicine?

- Although our Consortium members are all in academic EM, each individual has their own career and goals. Some are much more clinically and less academically focused. Others are the opposite. So when the shared group identity is focused on career advancement, there may be some tension with those in primarily clinical careers. But we do our best to embrace the diversity of careers in the group the best way we can.

4. Best Future Approaches: You make it clear in the article that solutions to gender inequity need to come both from current leadership and from the women seeking academic promotion. I think we need to be pursuing every option to close this gender gap in emergency medicine, I wonder if you have insight into what approaches might offer the biggest return on investment for institutions just starting on this journey?

- *First, there must be intentionality. I think Academic Emergency Medicine has been successful in being intentional in increasing awareness about gender inequities in EM. Similarly, institutions must be intentional in their interviewing practices for trainees and faculty to increase diversity, in building pipeline programs to increase diversity in medicine in general, and in achieving transparency around salaries, promotion, and leadership development. If you don't even know there are inequities in your department, then you can't even begin to work on them.*
- *For example for academic promotions, departments should critically examine how they are doing with academic rank in their faculty based on career track and years as faculty. Then they should be intentional in working with the individual faculty to improve equity in academic ranking, including with mentorship and sponsorship and career development coaching.*

5. Translation Into Long Term Goals: This program appeared to be quite successful in the short term in generating engagement and developing career skills for female faculty. How successful do you think these early successes will be in generating the desired gender equity in emergency medicine in the long run?

- *We are asking ourselves the exact same question. So our leadership group is developing metrics for the Consortium so we can hopefully measure our successes in gender equity over time—although it may take a long time. But ultimately I think we will be successful. At the individual level we will providing useful skills and actionable changes. And as a Consortium we will work with our department leaders to continue to intentionally work on gender inequity issues related to salary, academic rank, and leadership. Then hopefully this will also contribute to other important issues like faculty retention and physician well being.*

Time to Talk Nerdy:

- *But ultimately the goal is not about promotion—but about providing optimal care for our patients. And working towards diversity in medicine—not just around gender—is essential for us to achieve that goal.*

Those were the five nerdy questions. Is there anything else you think the SGEM audience should know about your study and its limitations?

- *I do want to acknowledge the formation of our Consortium was an important first step. But one of major limitations was we didn't have a true formal governance structure at the beginning. Just a leadership group comprised of the site champions. So one of the important lessons learned is to develop a formal governance structure from the beginning. But we are changing that now—which will improve the ultimate sustainability and success of the group.*

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

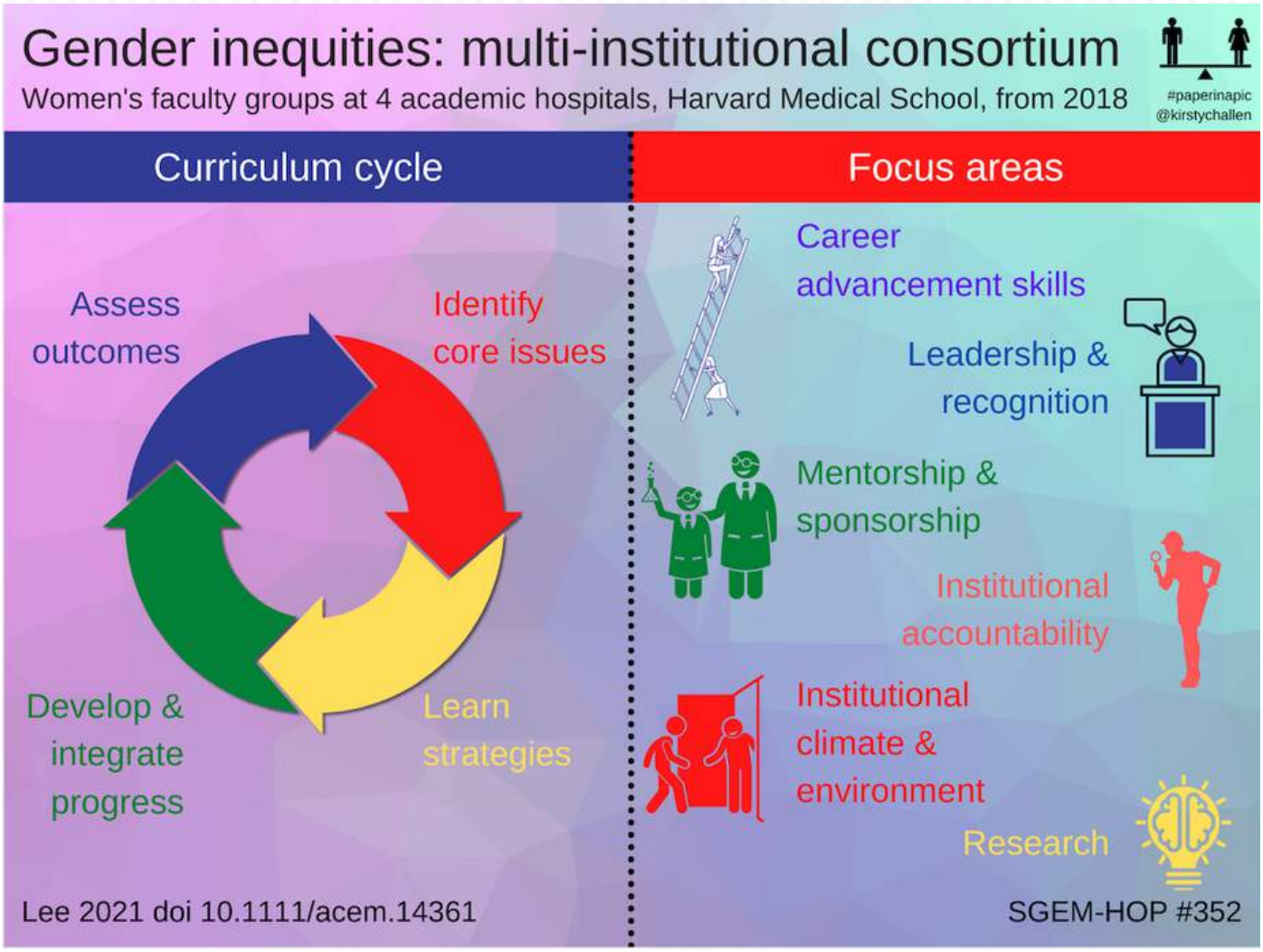
Clinical Application: This is an interesting publication to review and then consider if you could apply some of the ideas to your own workplace.

How do you think the SGEM listeners should apply this publication into their department/institution?

- Form a group! We literally give you a playbook on Table 4 on how to establish a career advancement consortium. And although we use women faculty as an example, this guideline can be used for any group with a shared background who is interested in career support and advancement. Or you can just start with data on faculty academic ranking and salaries to see where the inequities are. And then develop a plan to start addressing them.

What Do I Tell the Medical Student? Gender inequity exists in the house of medicine. There are many people trying to address this serious issue and implement solutions. While change is not happening quickly enough you should select the area of medicine that interests you the most.
What would you tell the medical student?

- Change will come slowly—but I feel it is coming. As the three of us know, emergency medicine is one of the most gratifying and also one of the most challenging jobs a person could have. So if that is where her passion lies, I wouldn't let gender inequity prevent her from pursuing it. Instead, I would challenge her to be a part of the solution. Only by increasing diversity in EM—including in the numbers of women—can we work towards gender equity and improved care of our patients.



What impact does talking about the gender disparities in medicine have on any stigma of gender inequities (G.I.) within medicine? #SGEMHOP @LoisLeeMD @First10EM @LWestafer @KirstyChallen thesgem.com/2021/12/sgem35...

No Impact on Stigma	14.7%
Increases Stigma	14.7%
Decreases Stigma	**64.7%**
G.I. Stigma Doesn't Exis	5.9%

353

AT THE COCA, COCA FOR OCHA

Clinical Question:

Does administration of Calcium during out-of-hosital cardiac arresst improve sustained return of sspontaneous circulation?

Bottom Line:

The routine use of calcium in an OHCA is not supported by the available evidence.

Guest:

Dr. Spencer Greaves is an Emergency Medicine resident at Florida Atlantic University. He received his Bachelors in Biomedical Engineering from Marquette University and his Masters in Public Health from Dartmouth College. Spencer completed his medical doctorate at the Medical College of Wisconsin. He and his wife live in Boynton Beach, FL where they recently celebrated the birth of their first child.

“WHILE I AM PROUD TO BE ATTENDING THIS INSTITUTION, MY OPINIONS EXPRESSED HERE ARE MINE ALONE AND DO NOT REPRESENT MY RESIDENCY PROGRAM, HOSPITALS I WORK AT, OR ANY OTHER AFFILIATED ORGANIZATIONS.”

Reference: Vallentin et al. Effect of Intravenous or Intraosseous Calcium vs Saline on Return of Spontaneous Circulation in Adults With Out-of-Hospital Cardiac Arrest – A Randomized Clinical Trial. JAMA 2021

This was an SGEM Journal Club and all the slides from the presentation can be downloaded using this LINK. As a reminder, here are the five rules for SGEM JC.

Rule	
1	You must talk/tweet about SGEM-JC
2	The evidence based medicine answer is: *“it all depends”*
3	Don’t Panic - Even your faculty is not sure of some of the answers
4	It’s all about the methods
5	Be skeptical of anything you learn, even if you heard it on SGEM-JC

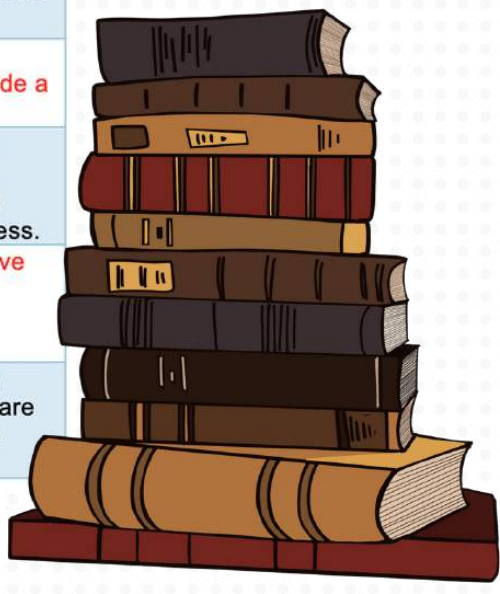
Case Overview:

An EMS crew arrives at the home of a 68-year-old suffering from a witnessed out-of-hospital cardiac arrest (OHCA). They have a history of hypertension, elevated cholesterol, and smoked cigarettes for 50+ years. Bystander CPR is being performed. The monitor is hooked up. The paramedics performed high-quality CPR and follow their ACLS protocol. Intraosseous access is quickly obtained, and a dose of epinephrine is provided. CPR is continued while a supraglottic airway is placed successfully. The patient is transported to the emergency department with vital signs absent (VSA).

Background:

We have covered adult OHCA multiple times on the SGEM. This has included the following issues:

Issue	Episode	Key Result	Bottom Line
BLS vs ACLS	SGEM#64	No statistical difference in survival to hospital discharge.	Addition of an ACLS algorithm to BLS management did not increase the survival to hospital discharge.
Mechanical CPR	SGEM#136	No superiority with mechanical chest compression devices	Mechanical chest compression devices do not appear superior to manual chest compression.
Targeted Temperature Management	SGEM#336	No statistical difference between hypothermia vs normothermia	TTM and TTM2 trials make it clear that hypothermia does not result in better outcomes
Amiodarone or Lidocaine	SGEM#162	No statistical difference compared to placebo	Neither lidocaine nor amiodarone is likely to provide a clinically important benefit.
IO vs IV Access	SGEM#231	Significantly fewer patients had a favourable neurologic outcome in the IO group vs the IV group	High-quality CPR and early defibrillation for shockable rhythms are more important than obtaining vascular access.
Epinephrine (PARAMEDIC 2 Trial)	SGEM#238	Survival was statistically higher in the epinephrine group vs placebo.	Use of epinephrine to improve survival with favorable neurologic outcome is not supported by the literature.
Supraglottic Airway	SGEM#247	Supraglottic airway was non-inferior to endotracheal intubation.	Key factors for survival with good neurological outcome are early defibrillation and high-quality CPR.



Background:

Calcium has a theoretical benefit on patients with cardiac arrest as it has inotropic and vasopressor effects. Previous small, randomized control trials (RCTs) have shown no superiority to calcium for return of spontaneous circulation (ROSC). However, the point estimated did favor calcium.

Reference: Vallentin et al. Effect of Intravenous or Intraosseous Calcium vs Saline on Return of Spontaneous Circulation in Adults With Out-of-Hospital Cardiac Arrest – A Randomized Clinical Trial. JAMA 2021

P

Population: Adults 18 years of age and older with OHCA in the central Denmark region from January 2020 to April 2021 who received at least one dose of epinephrine

- Exclusions: Traumatic cardiac arrest, known or strongly suspected pregnancy, prior enrollment in the trial, receipt of epinephrine outside the trial, or a clinical indication for calcium administration during the cardiac arrest.

I

Intervention: Calcium chloride 5 mmol given IV or IO immediately after first dose of ACLS epinephrine up to two doses

C

Comparison: Saline placebo given IV or IO immediately after first dose of ACLS epinephrine up to two doses

- **Primary Outcome:** Sustained ROSC defined as no further need for chest compressions for at least 20 minutes
- **Secondary Outcomes:** Survival, favorable neurological outcome, and quality of life assessment at 30 and 90 days
- **Trial:** Double-blind, placebo-controlled, parallel group, superiority, randomized clinical trial

Authors' Conclusions

"Among adults with out-of-hospital cardiac arrest, treatment with intravenous or intraosseous calcium compared with saline did not significantly improve sustained return of spontaneous circulation. These results do not support the administration of calcium during out-of-hospital cardiac arrest in adults."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [ ] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [x] 12. Financial conflicts of interest.

Results

Key Results:

- There were 1,221 OHCAs during the trial period. They excluded 824 for a variety of reasons with the most common reason (69%) because they did not receive any epinephrine. The mean age was 68 years, 71% male, more than 80% arrested at home, 85% received bystander CPR and half were in asystole.

- **Primary Outcome:** ROSC
  - 19% in the calcium group vs 27% in the saline group
  - Risk ratio (RR) 0.72 (95% CI; 0.49 to 1.03)
  - Risk Difference, −7.6% (95% CI; −16% to 0.8%); P = 0.09)
- **Secondary Outcomes:**
  - No statistically significant differences in 30-day survival, 30-day survival with a favorable neurological outcome or 90-day survival
  - Survival at 90-days with favorable neurological outcome was statistical better in the placebo group.
  - Quality of life assessment assessed by the patient was not statistically different at 30-days but was at 90-days favoring calcium

Time to Talk Nerdy:

1. Outcomes: It would be great if there was consistency in reporting outcomes. The trial was registered with ClinicalTrials.gov. Primary outcome was the same in the registration, protocol, and published manuscript. However, there was no quality-of-life assessment registered as an outcome, it was called a tertiary outcome in the protocol, categorized as a secondary outcome on the Table 2 of the manuscript and a tertiary outcome in the text of the manuscript. Same thing for the 90-day outcome which was not mentioned in the trial registry, was considered a tertiary outcome in the protocol but elevated to a secondary outcome in Table 2 and tertiary outcome in the body of the text.

2. External Validity: This trial was conducted in Denmark. They have a two-tiered EMS service that has an ambulance and a mobile emergency care unit with a physician. This is different from most places in north America that do not have physicians in the pre-hospital setting.

In addition, the latest statistics from the American Heart Association on cardiac arrests in the USA are different than the cohort included in this trial. The biggest difference was bystander CPR was 39% in the USA vs 85% in this Danish trial. These and other differences could limit the external validity to your own community.

	USA	Danish Trial
Mean Age	62 years old	68 years old
Sex	61% Male	71% Male
Location of Arrest	70% at Home	81% at Home
Witnessed	38%	51%
Bystander CPR	39%	85%
Initial Rhythm	50% Asystole	51% Asystole
Survival to Discharge	10%	7%
Survival Good Neuro	8%	6%

Time to Talk Nerdy:

3. Dose of Calcium: It is possible but not likely that a different dose of calcium may have made a difference. Proving a negative is harder than proving a positive. We start with a null hypothesis of no superiority. In this case, the null hypothesis is that calcium is not superior to placebo. The results did not support the alternative hypothesis of superiority, so we accept the null hypothesis. It would be a separate claim to say that calcium does not work for OHCAs. The more accurate statement would be there is no high-quality evidence to support the routine use of calcium in OHCAs.

4. OHCA: This data directly applies to OHCAs and not necessarily IHCA. There are longer times to drug administration in the pre-hospital setting. Time to drug administration was a median of 17 minutes. It could be hypothesized that early time to treatment could provide a patient-oriented outcome of benefit. However, that would need to be demonstrated.

5. Stopping Early: We have discussed the problem of stopping trials early before on the SGEM. It can introduce bias and increase uncertainty of the results. Stopping trials early over-estimates the effect size if there is a regression to the mean. Also, including trials that are stopped early can introduce bias into SRMA making them more difficult to interpret (Bassler et al JAMA 2010).

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

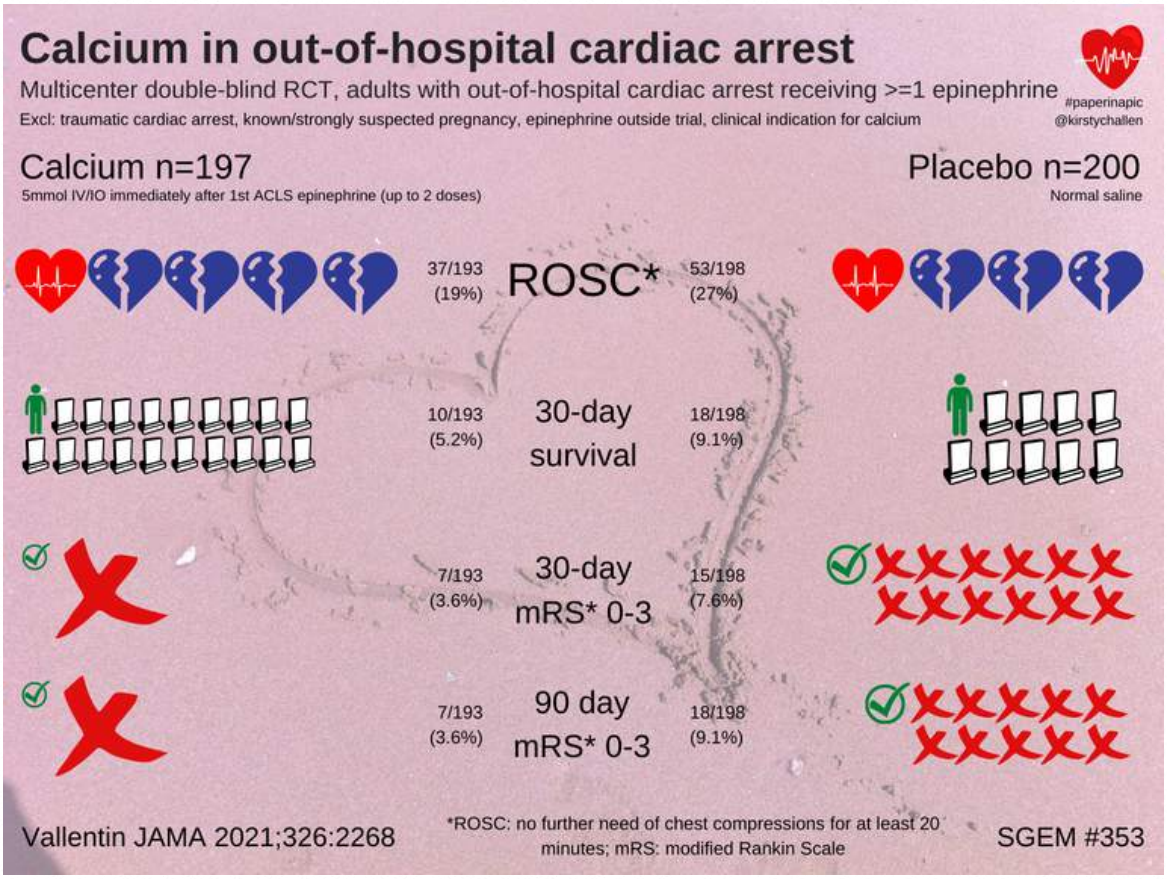
Clinical Application: We have not and will continue to not routinely give calcium to adult patients with OHCAs.

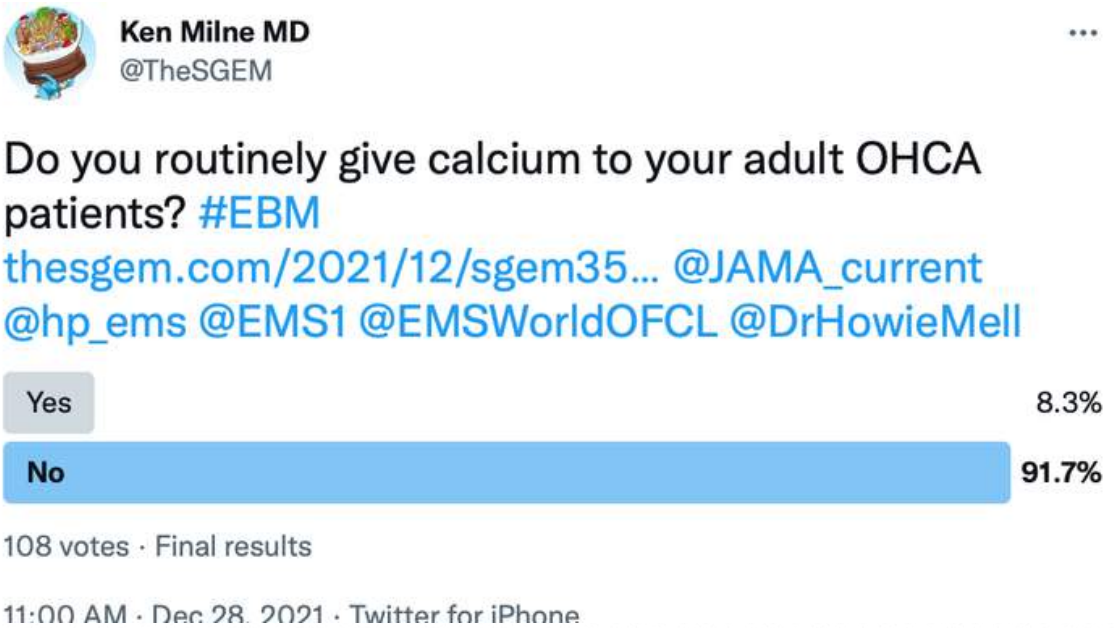
What Do I Tell My Patient? You tell the patients family that they had a cardiac arrest. The paramedics did great CPR, put in an airway to help breathing and gave epinephrine to try and restart the heart. Despite everyone's efforts we were not able to get their heart going again and they have died.

Case Resolution: Three rounds of epinephrine are eventually provided without ever achieving ROSC. ECG shows no electrical activity, pupils are fixed and dilated, and POCUS shows no cardiac activity. The patient is pronounced deceased in the ED.

Other FOAMed:

- First10EM: Calcium for OHCA – The COCA Trial
- The Bottom Line: COCA





354

EVERYBODY WALK THE DINOSAUR AND NOT TAKE THE MSU

Clinical Question:

Should mobile stroke units be purchassed and deployed in your community?

Bottom Line:

We still cannot recommend the use of MSU even with the addition of the best-MSU publication.

Guest:

Dr. Howard “Howie” Mell began his career as a firefighter / paramedic in Chicago. He became double board certified in Emergency Medicine (EM) and Emergency Medical Services (EMS). Howie also has a Master of Public Health.

Case Overview:

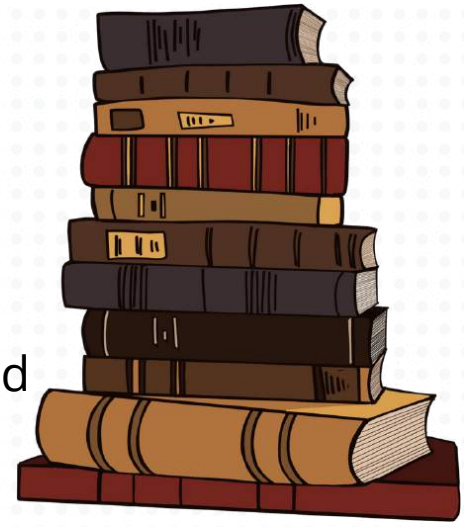
The Mayor of your community consults you as an expert in public health, EMS and as an EM physician on whether they should purchase a mobile stroke unit (MSU) ambulance.

Background:

No one who has listened to the SGEM will be surprised we are covering another paper looking at stroke. We have often discussed the use of thrombolysis for acute ischemic stroke (AIS) with or without endovascular therapy (EVT). However, the SGEM has also looked at secondary stroke prevention on previous episodes (SGEM#24, SGEM#303).

The SGEM has looked at pre-hospital stroke care using early administration of nitroglycerin by paramedics to see if it would improve neurologic outcome in patients with a presumed acute stroke (SGEM#269). The results from the RIGHT-2 trial reported no statistical difference in functional outcome as measured by the modified Rankin Scale (mRS) score at 90 days.

The SGEM bottom line was that very early application of transdermal nitroglycerin by paramedics in the pre-hospital setting cannot be recommended at this time in patients with a suspected stroke.



The issue of having a MSU has also been discussed on SGEM#330. A systematic review and meta-analysis which included seven randomized

Background:

controlled trials and four observational studies including 21,297 patients was critically appraised. The primary outcomes reported better neurologic outcome at seven days but not at one day post treatment by a MSU compared to conventional care (Fatima et al Int J Stroke 2020).

Reference: Grotta JC et al. Prospective, multicenter, controlled trial of mobile stroke units. NEJM 2021

P

Population: Patients calling EMS with a history and physical/neurological examination consistent with acute stroke who is last seen normal (LSN) possibly within 4 hours and 30 minutes and who had no definite tPA exclusions per guidelines, prior to CT scan or baseline labs. Daytime hours and mostly weekdays.

I

Intervention: Care by a mobile stroke unit (MSU)

C

Comparison: Care by traditional EMS referred to as standard management (SM)

- **Primary Outcome:** Score on the utility-weighted modified Rankin scale (uw-mRS) at 90 days in patients who were adjudicated to be eligible to receive tPA on the basis of subsequent blinded review

- **Secondary Outcomes:** There were twelve secondary endpoints in their final protocol listed in hierarchical sequence of importance

    - Agreement between on-board vascular neurologists (VN) and the remote VN
    - Exploratory cost-effectiveness analysis (CEA)
    - Outcomes comparing patients found eligible for tPA on MSU weeks compared to patients on SM weeks
        - Ordinal (shift) analysis of mRS at 90 days, and
        - Proportion of patients achieving 90 day mRS 0,1 vs 2-6
        - 30% improvement from baseline to 24hr NIHSS
    - Outcomes comparing all patients treated with tPA (whether or not adjudicated as tPA eligible) on MSU weeks compared to patients on SM weeks.
    - Uw-mRS at 90 days
        - Ordinal (shift) analysis of mRS at 90 days, and
        - Proportion of patients achieving 90 day mRS 0,1 vs 2-630%
        - Improvement from baseline to 24hr NIHSS
    - Outcomes of those treated within 60 min LSN compared to those treated from 61 to 270 minutes
        - Change in uw-mRS from baseline at 90 days
        - Ordinal shift analysis of MRS at 90 days

        - Proportion of patients achieving 90 day mRS 0,1 vs 2-6
        - 30% improvement from baseline to 24hr NIHSS
    - Outcomes all patients treated with IAT (separate analyses for those adjudicated as tPA eligible, all tPA treated, or all IAT with or without tPA) on MSU weeks compared to patients on SM weeks.
    - Uw-mRS at 90 days
        - Ordinal (shift) analysis of mRS at 90 days, and
        - Proportion of patients achieving 90 day mRS 0,1 vs 2-6
        - 30% improvement from baseline to 24hr NIHSS
    - The time from LSN to tPA treatment on all patients treated within 4.5 hours of LSN on MSU weeks compared to similarly eligible patients on SM weeks
    - Proportion of patients treated within 60 minutes of LSN on MSU weeks vs SM weeks.
    - The time from LSN and from ED arrival to start of endovascular procedure on MSU vs SM weeks
    - Proportion of all tPA-eligible patients having EVT on MSU vs SM weeks
    - The median/mean time from LSN to tPA therapy decision on all patients considered for treatment within 4.5 hours of LSN on MSU weeks compared to SM weeks
    - Time between 911 call and onset of etiology-specific BP management on MSU vs SM weeks.

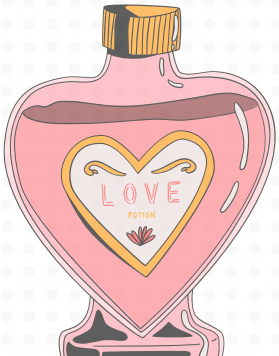
- **Safety Endpoints:**
  - Incidence of symptomatic intracranial hemorrhage (sICH) in enrolled tPA treated patients on MSU weeks compared to SM weeks. sICH was defined as any intracranial blood accumulation associated with a clinical deterioration of 4 points of the NIHSS for which the hemorrhage has been identified as the dominating cause of the neurologic deterioration)
  - Mortality up to one year
  - Incidence of stroke mimics and transient ischemic attacks (TIAs) in tPA treated patients on MSU weeks compared to SM weeks.
- **Trial:** Prospective cohort study with cluster randomized deployment weeks and blinded assessment of both trial entry and clinical outcomes. Cluster randomization can have both strengths and weaknesses just like any study design. For those less familiar with this methodology Taljaard and Grimshaw wrote a good article the topic in 2014.

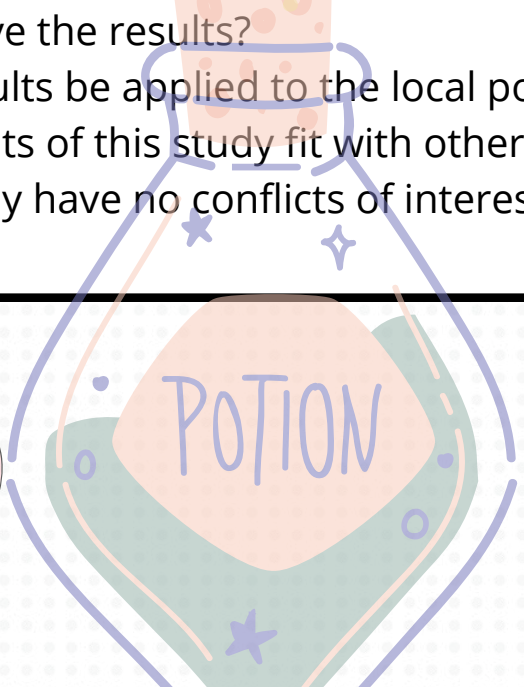
Authors' Conclusions

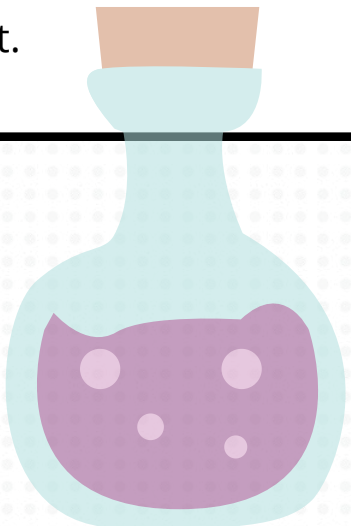
"In patients with acute stroke who were eligible for t-PA, utility-weighted disability outcomes at 90 days were better with MSUs than with EMS."

Quality Checklist for Observational Study

1. Did the study address a clearly focused issue?
2. Did the authors use an appropriate method to answer their question?
3. Was the cohort recruited in an acceptable way?
4. Was the exposure accurately measured to minimize bias?
5. Was the outcome accurately measured to minimize bias?
6. Have the authors identified all-important confounding factors?
7. Was the follow up of subjects complete enough?
8. How precise are the results? Fairly precise given the small sample size
9. Do you believe the results?
10. Can the results be applied to the local population?
11. Do the results of this study fit with other available evidence?
12. Did the study have no conflicts of interest.







Results

Key Results:

- This prospective observational study screened 10,443 patients and enrolled 1,515 patients (58.5% MSU vs 41.5% SM). Fourteen percent overall were not eligible for tPA due to intracranial blood seen on CT scan. Two-thirds in both groups (1,047 total) were decided post-hoc to be eligible for tPA. Of the tPA eligible patients, 97% in the MSU group received tPA compared to 79.5% in the SM group.
- This results section was a real struggle. It was unclear which primary and secondary outcomes we should highlight in the review. Should it be those published in the NEJM or do we discuss the original ClinicalTrials.gov outcomes, the current ClinicalTrials.gov outcomes or pre-specified published protocol outcomes (Yamal et al Int J Stroke 2018)?
- At the end of the day, we decided to provide the published primary outcome, mention the secondary outcomes and give a few of the safety outcomes.

- **Primary Outcome (NEJM):** Score on the uw-mRS at 90 days in patients who were adjudicated to be eligible to receive tPA on the basis of subsequent (post-hoc) blinded review
  - 0.72 in the MSU group and 0.66 in the SM group
  - Adjusted Odds Ratio (aOR) ≥0.91, 2.43 (95% CI, 1.75 to 3.36; P<0.001).
- **Secondary Outcomes:** Among the patients eligible for tPA, 55.0% in the MSU group and 44.4% in the SM group had a score of 0 or 1 on the mRS at 90 days. Among all enrolled patients, the mean score on the uw-mRS at discharge was 0.57 in the MSU group and 0.51 in the SM group (aOR for a score of ≥0.91, 1.82; 95% CI, 1.39 to 2.37; P<0.001). For more secondary outcomes see the NEJM publication.

Case Outcomes

- **Safety Endpoints:**
  - sICH in ~2% of patients who received tPA in each group and none of the patients considered to be stroke mimics.
  - Mortality at 90 days was 8.9% in the MSU group vs 11.9% SM group.

Table S5. Final diagnoses among tPA-eligible (blinded review) and all enrolled patients

	tPA-eligible		All enrolled	
N (%)	MSU (N=617)	EMS (N=430)	MSU (N=886)	EMS (N=629)
Definite stroke	420 (68.1)	311 (72.3)	594 (67.0)	457 (72.7)
Probable stroke	31 (5.0)	23 (5.3)	38 (4.3)	28 (4.5)
Stroke reversed by tPA	104 (16.9)	38 (8.8)	111 (12.5)	40 (6.4)
TIA	5 (0.8)	17 (4.0)	24 (2.7)	32 (5.1)
Stroke mimic	56 (9.1)	41 (9.5)	118 (13.3)	72 (11.4)
Missing	1 (0.2)	0 (0.0)	1 (0.1)	0 (0)

Time to Talk Nerdy:

1. Houston, We Have a Problem: They changed their protocol at least four times over the course of the study. These changes were described in the PDF of their protocol. Sometimes the changes were minor and other times they were major. You can also see how their primary outcomes changed on ClinicalTrials.gov, in their pre-published protocol and through to their published manuscript in the NEJM.

We were unable to find the any data in the manuscript or supplemental material on the other three “original” or “current” primary outcomes. This included the kappa value for the agreement between on scene vascular neurologist and remote vascular neurologist, cost effectiveness or the change in uw-mRS from baseline at 90 days. We have reached out to the lead author Dr. Grotta and will update the blog if this information becomes available.

UPDATE: The Cohen kappa was published by Wu et al in 2017 with a value of 0.73 which is considered moderate inter rater reliability according to McHugh 2012. This does not explain why this outcome was considered a primary outcome when the trial was registered in 2014 and in the update in August 2018 and then considered a secondary endpoint in the 2021 published manuscript supplementary protocol material dated 2015.

These multiple changes and selective reporting make me skeptical of the publication. This position is based upon studies by Chan et al JAMA 2004, Chan et al 2004 CMAJ, Dwan et al PLoS 2013, Hartung Annals Int Med 2014, and Chen et al JAMA Network Open 2019.

Here are the details of the changes to the primary outcome over time:

Time to Talk Nerdy:

- Original Primary Outcomes (2014 ClinicalTrials.gov):
  - Time LSN to tPA treatment
  - Agreement between on scene VN and remote VN
  - Cost effectiveness
- Current Primary Outcomes (2018 ClinicalTrials.gov):
  - Uw-mRS score change from baseline to 90 days
  - Agreement between on scene VN and remote VN
  - Cost effectiveness
- Published Protocol Co-Primary Outcome (2018):
  - Score on the uw-mRS at 90 days
  - Cost-effectiveness based on two measures
- Published Primary Outcome (NEJM 2021):
  - Score on the uw-mRS at 90 days
- Summary of protocol changes, Original protocol, Final protocol (2021)

2. Hours of Operation: The seven different sites operated daytime only and not on Sundays. Most patients came from Houston (77%) which operated from 8 am to 6 pm Monday through Saturday. These restricted hours and days of operation could have contributed to only 2.4 patients/week at the Houston site and 2.4 patients/month at the six other non-Houston sites. We will talk more about these low numbers in another nerdy point. However, it is unclear if these limited times and days can be extrapolated to evenings, nights, and Sundays.

It is also unclear if this data has external validity to a Canadian community setting beyond just the limited hours of operation.

Time to Talk Nerdy:

3. Secondary Outcomes: This refers to the first nerdy point. The secondary outcomes were also changed. The original 2014 protocol had just two secondary outcomes. This was updated to a total of six in 2016 on ClinicalTrials.gov. The published protocol with the manuscript lists twelve secondary outcomes plus three safety outcomes for a grand total of fifteen non-primary outcomes (NEJM 2021).

- Original Secondary Outcomes (2014 ClinicalTrials.gov): Two secondary outcomes
  - mRS at 90d 0,1 vs 2-6 of patients treated with tPA within 60min on either MSU or SM weeks, compared to similar patients treated 61 to 270min and
  - mRS 0,1 vs 2-6 at 90 days of all patients meeting published guidelines for treatment with tPA within 4.5 hours of symptom onset on MSU vs SM weeks, adjusting for any imbalances in stroke severity (baseline NIHSS) between the groups at the time of treatment.
- Current Secondary Outcomes (2016 ClinicalTrials.gov): Added four more secondary outcomes for a total of six
- Published Protocol Secondary Outcomes (2018): 90-day mRS; time metrics including LSN, alert, scene arrival and departure, tPA decision, tPA bolus, ED arrival, and start of IAT; healthcare utilization during the first year after the stroke; QoL. Safety outcomes include mortality and symptomatic hemorrhage.
- Published Secondary Outcomes (2021 NEJM): Lists twelve secondary outcomes plus three safety outcomes for a total of fifteen non-primary outcomes.

Secondary outcomes should usually be considered hypothesis generating. With all the changes made in the secondary outcomes it is hard to have much confidence in the results and their interpretations.

Time to Talk Nerdy:

4. Observer's Paradox or Hawthorne Effect: This study is the observer's paradox personified. It was impossible to blind the ED staff or patients to the use of an MSU to transport the patient. No outcomes were reported based on the treatment provided (e.g., tPA). The only variable reported on was treatment by the MSU or SM. This introduces a plethora of variables from the Hawthorne Effect to the attention paid to a prehospital report given by a specialist physician or specialty team to the one given by a standard EMS provider.

Compounding this is the fact that ~77% came from one city (Houston), with one EMS system as the control. Without some breakdown as to why the patients treated in the MSUs did better, these data are very difficult to generalize. It is interesting that outcome data was not reported by the type of therapeutics provided (i.e., IV tPA, clot retrieval +/- tPA, IA tPA, or medical management only).

5. Outcome Measure: This study outcome of uw-mRS may be a bit more confusing to some readers. Most of us are familiar with the mRS and even the ordinal shift analysis that is used in some stroke studies.

The uw-mRS translates the seven levels (0 to 6) of the mRS to values between 0 and 1. The distances between the levels reflecting patient and societal valuation of each disability state (Chaisinanunkul et al Stroke 2015). A higher score indicates a better outcome. This is in contrast to the mRS where a higher score indicating more disability.

The authors posit two advantages of using the uw-mRS over the dichotomized mRS and ordinal shift approach. Dichotomizing and ordinal outcome results in loss of information in contrast to the uw-mRS which provides a way to use all points in the scale in a more patient-oriented way.

Time to Talk Nerdy:

Ordinal analyses also assume that each change between ordinals has the same clinical impact. The uw-mRS adjusts each ordinal to be more patient-oriented.

To make things more complected, different studies will assign different weights to each level making it even harder to compare studies.

Table S1: Utility weights for the modified Rankin Scale

Modified Rankin Scale	BEST-MSU derived utility weights*	DAWN utility weights†
0	1	1
1	0.91	0.91
2	0.74	0.76
3	0.65	0.65
4	0.19	0.33
5	0.03	0
6	0	0

* The BEST-MSU weights were derived using a tobit model to convert EQ5D-5L to a United States-based utility

† Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA, Sila CA. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. New England Journal of Medicine. 2018 Jan 4;378(1):11-21.

6. Table S5: There is an amusing table included in the supplement (Table S5). Now what I find amusing here is that 16.9% of MSU treated patients had their strokes "reversed by tPA" whereas only 8.8% of EMS patients did, but somehow only 0.8% of the MSU patients had TIAs, whereas 4.0% of the SM patients did. It seems that in the post analysis, symptomatic patients seen on the MSU were cured by tPA, instead of the more likely explanation that they would've recovered regardless. The other thing this shows is that at least seven patients "ineligible" for tPA in the MSU group and two patients "ineligible" for tPA in the SM group received IV tPA (more on this below).

Table S5. Final diagnoses among tPA-eligible (blinded review) and all enrolled patients

	tPA-eligible		All enrolled	
N (%)	MSU (N=617)	EMS (N=430)	MSU (N=886)	EMS (N=629)
Definite stroke	420 (68.1)	311 (72.3)	594 (67.0)	457 (72.7)
Probable stroke	31 (5.0)	23 (5.3)	38 (4.3)	28 (4.5)
Stroke reversed by tPA	104 (16.9)	38 (8.8)	111 (12.5)	40 (6.4)
TIA	5 (0.8)	17 (4.0)	24 (2.7)	32 (5.1)
Stroke mimic	56 (9.1)	41 (9.5)	118 (13.3)	72 (11.4)
Missing	1 (0.2)	0 (0.0)	1 (0.1)	0 (0)

7. Protocol Violators: The authors report that 16.7% of those in the MSU group and 11.6% of those in the SM group were treated with tPA despite not being eligible for tPA. These are the numbers of patients being exposed to a treatment in the context of a prospective cluster cohort study that has potential harm (sICH). It would be likely the number of protocol violators outside a study would be larger and this would lead to more potential harm. This position is informed by the Cleveland area experience when tPA was first introduced (Katzan et al JAMA 2000). They had 50% of patients deviate from national treatment guidelines (protocol violations) with an in-hospital mortality rate three times higher than those who did not receive tPA (15% vs 5%).

8. Figure S3 Consort Diagram: This is an interesting figure that breaks down the 1,492 patients enrolled. Why were only 350 of the 430 (81.3%) *"tPA eligible"* patients in the SM arm given tPA or EVT direct when 599 of the 617 (97.1%) *"tPA eligible"* patients in the MSU arm were? While I do not accept that IV tPA represents the best treatment for these patients, it is certainly clear that the authors do. Given that, why the discrepancy? By the definitions of the protocol, these patients were within the timing window for administration, so why wasn't tPA given? This provides further evidence that the ED staff responded differently to the MSU than they did to a standard SM unit. Eliminating these differences should be the focus of this paper, not the expansion of MSUs.

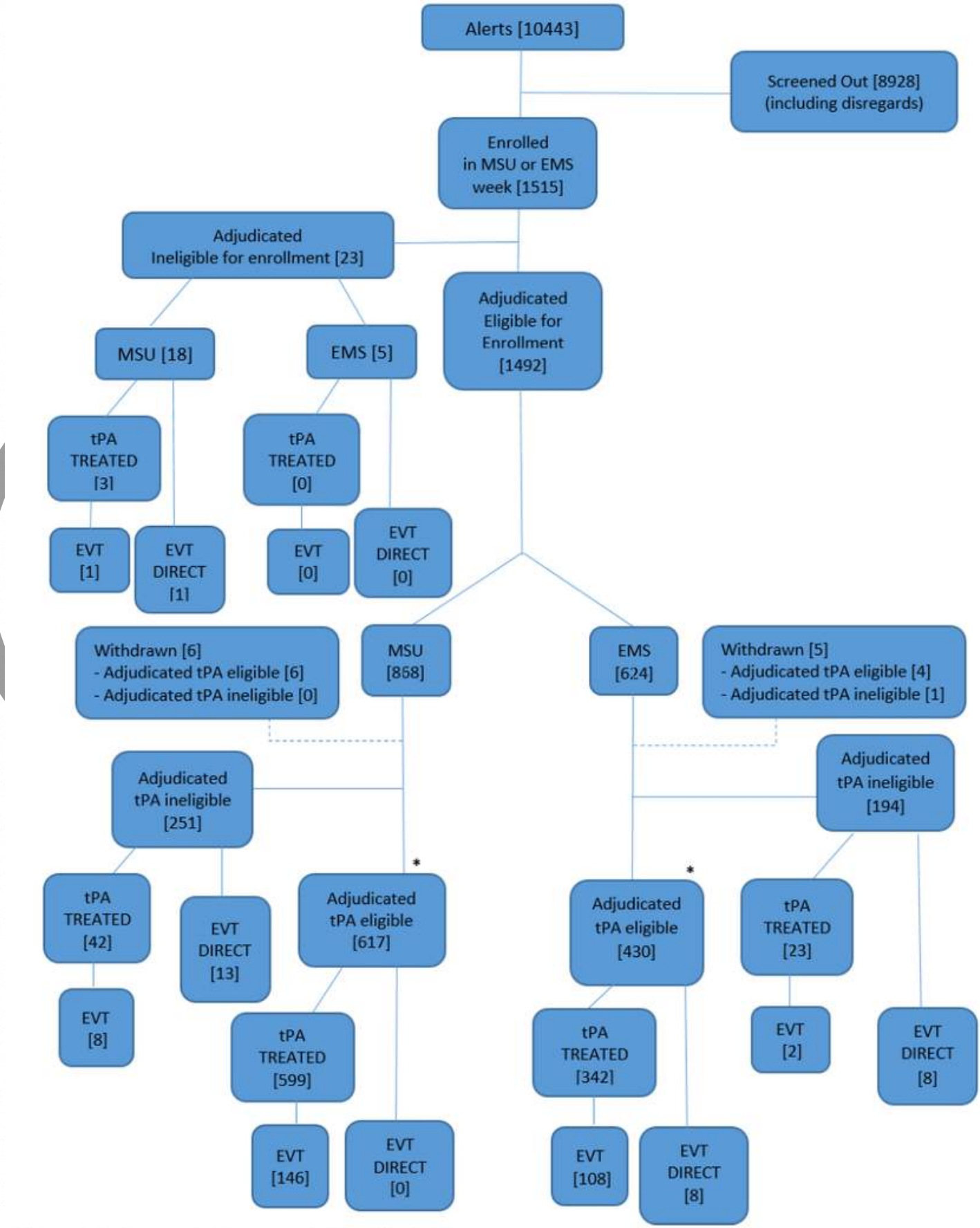


Figure S1. Consort diagram of all patients

Time to Talk Nerdy:

9. Change in uw-mRS Score: No data are provided regarding change in uw-mRS scores. This was one of their three *"primary"* outcomes listed in the trial registry in 2018 ClinicalTrials.gov. Yet according to their supplemental material published in 2021, they changed the primary outcome on April 18, 2018. The new version changed the primary outcome from a change in mean uw-mRS from pre-stroke to 90 days to mean uw-mRS at 90 days. This is confusing because they published their protocol in 2018 with a primary outcome of mean uw-mRS at 90 days. This changing back and forth of the primary outcome without publishing the results of the change in uw-mRS increases my level of skepticism.

One secondary outcome that they did report and relates to change in function is if there was a 30% reduction in NIHSS score from baseline to 24 hours. They observed such an improvement in 75.0% of the patients eligible for tPA in the MSU group and in 67.8% of those in the SM group (aOR, 1.45 [95% CI, 1.09 to 1.91] with inverse probability weighting and 1.45 [95% CI, 1.10 to 1.93] without inverse-probability weighting). These data are interesting for two reasons: They demonstrate that the data regarding change and degree of change were collected at least for NIHSS score at 24 hours, but nothing is reported on the change in uw-mRS at 90 days.
The other interesting aspect is the improvement at 24 hours in this prospective observational study contrasts with the NINDS RCT which did not report an improvement in NIHSS score at 24 hours. This suggests something is confounding the data and tPA is not responsible for the observed differences between groups in BEST-MSU.

10. Jurassic Park: There is a great line from the early scenes of the 1993 film Jurassic Park: "Your scientists were so preoccupied with whether they could, they didn't stop to think if they should." Any

conversation of mobile stroke units needs to include this issue in the discussion.

This study ran for five years to get 1,515 patients enrolled. That equals 303 patients per year that possibly could be aided by the intervention. Now let's look at some of the data.

In 90-day mortality, MSU was 3% better (NNT ~33). Improvement at 24 hours favored MSUs as well with 7.2% more MSU patients improving (NNT ~14). This is interesting because NINDS 1995 did not show a statistically significant benefit with tPA at 24 hours over placebo for their primary outcome using the NIHSS score. The SGEM did a structured critical appraisal of the NINDS trial on SGEM#70.

If we look at the difference in patients with an mRS < 2 at 90 days, the MSU patients do better by 7.2% again (NNT ~14). Now that means that if all 303 patients enrolled annually had received care in an MSU, 22 of them would have better outcomes for it. So far so good. But what is the population protected by the MSUs in this study?

Patients were enrolled from Houston (807), Colorado (100), Memphis (54), New York City (28), Los Angeles (23) Sutter Health in Burlingame, CA (22), and Indianapolis (13). So how many people, if they called 9-1-1 for a stroke during the study period would've been eligible to be enrolled? The answer is impossible to know but given the number of sites and the size of the respective cities, using a million people as a benchmark seems more than fair (as the actual number is likely three to five million). If we accept that a million people were protected by these units, and 22 patients would have had improved outcomes (which I'm only accepting for the sake of this argument), then one outcome was improved for every 45,455 persons in the population

protected per year.

Data I collected and reported at the 2020 Annual Meeting of the Society of Vascular and Interventional Neurology showed that in previous MSU studies with better defined populations, there was roughly one person treated for roughly every 12,000 – 14,000 persons protected (Berlin 1 per ~12,000 pop per year, Toledo 1 per ~14,000 pop per year, Cleveland 1 treated per ~14,000 pop per year). Those studies focused on tPA administration however, whereas BEST-MSU solely focused on the mere presence of the MSU. With a NNT in those studies of ~7 (if you accept their findings), one outcome was improved for every ~91,000 persons protected per year (which would fit the BEST-MSU data neatly if two million persons were protected by its participants).

Ok, but what does that mean? For the average US EMS agency, millions will have to be spent to improve one outcome a year. Even in high population cities, population density would require multiple MSUs, so again, millions would have to be spent to "save" one person. In most North American cities, putting two or three additional regular EMS units (which could be done for the cost of one MSU) would have much better outcomes in terms of overall population health. Can MSUs improve outcomes? Maybe (probably not). Is the juice worth the squeeze? Absolutely not.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We don't disagree with the authors' conclusion. We disagree with how that conclusion is interpreted in the paper. This paper doesn't prove that MSUs should be in wider use, it probably proves that the handoff of a suspected stroke patient between EMS and ED staff can be improved on, and this would likely improve patient outcomes.

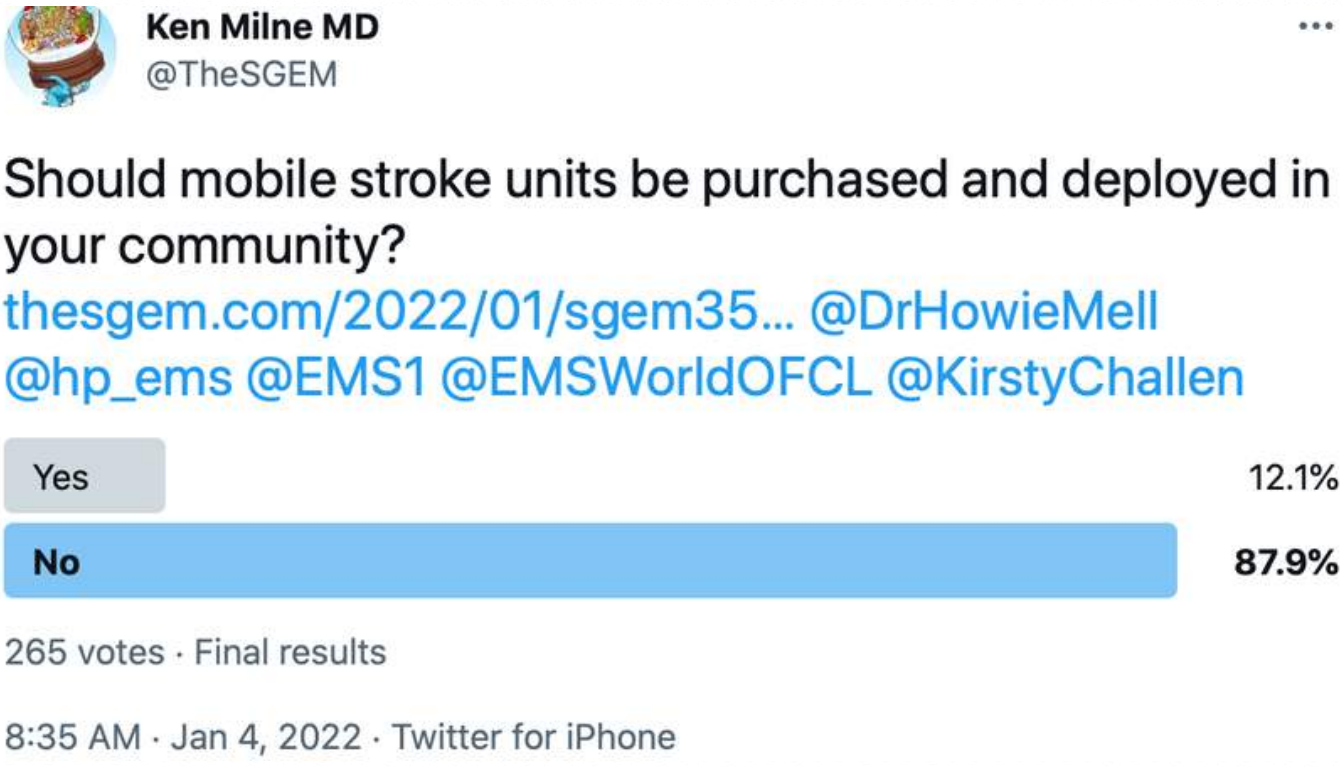
Clinical Application: We do not have high-quality evidence to support the use of MSUs and these initiatives should not be supported by EM or EMS physicians.

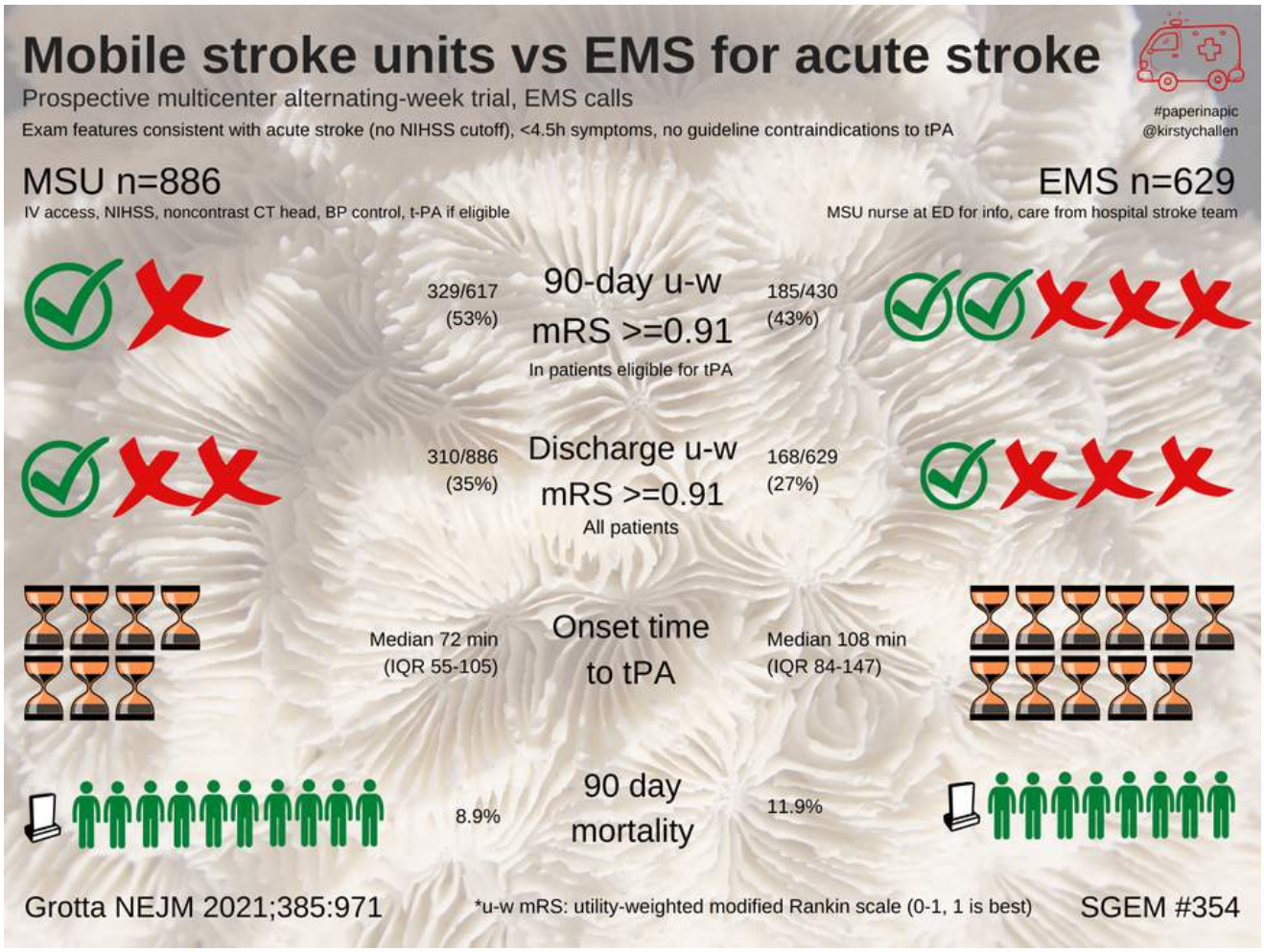
What Do I Tell the Mayor? I would tell a mayor, EMS chief, or health system that MSU's are an expensive boondoggle that won't change the health of the population they serve. I would point out that this study suggests that there may be issues with the handoff between EMS and the ED regarding suspected stroke patients that could be improved on to increase favorable outcomes.t their heart going again and they have died.

Case Resolution: You tell the mayor that given the choice of spending lots of money on one MSU ambulance vs. two to three regular ambulances you would advise the latter. This would not just improve response times for stroke patients but for all patients who call 911.

Other FOAMed:

- EM Ottawa
- POEM Research Summary





355

BIGGER ISN'T BETTER WHEN IT COMES TO CHEST TUBES

Clinical Question:

Are small (14Fr) pigtail catheters as effective as alrge (28-32 Fr) chest tubes for the treatment of hemoddynaically stable paatient with trauamatic hemothorax?

Bottom Line:

It is reasonable to offer a pigtail catheter instead of a large bore chest tube for the evacuation of a traumatic hemothorax in a hemodynamically stable patient

Guest:

Dr. Chris Root is a second-year resident physician in the Department of Emergency Medicine at the University of New Mexico Health Sciences Center in Albuquerque, NM. He is also a resident flight physician with UNM's aeromedical service, UNM Lifeguard. Prior to earning his MD, he worked as a paramedic in the New York City 911 system.

Case Overview:

A 43-year-old male presents to your emergency department (ED) the day after being involved in an all-terrain vehicle (ATV) accident. He reports he was riding his ATV along an embankment when it rolled, landing on top of him briefly. He did not seek medical attention at the time of the incident, but he has had persistent chest wall pain and worsening shortness of breath since yesterday evening. He is hemodynamically stable, oxygen saturation is 91% on room air, physical exam reveals ecchymosis and tenderness over the right chest wall with diminished right sided lung sounds. CT scans reveal multiple right sided rib fractures and a hemothorax estimated to measure 500cc with no additional injuries.

Background:

We have discussed chest tubes a couple of times on the SGEM. This is usually with the master himself, Dr. Richard (Thoracic Rick) Malthaner. The first time was looking at a study about where to put the chest tube in a trauma patient. It turns out location (high or low) does not matter. The most important thing is placing the chest tube in the triangle of safety in the plural space (SGEM#129).

The other episode on chest tubes looked at conservative vs interventional treatment for spontaneous pneumothorax (SGEM#300). This randomized controlled trial demonstrated that conservative management was non-inferior to placing a chest tube in a patient with a large first-time spontaneous pneumothorax.

Background:

Another SGEM episode we did looked at the location of needle decompression for tension pneumothorax (SGEM#339). This was done with our good friend and frequent guest skeptic Dr. Robert Edmonds. This observational study did not support the claim that the second intercostal space-midclavicular line is thicker than the fourth/fifth intercostal space-anterior axillary line.

This new SGEM episode looks at the size of chest tubes needed to successfully treat a traumatic hemothorax. Traditionally, these are treated by inserting a large bore chest tube (LBCT). There is increasing evidence supporting the use of smaller, percutaneously inserted chest tubes or pigtail catheter (PC) for the drainage of pleural effusions and pneumothoraces as well as some evidence of their efficacy for hemothorax.

Reference: Kulvatunyou et al. The small (14 Fr) percutaneous catheter (P-CAT) versus large (28–32 Fr) open chest tube for traumatic hemothorax: A multicenter randomized clinical trial. J Trauma and Acute Care Surgery. November 2021.

P

Population: Hemodynamically stable adult patients 18 years or older suffering traumatic hemothorax or hemopneumothorax requiring drainage at the discretion of the treating physician.

- E**xclusions:** Emergent indication, hemodynamic instability, patient refuses to participate, prisoner or pregnancy

I

Intervention: Placement of small (14 fr PC) chest tube using a percutaneous seldinger technique

C

Comparison: Placement of a large (28-32 fr LBCT) chest tube using a traditional surgical thoracostomy

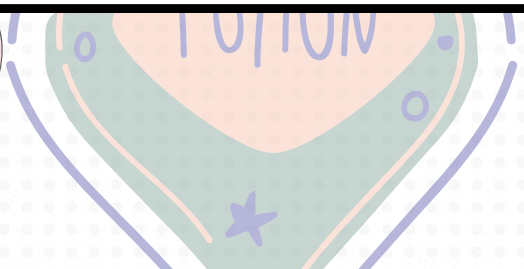
- **Primary Outcome:** Failure rate defined as radiographically apparent hemothorax after tube placement requiring an additional intervention such as second tube placement, thrombolysis or video-assisted thorascopic surgery
- **Secondary Outcomes:** Insertion complication rate; drainage output (30 minutes, 24-hour, 48-hour, and 72-hour); hospital course outcome up to 30 days (total tube days, ICU LOS, hospital LOS, and ventilator days); and insertion perception experience (IPE) score (1-5 score subjective score,1 – it was okay to 5 – it was the worst experience of my life).
- **Trial:** Multicenter, non-inferior, unblinded, randomized, parallel assignment comparison trial

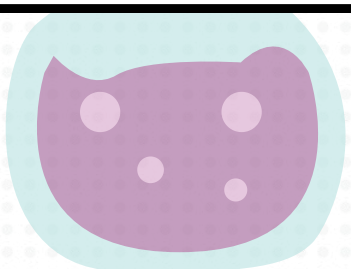
Authors' Conclusions

"Small caliber 14-Fr PCs are equally as effective as 28- to 32-Fr chest tubes in their ability to drain traumatic HTX with no difference in complications. Patients reported better IPE scores with PCs over chest tubes, suggesting that PCs are better tolerated."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [?] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [?] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [x] 12. Financial conflicts of interest.





Results

Key Results:

- There were 222 eligible patients identified over five years. The final cohort consisted of 119 patients (56 PC and 63 LBCT). The mean age was 55 years, 82% were male, 81% blunt trauma and median time to tube placement was 1 to 2 days from injury.

- **Primary Outcome:** Failure rate between PC and LBCT for the drainage of traumatic hemothorax 11% vs 13% (p=0.74).
- **Secondary Outcomes:** There were two insertion-related complications one from each group (bleeding from PC necessitated a thoracotomy and extra pleural position from chest tube placement required another tube placement). There were two deaths, one from each group (PC group had a PE on postinjury day 10 and the tube had already been removed and chest tube group had a nontrauma-related death at an outside institution). No statistical difference between PC and LBCT in terms of drainage tube output except at 30 minutes. No statistical difference in hospital course (tube days, ICU LOS, total hospital LOS or ventilatory days). Patients reported better IPE scores in the PC group compared to the LBCT group.

TABLE 3 Comparison of Outcomes Full Size Table

	Pigtail Catheters (n = 56)	Chest Tubes (n = 63)	p
Failure rate, n (%)	7 (11)	8 (13)	0.74
Initial output, median (IQR), mL	600 (375–1,037)	400 (250–650)	0.005
24 h	930 (600–1,350)	685 (450–1,000)	0.05
48 h	150 (60–310)	180 (80–300)	0.77
72 h	45 (0–200)	130 (0–272)	0.28
Tube days, median (IQR), d	4 (3–6)	5 (3–7)	0.31
IPE score, median (IQR)	1 (1–2)	3 (2–5)	<0.001
VATS, %	7	5	0.58
Ventilator day, median (IQR)	0 (0–2)	0 (0–0)	0.13
ICU day, median (IQR)	2.5 (0–3.5)	2 (0–4)	0.28
Hospital length of stay, median (IQR), d	8.5 (5.5–15)	8 (5–12)	0.30

ICU, intensive care unit; VATS, video-assisted thoracoscopy.

Time to Talk Nerdy:

1. Selection Bias: There was no explicit statement that patients were consecutively recruited into the trial. They identified 222 eligible patients over five years. There were 102 excluded with 27 for "MD preference".This means 27/102 (26%) of exclusions were for a subjective reason. This could have introduced some selection bias into the trial.

2. Exclusion of Hemodynamically Unstable Patients: Hemodynamically unstable trauma patients were excluded from study enrollment. Open thoracostomy and the placement of a LBCT is still considered by many to be the primary treatment for the evacuation of hemothorax in the hemodynamcailly unstable trauma patient. The authors did not seek to deviate from that idea in this study. However, they do allude to anecdotal experience placing PCs in hemodynamically unstable patients, and the output from PCs in the first hour was greater than that from LBCT in their trial, but further studies are needed to investigate the utility of PCs in hemodynamically unstable trauma patients. The exclusion of hemodynamically unstable patients could also explain the lower than anticipated failure rate which will be discussed later.

3. Patient Oriented Outcome: Tube failure rate is a simple, dichotomous, and clinically important primary outcome. However, the IPE score is a critical patient-oriented outcome (POO) that should be considered when managing these patients. The lead author, Dr. Kulvatanyou, alludes to having had friends and family members who have undergone LBCT placement express how horrible it was. Although the IPE scale developed by the investigators was not externally validated it is a straightforward and effective means of comparing the subjective experience of patients receiving either intervention. If you had a traumatic hemothorax, would you like the

big tube or the small tube?

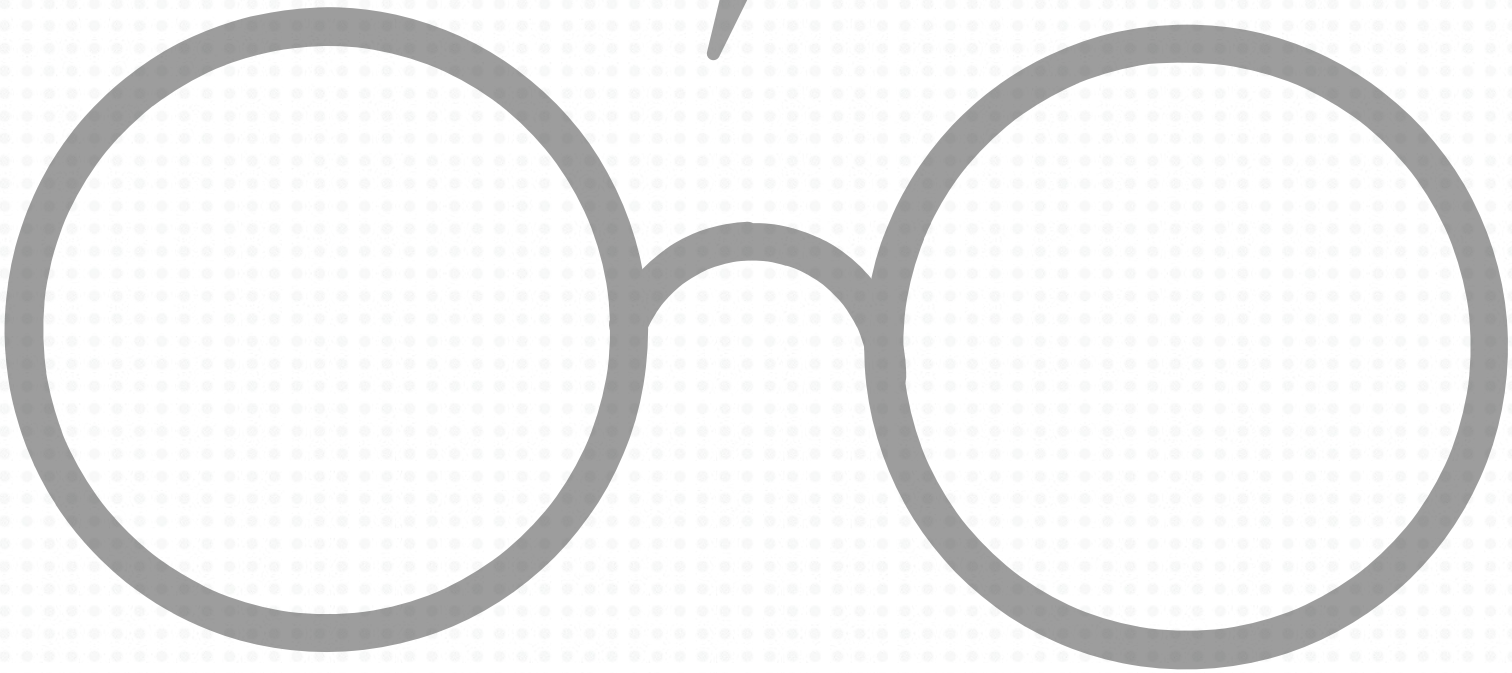
4. Low Overall Failure Rates: This study reports failure rates of 11% and 13% for PCs and LBCT respectively. These figures are significantly lower than a rate of 28.7% reported in a recent multi-institutional study from the Eastern Association for the Surgery of Trauma (EAST). The authors comment that this may be because their study excluded patients in extremis who may have additional injuries or require a level of procedural urgency that predisposes them to complications, however it is interesting to note that the study population in this trail had a mean hemothorax volume of 612mL vs 191 mL is the EAST study indicating that volume of blood did not appear to influence rate of failure compared to what has been published elsewhere (Prakash et al 2020).

5. Stopped Early: This is a multi-center RCT building on this groups previously published single center experience using PCs for the treatment of traumatic hemothorax (Kulvatunyou JTACS 2012). Despite enrolling at four sites for five years, they only enrolled 119 total patients. The authors initially estimated that they would have had to enroll 95 patients in each arm to have adequate power to detect a 15% absolute difference in efficacy between PCs and LBCTs. This was also based on the assumption of a failure rate of 15% for PC and 30% for LBCT.

Unfortunately, due to slow enrollment and the disruption to research caused by the COVID19 pandemic the authors stopped the study early after enrolling 56 patients in the PC arm and 63 patients in the LBCT arm. They report they conducted an interim analysis prior to stopping enrollment and their primary endpoint still met the non-inferior margin.

Time to Talk Nerdy:

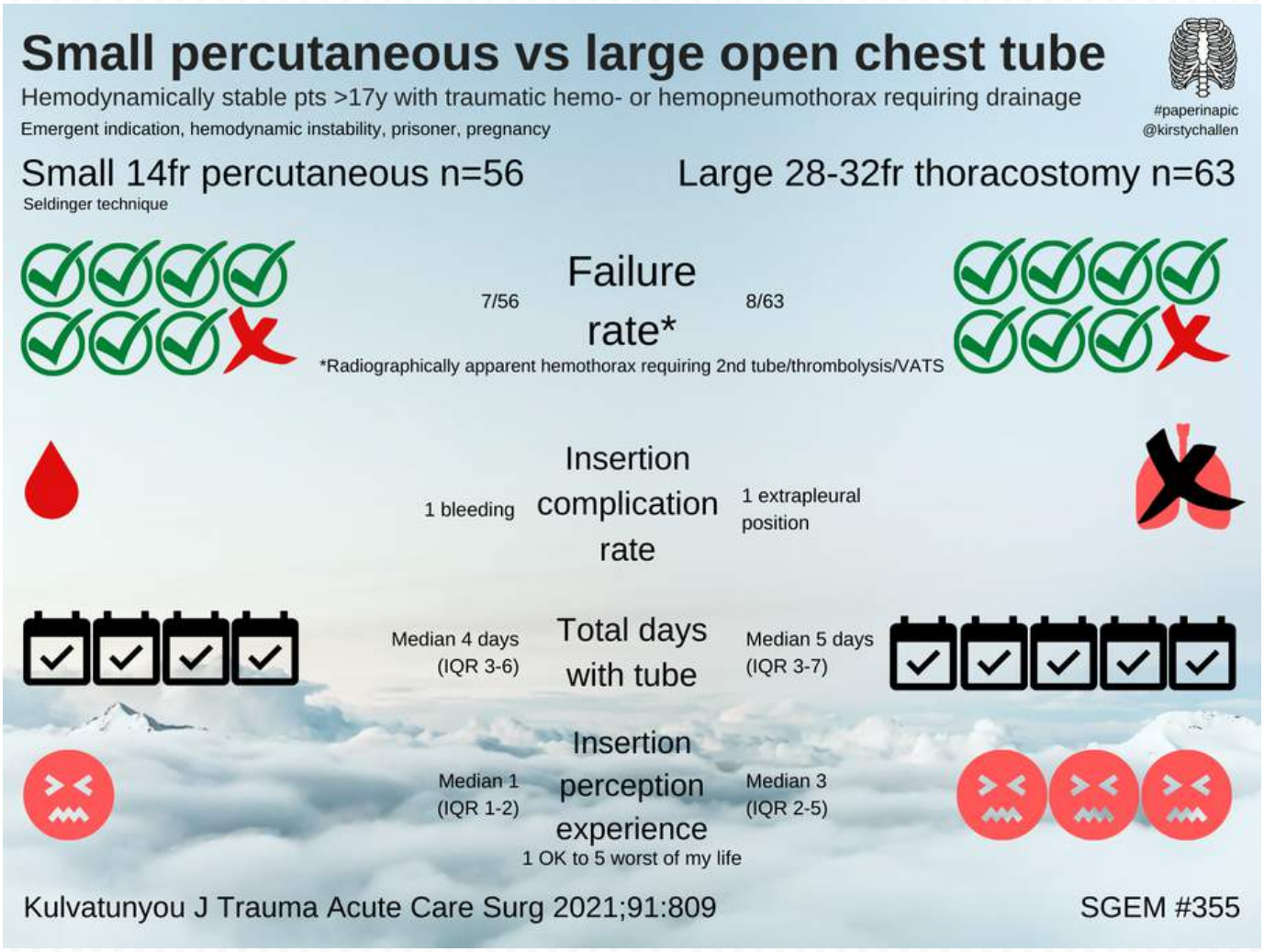
Comment on Authors' Conclusion Compared to SGEM Conclusion: The authors concluded that PC are "equally" as effective as LBCTs for the evacuation of traumatic hemothorax and that patients tolerate the placement of PCs better than LBCTs. A friendly amendment would be to say that PCs are non-inferior to LBCT and that patients prefer PC. They would have needed to show the 95% CI and demonstrate equivalence to claim "equally" effective. We have reached out to the authors to see if we can get this information and will update the blog if/when it becomes available.



Clinical Application: This trial provides more information that bigger is not necessarily better means of treating traumatic hemothorax.

What Do I Tell My Patient?You have a collection of blood between your chest wall and lung. This is called a hemothorax. To relieve your discomfort and prevent your breathing from becoming worse we recommend inserting a tube to drain the blood out. Traditionally this was done with a large tube. However, there's evidence that it is effective, safe, and more comfortable for patients to use a smaller tube. This smaller tube is called a pigtail catheter. We would give you numbing medicine and some sedation to make it as comfortable as possible. You will be admitted to the hospital for monitoring and pain management while it drains. The tube will stay in place for a few days. Would you like the small tube or the big tube?

Case Resolution: The patient is consented for the placement of a PC in the ED. He is admitted to the trauma service for monitoring and pain management. The PC is removed on hospital day three and the patient is discharged on hospital day five.



I you personally had a traumatic hemothorax & were hemodynamically stable what size of chest tube would you prefer? #EBM #FOAMed thesgem.com/2022/01/sgem35...

@JTraumAcuteSurg @gueromedico @rob_leeper @KirstyChallen @ThoracikRick @STS_CTsurgery @kari_jerge @EAST_TRAUMA @traumadoctors

Small Pigtail Catheter	**75.3%**
Large Bore Chest Tube	24.7%

356

DRUGS ARE GONNA KNOCK YOU OUT – ETOMIDATE VS. KETAMINE FOR EMERGENCY ENDOTRACHEAL INTUBATION

Clinical Question:

Which induction agent has a bettre day 7 survival for critically ill patients requiring emergency endotracheal intubatoin, ketamine or etomidate?

Bottom Line:

It likely does not make a patient-oriented difference hethre you use ketamine or etmoidate for emergency endotracheal induction in most critically ill patients.

Guest:

Missy Carter, former City of Bremerton Firefighter/Paramedic, currently a professor of Emergency Medical Services at Tacoma Community College's paramedic program. Missy is currently working in a community emergency department as a physician assistant and recently accepted a critical care position in Tacoma Washington.

Case Overview:

You respond to a rapid response on the floor for a 58-year-old woman in septic shock who is requiring emergent rapid sequence intubation (RSI). As you prepare to intubate the pharmacist asks if you would prefer ketamine or etomidate for induction in this patient.

Background:

We have covered the issue of intubation multiple times on the SGEM. This has included looking at supraglottic airways for out-of-hospital cardiac arrests (SGEM#247), video vs. direct laryngoscopy (SGEM#95), tracheal intubation for in-hospital cardiac arrests (SGEM#197), apneic oxygenation (SGEM#186) and confirming intubation with POCUS (SGEM#249). One thing we have not covered is the choice of induction agent for intubation.

There has been much debate regarding the use of etomidate verses ketamine for induction in the critically ill [1-4]. A 2009 randomized control trial conducted in French ICUs supported the use of ketamine in this patient population [5]. Both agents are considered hemodynamically stable, but any induction agent may precipitate shock in the critically ill.

There is some conflicting evidence as to which agent is preferred for patients who are at high risk of peri intubation complications. Historically there has been concern about adrenal insufficiency caused by etomidate being harmful for patients with sepsis but this has not been shown to cause increased mortality in the literature [6, 7].

Background:

Ketamine has emerged as a reasonable alternative but in recent years there has been concern about increased cardiovascular collapse with ketamine especially in those with sepsis or a high shock index [1, 8].

Reference: Matchett, G. et al. Etomidate versus ketamine for emergency endotracheal intubation: a randomized clinical trial. Intensive Care Med 2021

P

Population: Adults 18 years of age and older in need of emergency endotracheal (ET) intubation

- **Exclusions:** Children, pregnant patients, patients needing ET intubation without sedation or allergic to one of the agents being used

I

Intervention: Ketamine 1-2mg/kg IV

C

Comparison: Etomidate 0.2-0.3mg/kg IV

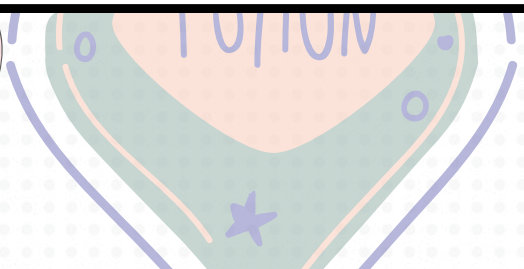
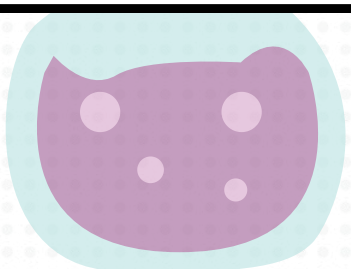
- **Primary Outcome:** 7-day survival
- **Secondary Outcomes:** 28-day survival, duration of mechanical ventilation, ICU length of stay, need for vasopressor use, SOFA scores and an assessment of a new diagnosis of adrenal insufficiency by the treating critical care teams.
- **Trial:** Prospective, randomized, parallel-assignment, open-label, single-center trial (NCT02643381

Authors' Conclusions

"While the primary outcome of Day 7 survival was greater in patients randomized to ketamine, there was no significant difference in survival by Day 28."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [?] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [?] 10. All patient-important outcomes were considered.
- [?] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [x] 12. Financial conflicts of interest.

Results

Key Results:

- The cohort consisted of 801 critically ill patients that required ET. The mean age was 55 years, 38% female, 69% were in the MICU, and 51% had diagnosis of sepsis

- **Primary Outcome:** 7-day survival favored
  - Ketamine (85.1%) vs etomidate (77.3%), difference − 7.8, (95% CI; − 13 to − 2.4) p = 0.005
- **Secondary Outcomes:** There was no statistical difference in 28-day survival between groups (ketamine 66.8% vs etomidate 64.1%)

Time to Talk Nerdy:

1. Selection Bias: These were not consecutive patients. The manuscript says physicians were "encouraged to consider screening and enrolling patients whenever clinical circumstances reasonably permitted but were under no obligation to do so."

When you look at the number of patients excluded due to "clinical circumstances, clinician preference for usual care" in each arm of trial they were similar (n =396 for etomidate, and n = 398 for Ketamine). The reasons for these exclusions are unclear and may have biased the results towards whichever medication the physician favored. How these exclusions would ultimately impact the over-all results is also unclear.

2. Blinding: This was an open label trial. The authors said: "After extensive discussions with hospital and community stakeholders, we were unable to arrive at a satisfactory plan for masking." This lack of blinding could have been responsible for the reported higher level of adrenal insufficiency was found in the etomidate arm. Having knowledge of group allocation may have led clinicians to more testing for adrenal insufficiency in the etomidate arm verses the ketamine arm.

3. Outcome Measure: The authors recognize that selecting 7 day survival is an unconventional outcome measure in an RCT of critically ill patients. They chose one Constantine unit (7 days) as the outcome because of their quality improvement data and to have the endpoint close to randomization. While the 7 day mortality was statistically better in the ketamine group compared to the etomidate group, there was not statistical difference reported at 28 days. Also, a more patient oriented outcome would be survival with good neurologic status.

Time to Talk Nerdy:

4. External Validity: This trial was a single center trial including largely ICU patients who were intubated by an anesthesia lead airway team. This airway team uses the Montpellier Intubation protocol which includes the presence of two skilled operators, head-up positioning, deliberate preoxygenation, routine use of neuromuscular blocking agents and intubating stylets and frequent use of VL. They use EtCO2 detection for tube confirmation and are focused on prompt treatment of post intubation hypotension with vasopressors and IVF. This practice produced a 91% first pass success rate and likely contributed to standardized care in each group. The practice may not be generalizable to other centers who do not use such standardized protocols.

5. Hypothesis Generating: There were some interesting secondary outcomes regarding hemodynamics and cardiovascular collapse that are thought provoking and hypothesis generating. Ketamine had higher rates of vasopressors use, more frequent post intubation CPR, and higher incidence of post induction cardiovascular collapse compared to etomidate. This is very interesting given the 7-day mortality was better with ketamine. It may be that the airway team was so aggressive about post intubation management that they were able to overcome these complications.

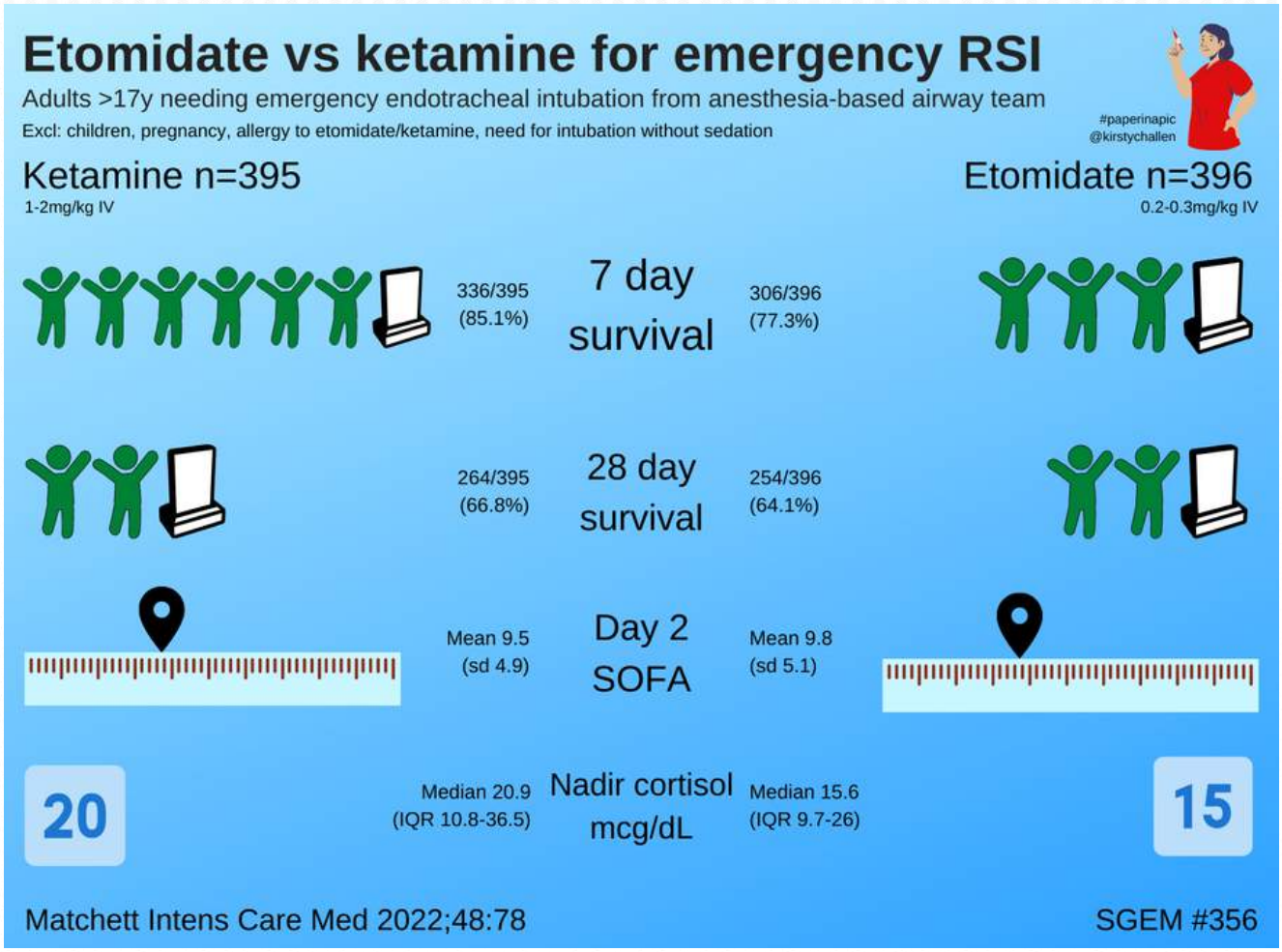
This circles back to nerdy point #4 and raises another question about generalizability. If these complications are encountered in other practice settings, such as the pre-hospital setting where there are less resources, would the patient receive the same aggressive post intubation management for these complications and might that change the outcomes.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusion.

Clinical Application: Both ketamine and etomidate have similar hemodynamic stability, but both should be used with caution in the critically ill patient. There may be certain patient populations who might benefit from one medication over the other, but more research is needed on this topic. Regardless of which agent used there should be a focus on optimizing patient physiology by aggressively resuscitating before you intubate. Considering lower dosing for either induction agent in the critically ill may be further protective.

What Do I Tell My Patient? You tell the patients family she is requiring a breathing tube to keep her safe while we manage her illness. She will be given medications to make them comfortable during and after the procedure. Although complications are possible, we will be doing everything we can to reduce her risk and keep her safe and comfortable.

Case Resolution: You tell your pharmacist you would like to use etomidate at a half dose but prior to intubation. First you would like to optimize hemodynamics and oxygenation and have a vasopressor ready in case you encounter post intubation hypotension.



Ken Milne MD
@TheSGEM

What induction agent do you prefer for adults who require emergency endotracheal intubation?
thesgem.com/2022/01/sgem35... @emcrit

Etomidate	31.9%
Ketamine	**68.1%**

317 votes · Final results

8:55 AM · Jan 18, 2022 · Twitter Web App

357

COVID IT'S GETTING HARDER AND HARDER TO BREATHE BUT WILL BUDESONIDE HELP?

Clinical Question:

Does inhaled budesonide improve clinical outcomes in high-risk outpatients with COVID-19?

Bottom Line:

Currently, there does not appear to be a role for the rooutine uses of inhaled budesonide in the management of COVId-19.

Guest:

Dr. Justin Morgenstern is an emergency physician and the creator of the #FOAMed project called First10EM.com.

Case Overview:

A 65-year-old woman with a history of diabetes, hypertension, and gastroesophageal reflux disease (GERD) presents with three days of fever, cough, and myalgias. She is fully vaccinated against COVID-19. Her husband tested positive for COVID-19 yesterday, and she used a home rapid test this morning that is also positive. Her vitals signs are all normal and she feels well enough to isolate at home. As you are preparing to discharge her, she asks if there is anything you can prescribe her to help. She thinks her friend might have been prescribed a puffer of some sort.

Background:

I've tried not to focus too much on COVID-19. There are many great FOAMed resources that have done a good job of covering the topic. The SGEM has only done a few shows over the two years including:

- Debate regarding a universal mandate for masks early in the pandemic with Dr. Joe Vipond (SGEM Xtra: Masks4All in Canada Debate)
- Skeptical review of the early therapeutics with Dr. Sean Moore for the Canadian Association of Emergency Physicians (CAEP) Town Hall (SGEM Xtra: COVID19 Treatments – Be Skeptical)
- Diagnostic accuracy of various tests for COVID19 with Dr. Chris Carpenter (SGEM#299: Learning to Test for COVID19)
- Structured critical appraisal of the DANMASK trial with Dr. Joe Vipond (SGEM#309: That's All Joe Asks of You – Wear a Mask)

Background:

IThe First10EM has done more than 30 blog posts about COVID-19 at this point, with a lot more to come. I know we all wish COVID-19 would just go away. But unfortunately, wishful thinking won't help us, but hopefully science will. There is strong evidence that systemic steroids improve outcomes in patients with severe COVID-19 (First10EM: Steroids for COVID). This has raised the question of whether inhaled steroids might be helpful. After all, the infection is primarily in the lungs.

Early in the pandemic, there was some observational data that concluded that inhaled steroids were associated with an increased mortality from COVID-19 in patients with asthma and COPD (Schultze Lancet Resp Med 2020). However, the most likely explanation was not causal. Sicker patients are prescribed steroids more often, and so the association is not surprising.

The STOIC trial was an initial phase 2 open-label randomized control trial of inhaled budesonide for patients with mild symptoms of COVID-19 (Ramakrishnan et al Lancet Resp Med 2021). It did report positive results.

Their primary outcome was a 'COVID-19 related' urgent care visit, emergency department assessment, or hospitalization, and was significantly reduced in the budesonide arm (15% vs 3%, p=0.009).

However, the unblinded trial design, less relevant composite outcome, and fact that the trial was stopped early limit confidence in the results. That bring us to the PRINCIPLE trial.

Background:

Reference: Yu et al. Inhaled budesonide for COVID-19 in people at high risk of complications in the community in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial. Lancet 2021

P

Population: Outpatients with symptomatic COVID-19 within 14 days of symptom onset who were considered high risk for adverse events. This included adults over 65 years of age, or over 50 years of age with co-morbidities.

- **Exclusions:** Known allergy or contraindication to inhaled budesonide, were unable to use an inhaler, or already using inhaled or systemic glucocorticoids.

I

Intervention: Inhaled budesonide 800 ug BID for 14 days

C

Comparison: Usual care (there was no placebo)

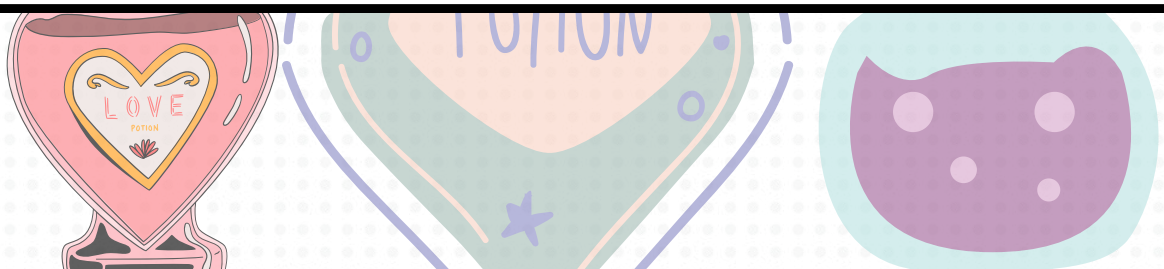
- **Primary Outcome:** Composite outcome of COVID-19-related hospital admission or death within 28 days. However, partway through the trial they realized hospitalization was lower than normal, and so they added a second primary outcome: illness duration.
- **Secondary Outcomes:** Recovery by 14 days, daily symptoms rating, time to sustained alleviation of symptoms, time to initial reduction of symptoms, contact with health services, oxygen administration, ICU admission, mechanical ventilation and adherence to study medication
- **Trial Design:** Multicentre, open-label, multi-arm, randomised, controlled, adaptive platform trial

Authors' Conclusions

"Inhaled budesonide improves time to recovery, with a chance of also reducing hospital admissions or deaths (although our results did not meet the superiority threshold), in people with COVID-19 in the community who are at higher risk of complications."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [?] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [?] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [x] 12. Financial conflicts of interest.



Results

Key Results:

- They recruited 1,959 into the trial for the primary analysis (833 budesonide and 1,126 usual care). Mean age was 64 years, 81% had comorbidities, 52% female, 11% had been vaccinated (1 or 2 shots), 5% were current smokers and median duration of illness was 6 days.

- **Primary Outcome:**
  - There was no statistical difference for the original primary outcome of hospital admission or death due to COVID-19: 6.8% with budesonide versus 8.8% with usual care (ARR 2.0%, 95% CI -0.2 to 4.5%)
  - For the added primary outcome of time to first reported recovery, budesonide was better at 11.8 vs 14.7 days, absolute benefit 2.9 days (95% CI: 1.2-5.1 days)
- **Secondary Outcomes:**
  - No statistical difference in mortality (1% v 1%), mechanical ventilation (2% v 2%), need for supplemental oxygen (7% v 9%) or need for ICU (1% v 3%)
  - There are a large number of symptom-based outcomes. In general, they demonstrate statistically less symptoms with budesonide, although the actual clinical difference seems small, and this is an unblinded study. We will discuss this further in the Talk Nerdy section.

Case Outcomes

	Inhaled budesonide	Usual care	Estimated treatment effect (95% CI)	p value
Early sustained recovery	251/781 (32%)	173/794 (22%)	1·48 (1·26 to 1·75)*	<0·0001
Sustained recovery	462/787 (59%)	390/799 (49%)	..	..
Time to sustained recovery, days	23 (9 to not reached)	28 (15 to not reached)	1·39 (1·21 to 1·59)†	<0·0001
Alleviation of all symptoms	630/701 (90%)	666/732 (91%)	..	..
Time to alleviation of all symptoms, days	4 (2 to 9)	5 (2 to 10)	1·07 (0·96 to 1·19)†	0·26
Sustained alleviation of all symptoms	579/701 (83%)	597/731 (82%)	..	..
Time to sustained alleviation of all symptoms, days	8 (3 to 24)	12 (5 to 26)	1·13 (1·01 to 1·27)†	0·037
Initial reduction of severity of symptoms	662/786 (84%)	650/797 (82%)	..	..
Time to initial reduction of severity of symptoms, days	7 (3 to 14)	8 (3 to 20)	1·19 (1·07 to 1·32)†	0·0019
Illness severity rating (1 worst, 10 best), mean (SD) [n]				
Day 7	7·0 (1·8) [747]	6·6 (1·9) [759]	0·33 (0·14 to 0·52)‡	0·0001
Day 14	7·9 (1·7) [745]	7·5 (1·7) [763]	0·37 (0·17 to 0·57)‡	<0·0001
Day 21	8·4 (1·5) [623]	7·9 (1·6) [612]	0·38 (0·15 to 0·61)†	0·0001
Day 28	8·4 (1·5) [759]	8·2 (1·5) [772]	0·19 (−0·07 to 0·44)‡	0·16
WHO-5 Well-Being Index, mean (SD) [n]				
Day 14	42·5 (25·0) [713]	39·4 (24·4) [724]	2·97 (0·64 to 5·30)‡	0·013
Day 28	54·6 (25·1) [713]	52·0 (24·8) [721]	2·36 (0·03 to 4·69)‡	0·047
Self-reported contact with at least one health-care service	416/778 (54%)	466/787 (59%)	0·90 (0·83 to 0·98)*	0·017
General practioner reported contact with at least one health-care service	305/602 (51%)	351/607 (58%)	0·87 (0·79 to 0·97)*	0·010
New infections in household	197/772 (26%)	214/782 (27%)	0·93 (0·79 to 1·10)*	0·40
Prescription of antibiotics	42/550 (8%)	53/543 (10%)	0·78 (0·53 to 1·15)*	0·24
Hospital assessment without admission	22/786 (3%)	22/797 (3%)	1·01 (0·57 to 1·82)*	>0·99
Oxygen administration	50/774 (7%)	73/785 (9%)	0·69 (0·49 to 0·98)*	0·039
Mechanical ventilation	13/776 (2%)	14/784 (2%)	0·94 (0·44 to 1·98)§	>0·99
Intensive care unit admission	10/771 (1%)	21/779 (3%)	0·48 (0·23 to 1·01)§	0·068
Duration of hospital admission, days, median (IQR) [n]	9·5 (5 to 28) [70]	10 (4 to 29) [95]	−0·70 (−6·34 to 4·94)¶	0·81
WHO ordinal scale of clinical progression				
Not admitted to hospital	715/787 (91%)	701/799 (88%)	0·73 (0·53 to 1·01)‖	0·056
Admitted to hospital without need for supplemental oxygen	17/787 (2%)	21/799 (3%)	..	..
Admitted to hospital with need for supplemental oxygen	36/787 (5%)	56/799 (7%)	..	..
Admitted to hospital with need for non-invasive positive pressure ventilation or high-flow nasal cannula	0/787	1/799 (<1%)	..	..
Admitted to hospital with need for mechanical ventilation or extracorporeal membrane oxygenation	13/787 (2%)	10/799 (1%)	..	..
Death	6/787 (1%)	10/799 (1%)	..	..

Data are n/N (%) or median (IQR) unless otherwise stated. Patients with data not available were not included in analyses. *Relative risks adjusted for age, comorbidity at baseline, duration of illness, and vaccination status at baseline. †Estimated hazard ratio derived from a Cox proportional hazard model adjusted for age, comorbidity at baseline, duration of illness, and vaccination status at baseline, with 95% CI. ‡Mixed-effects model adjusting for age, comorbidity, duration of illness, vaccination status at baseline, and time; participant was fitted as a random effect; WHO-5 score was also adjusted for the score at baseline. §Unadjusted relative risks due to low event rate. ¶Adjusted difference in medians derived from quantile regression adjusted for age, comorbidity at baseline, duration of illness, and vaccination status at baseline. ‖Proportional odds ratio derived from ordinal logistic regression adjusted for age, comorbidity at baseline, duration of illness, and vaccination status at baseline.

Table 3: **Secondary outcomes**

Time to Talk Nerdy:

1) Unblinded Trial: The biggest limitation in this study is its lack of blinding, especially considering they added a second primary outcome that was entirely symptom based. In any unblinded trial, we should expect that the treatment group will have fewer symptoms, so those results are unreliable here. However, even seemingly objective outcomes like hospitalizations can end up biased in unblinded trials. Imagine a patient who feels like 'nothing is being done for them', struggling with the cough and fatigue of COVID-19. They may not meet any formal admission criteria for COVID-19, but if it is there third ED visit, they might end up admitted anyway. (I have seen this happen many times.) Therefore, symptoms translate into hospitalizations, and so the unblinded nature of the trial even biases their original primary outcome.

2) Disease Specific Outcomes: For their original primary outcome, they looked at "COVID-19-related hospital admission or death" rather than just hospital admission or all death. This is an issue and can bias a trial from the outset. These outcomes fundamentally ignore harms of medications. If a patient is admitted to hospital because of a medication-related adverse event, then don't get counted in this primary outcome. Luckily, adverse events are rare from inhaled budesonide, so this bias probably did not have a huge impact on these results.

3) Adding a Second Primary Outcome: The original primary outcome was a composite of COVID-19-related hospital admission or death within 28 days. This was changed to add a co-primary outcome of illness duration. The rationale was that the hospital admission rates in the UK were lower than the authors initially expected. Ethics approval was provided for this amendment and implemented before performing any interim analyses.

Time to Talk Nerdy:

The more objective primary outcome of hospitalization and death were not statistically different, but the subjective outcome of illness duration was better with budesonide. As mentioned in nerdy point #1 the lack of blinding likely impacted the additional primary outcome and may have impacted hospitalizations.

4) Extrapolation: Most of these patients were unvaccinated. Vaccinated patients have better outcomes after COVID-19 infection, and therefore are much less likely to benefit from treatment. Therefore, we shouldn't expect to see the same degree of benefit in vaccinated populations. The same concern may apply to the shifting severity we see from new COVID-19 variants.

5) Threshold for Evidence During a Pandemic: This is a longer and more philosophical discussion. For any study, we will see a range of possible interpretations. During COVID-19, in particular, I have found myself disagreeing with some very smart evidence-based doctors who I usually agree with, and I think the difference comes down to a question of philosophy of science. Personally, I think we should be using the same standards for science now as we always have.

I agree that we should not lower our standards during a global pandemic. We discussed this with our good friend Dr. Simon Carley from St. Emlyns on an SGEM Xtra. He said, *"the principles of EBM are more important now than at any other time in our careers".*

There is an alternative argument that, I will admit, sounds very convincing on the surface. The arguments states that we have an urgent need for action right now. Our health care systems are crumbling around us. We need to do anything we can to improve COVID-19 outcomes. There is just not time to wait for more certainty.

Time to Talk Nerdy:

This argument seems very reasonable, but I think it is flawed. It contains the inherent assumption that unproven medications will cause more good than harm, which may not be a very good assumption.

This is an example of intervention bias. It is a form of bias to intervene (tests, medication, or procedures) when non-intervening would be a reasonable alternative (Foy and Filippone 2013). One of my favourite papers of all times is titled "Don't just do something, stand there! The value and art of deliberate clinical inertia" by Keijzers et al 2018. This is something our mentor Dr. Jerome Hoffman has been saying for years.

All treatments may cause harm. Any unproven treatment could actually end up increasing demands on hospital resources through adverse events, especially as use expands beyond the tightly controlled trial setting. For a variety of reasons, medical studies generally overestimate benefits and underestimate harms. Harms are also known to be under-reported in randomized control trials and systematic reviews and meta-analyses (Saini et al BMJ 2014, Hodgkinson et al BMJ 2013 and Zorzela et al BMJ 2014). Therefore, we should advocate for solid evidence of benefit before implementing new therapies. The same should apply to COVID-19.

Empirically, throughout the history of medicine, most new potential therapies fail. The overall chance that a drug entering clinical development will be approved for marketing is just over 10% (DiMasi et al J Health Econ 2016). Even if treatments are approved, close to one-third are withdrawn due to safety concerns, receive FDA black box warnings, or FDA safety communications (Downing et al JAMA 2017). It is hard to have a positive impact on the complex homeostasis that is human biology.

Time to Talk Nerdy:

We also know that a huge number of apparently positive trials are never replicated (Begley and Ellis Nature 2012, Prinz et al Nature Reviews Drug Discoveries 2011, and Ioannidis JPA JAMA 2005). If we have a problem in medicine, it is with overestimating the benefit of our purported therapies.

The argument that novel therapies could reduce healthcare demands during a pandemic contains the hidden assumption that the therapy will work, which historically and empirically speaking, may be a bad assumption.

The problem of overestimating benefit is almost certainly magnified during the COVID-19 pandemic. Around the world, scientists and clinicians have thrown essentially any chemical they can think of at COVID-19. If we throw hundreds of potential drugs randomly towards a target, we shouldn't be surprised that some hit the bullseye. The problem is that at least some of the options will hit the bullseye by statistical chance alone.

If 20 different drugs were tested in a single trial, and one happened to have a statistically significant result, we would know to be cautious. But that is exactly what is happening worldwide; the drugs just happen to be tested in separate trials. Since early 2020 it was obvious, given the sheer number of randomized control trials being run, that some COVID-19 trials would be positive by for reasons unrelated to treatment efficacy.

When you combine the ongoing chance of harm from novel therapeutics with the increased risk of false positives during the COVID-19 research frenzy, we need to maintain the same stringent scientific standards we always use to keep patients safe.

Time to Talk Nerdy:

Comment on Authors' Conclusion Compared to SGEM Conclusion: The unblinded nature of this study leave us very skeptical about the claim that budesonide improves symptoms. We agree with the authors that is still a chance that budesonide could improve objective outcomes like hospitalization, but that their data were not statistically significant for that claim, and so more research would be needed.

Clinical Application: After two randomized control trials, it remains unclear if inhaled budesonide has any role in the management of COVID-19. It may relieve symptoms, but it also may just be an expensive placebo. This is a well-known medication with a relatively low risk of side effects, so shared decision making is reasonable in the face of this uncertainty.

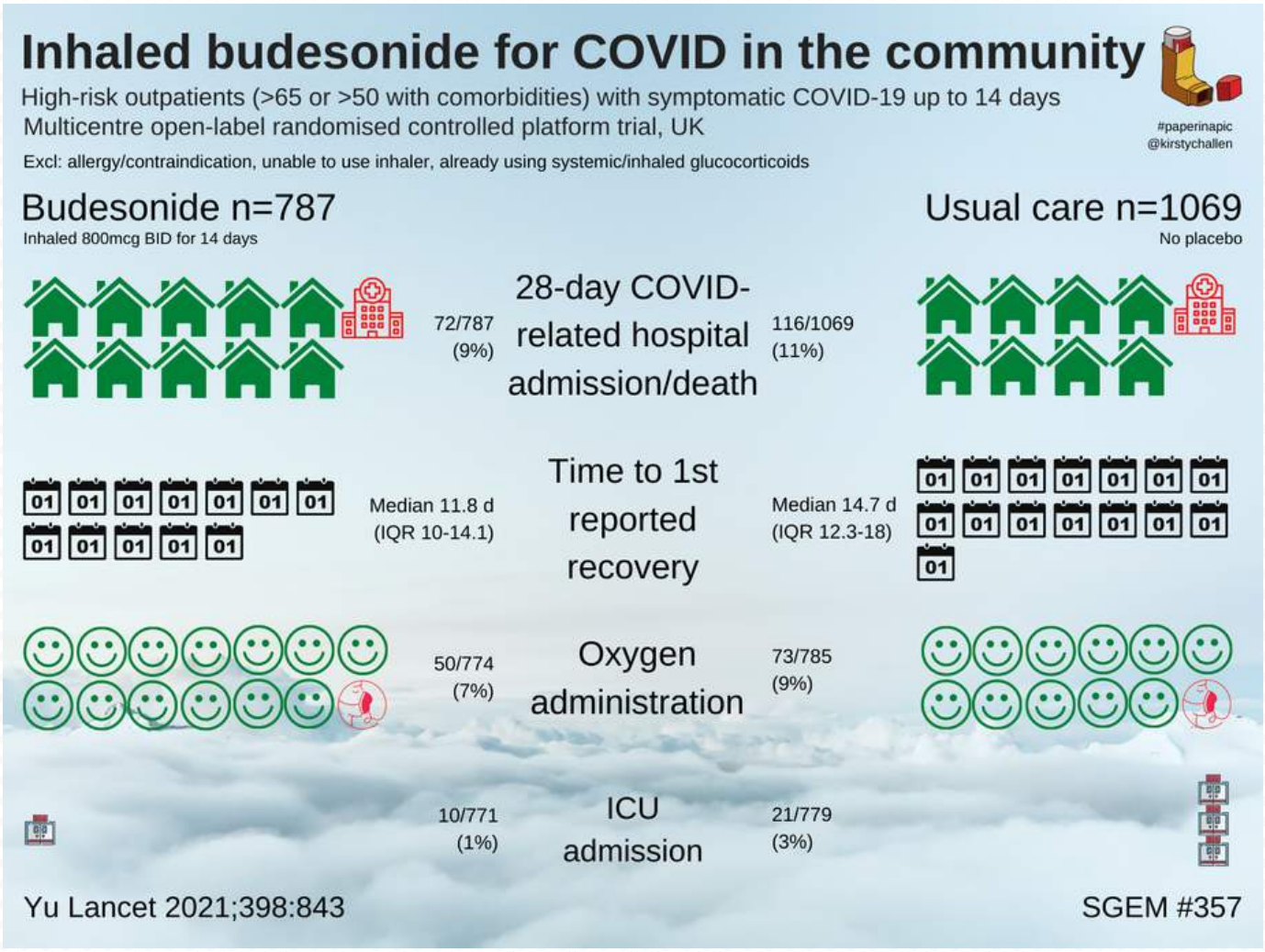
What Do I Tell My Patient? There is a puffer that has been tested against COVID-19. At this point, we don't know if it provides any real help, but it might help relieve your cough a day or two earlier.

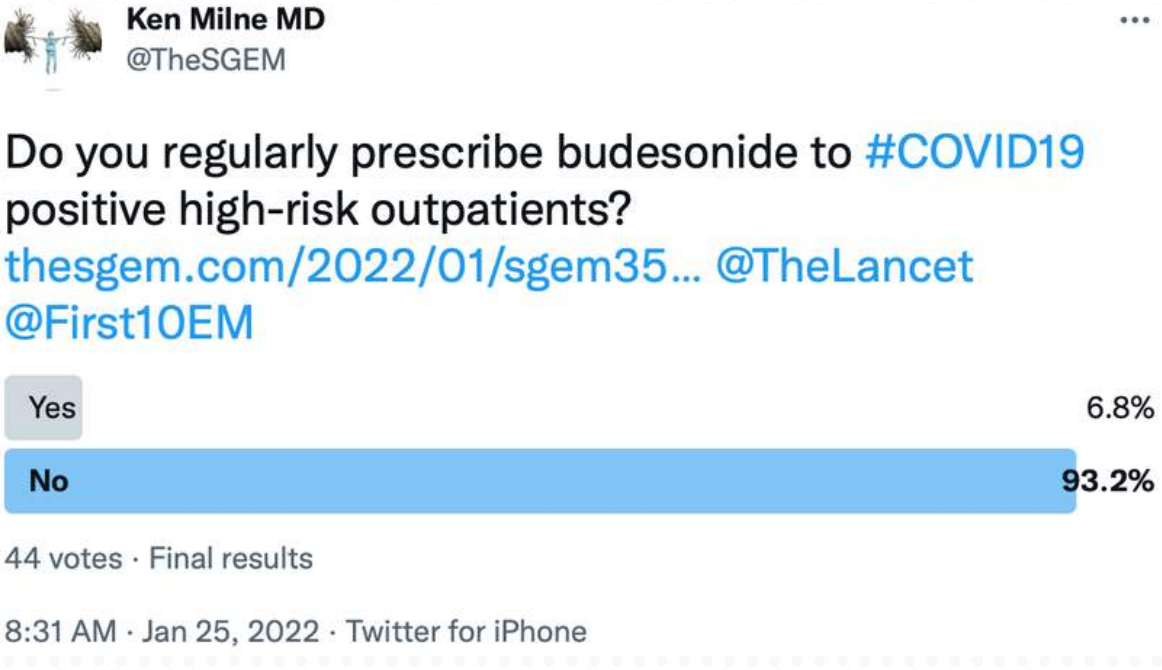
However, all medications have possible side effects. This is a steroid puffer that has been used for a long time, and its pretty safe if used for the short term, but side effects like thrush, sort throats, and pneumonia do occur. It is also relatively expensive. I do not routinely recommend it, but if you want to know more, I am happy to discuss further.

Case Resolution: You discuss the risks, benefits, and costs of inhaled budesonide, as well as the significant remaining uncertainty with your patient. She decides against treatment.

Other FOAMed:

- First10EM: COVID therapy evidence updates (budesonide)
- REBEL EM: The STOIC Trial: Inhaled Budesonide in the Treatment of Early COVID-19





358

I WOULD DO ANYTHING FOR SEPTIC OLECRANON BURSITIS BUT I WON'T TAP THAT

Clinical Question:

What is the efficacy and outcomes associated wwith empiric antiobitic threapy, withuot aspiraation, for septci olecranon bursitis?

Bottom Line:

Most patients with suspected septic olecranon bursitis had na uncomplicated resolution of their bursitis.

Guest:

Dr. Corey Heitz is an emergency physician in Roanoke, Virginia. He is also the CME editor for Academic Emergency Medicine.

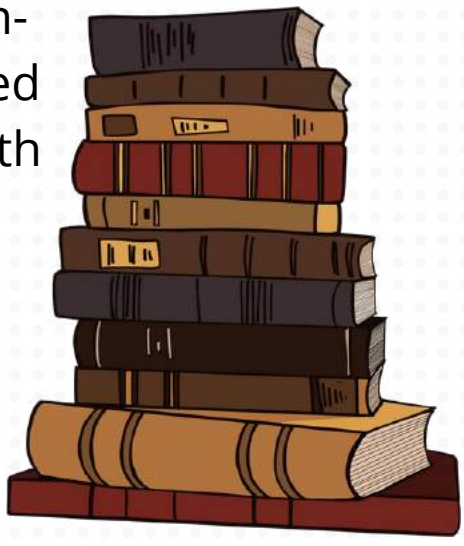
Case Overview:

You're working in your busy freestanding emergency department (ED) getting absolutely crushed handing out COVID19 tests like candy and are relieved to see a patient with something different. A 27-year-old male construction worker building a local house presents with a tender, warm, erythematous olecranon and you diagnose him with septic olecranon bursitis. You offer to drain the bursa and get him back to work ASAP, and the patient looks very anxious and asks if you really must.

Background:

We have covered skin and soft tissue infections multiple times on the SGEM. The most recent time was with guest skeptic and SAEM FOAMed Excellence in Education Award winner Dr. Lauren Westafer (SGEM#348). We reviewed Dr. David Talan and colleagues' study that was the October 2021 SGEM Hot Off the Press. That study investigated if a single-dose long-acting intravenous antibiotic could reduce hospitalization in patients with skin infections.

The SGEM bottom line from that episode was in hospital systems with access to IV dalbavancin and the ability to establish expedited telephone and in-person follow up, this clinical pathway is associated with a decrease in hospitalizations for patients with moderately severe cellulitis.



A couple of other SGEM episodes have looked at the management of cellulitis including SGEM#131 and SGEM#209. The treatment of abscesses has been covered four times on the SGEM (SGEM#13, SGEM#156, SGEM#164 and SGEM#311).

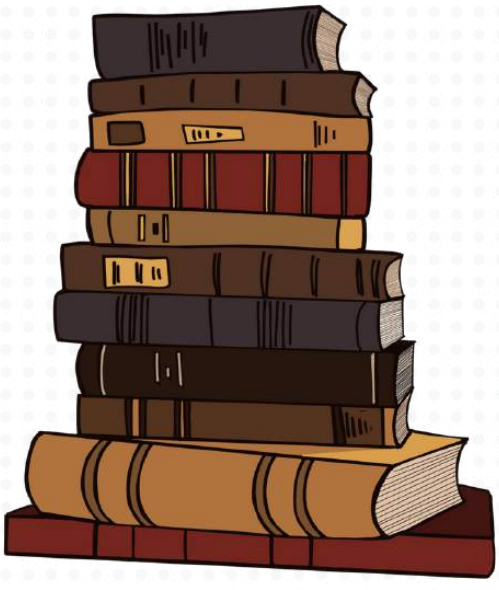
Background:

The latest episode looked at the loop technique to drain uncomplicated abscesses. One topic we have not looked at is infected bursa.

It's estimated that about half of olecranon bursitis cases are septic[1]. Often, diagnostic aspiration is performed, but complications include fistula formation, further infection, and need for bursectomy [2-6].

Often the workup of septic bursitis is based upon anecdotal evidence [7]. This is likely due to the lack of high-quality evidence to direct our care. One area with limited information is the efficacy of empiric antibiotics without bursal aspiration.

Reference: Beyde et al. Efficacy of empiric antibiotic management of septic olecranon bursitis without bursal aspiration in emergency department patients. AEM January 2022



P **Population:** Adults >18 years old with olecranon bursitis
- **Excluded:** Declined authorization, underlying fracture, or surgery on the joint within 3 months

I **Intervention:** Exposures- Antibiotics, aspiration, surgery or admission to hospital

C **Comparison:** None

- **Primary Outcome:** Complicated versus uncomplicated bursitis resolution (Uncomplicated was defined as bursitis resolution without the need for bursal aspiration, surgery, or hospitalization)
- **Secondary Outcome:** Descriptive statistics of the cohort
- **Study Design:** Retrospective observational cohort study

This is an SGEMHOP episode which means we have the senior author on the show. Dr. Ronna Campbell is an emergency physician practicing since 2007 in Rochester, MN. She enjoys mentoring medical students, residents and others in research.

Authors' Conclusions

"Eighty-eight percent of ED patients with suspected septic olecranon bursitis treated with empiric antibiotics without aspiration had resolution without need for subsequent bursal aspiration, hospitalization, or surgery. Our findings suggest that empiric antibiotics without bursal aspiration may be a reasonable initial approach to ED management of select patients with suspected septic olecranon bursitis."

Quality Checklist for Observational Study

- [x] 1. Did the study address a clearly focused issue?
- [x] 2. Did the authors use an appropriate method to answer their question?
- [x] 3. Was the cohort recruited in an acceptable way?
- [x] 4. Was the exposure accurately measured to minimize bias?
- [x] 5. Was the outcome accurately measured to minimize bias?
- [?] 6. Have the authors identified all-important confounding factors?
- [x] 7. Was the follow up of subjects complete enough?
- [ ] 8. How precise are the results? Fairly wided 95% CI aaround some of the point estimates
- [x] 9. Do you believe the results?
- [?] 10. Can the results be applied to the local population?
- [x] 11. Do the results of this study fit with other available evidence?
- [ ] 12. Funding of the study? NCATS/NIH grant

Results

Key Results:

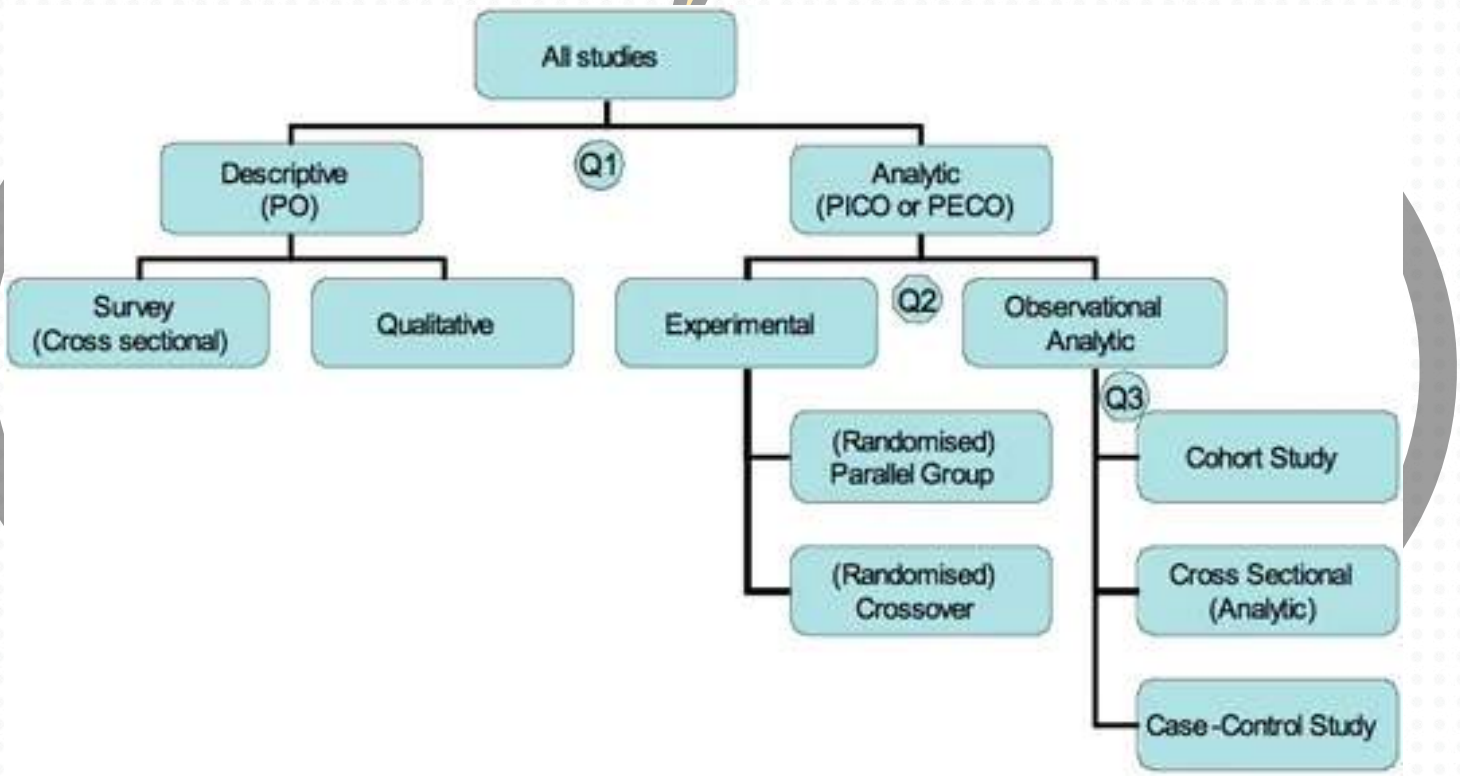
- 264 patients included in the study, 229 with three months of follow up, 220 with six months. The age ranged from 42-69 years with 85% male. The most common presenting symptoms were swelling (94%), erythema (77%), and pain (85%).

- **Primary Outcome:** Complicated vs uncomplicated resolution
  - 88.1% were uncomplicated (95% CI: 81.1%–92.8%)
  - 6.0% had subsequent bursal aspiration (95% CI: 2.8%–11.8%)
  - 6.7% were subsequently admitted to hospital for antibiotics (95% CI: 3.3%–12.7%)
- **Secondary Outcomes:**
  - 1.5% (4) had ED aspiration with no known complications (one lost to follow-up)
  - 15% (39) were admitted to hospital on the initial visit
  - 56% (147) were discharged from the ED with antibiotics
  - 8.8% (13) lost to follow up, 17.2% (27) 95% CI 11.4%-25.9% had subsequent bursitis-related visit, 88.1% (118) 95% CI 81.1-92.8% uncomplicated resolution and 8 (6.0%, 95% CI 2.8%-11.8%) underwent subsequent bursal aspiration
  - 29% (76) were discharged from the ED without Antibiotics
  - 12% (9) lost to follow up, 97% (65) 95% CI 89-99% resolved without antibiotics, 91% (61) 95% CI 81.96% had an uncomplicated resolution and 3% (2) 95% CI 1-11% received inpatient antibiotics in a subsequent hospitalization

Time to Talk Nerdy:

Listen to the SGEM podcast to hear Ronna answer our five nerdy questions about her study.

1. Study Design: You decided to perform a retrospective observational study. This really limits the strength of conclusions that can be made from the data. Can you comment on the decision not to perform a prospective observational study or a randomized control trial (CEBM)?



2. STROBE – You mentioned the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology). Some of the SGEM listeners may not be familiar with these guidelines. Can you tell us a little about these guidelines and why it is important to follow them?

Time to Talk Nerdy:

3. Lack of Blinding – The abstractors were not blinded to the study objectives. Do you think that could have impacted the results and what did you do to mitigate this potential bias?

4. Gold Standard – Was there any gold standard for the diagnosis of septic olecranon bursitis other than provider impression?

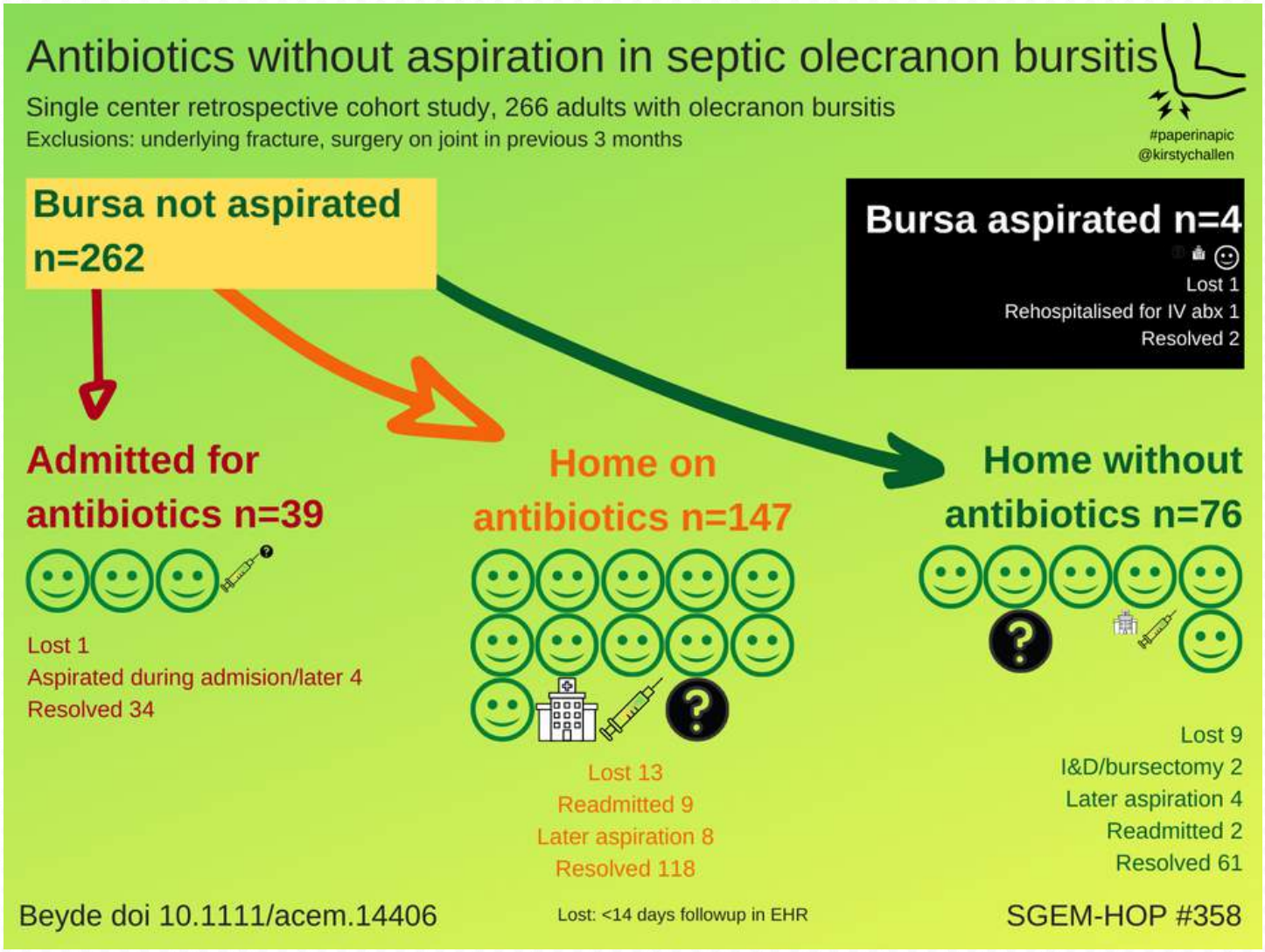
5. External Validity – This study was conducted at a single centre. In addition, it was the Mayo Clinic which is a quaternary care ED. Practice patterns of clinical staff (MD/DO/NP/PA) and management may be different here than at other quaternary EDs or community and rural EDs. Do you think your study has external validity to other practice environments?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with their conclusions

Clinical Application: The evidence base is weak and does not provide a clear answer. When deciding on a treatment plan, it is reasonable to not perform an aspiration for suspected septic olecranon bursitis.

What Do I Tell My Patient? You have what appears to be an infected elbow bursa. A bursa is a fluid-filled pad around our joints. We can either stick a needle in the bursa (aspirate) and try to get some fluid. This fluid can be tested for infection. Aspiration of a bursa can have complications such as bleeding, causing an infection or hitting a nerve. Another option is to not do the aspiration and treat you with antibiotics. If this does not work or you are getting worse, you can always return to the ED. Would you prefer aspiration plus antibiotics or no aspiration plus antibiotics?

Case Resolution: You discuss the options with the patient and using shared decision making, decide on an empiric antibiotic approach, without aspiration. The patient has a full and uncomplicated resolution.



@TheSGEM

Do you usually aspirate a suspected septic olecranon bursitis? #SGEMHOP thesgem.com/2022/01/sgem35... @MayoClinicEM @CHeitzMD @SAEMEBM @AcademicEmerMed @KirstyChallen

Yes	29.3%
No	**70.7%**

147 votes · Final results

359

MEET ME HALFWAY ON THE DURATION OF ANTIBIOTICS FOR NON-SEVERE PEDIATRIC COMMUNITY-ACQUIRED PNEUMONIA

Clinical Question:

Is a 5-day course of antibiotics superior to a 10-day course for the tretament of non-severe community-acquired pneumonia in children with respect to clinical outcomes, adverse effects, and antimicrobilal resistance?

Bottom Line:

This study suggests that a short-course of antibiotics is just as effective a a standard-course of antibiotics for the treatment of CAP in children with non-severe illnes and may lead to better antimicrobial stewardship.

Guest:

Dr. Dennis Ren is a pediatric emergency medicine fellow at Children's National Hospital in Washington, DC.

Case Overview:

A three-year-old boy presents to the emergency department (ED) with fever and cough. On exam, he is breathing a little fast and his oxygen saturation is 94% on room air but otherwise appears comfortable. You appreciate some decreased breath sounds and crackles on your lung exam. You make a clinical diagnosis of community-acquired pneumonia (CAP) and plan to send him home with a 10-day course of amoxicillin. His mother asks you, “Last time he took antibiotics for that long, he had terrible diarrhea. Do you think we can do fewer days of antibiotics and still treat the pneumonia?”

Background:

We have covered the topic of pediatric community-acquired pneumonia before on the SGEM #338 (Are Children with CAP Safe and Sound if Treated for 5 days rather than 10 days of antibiotics?) with Dr. Andrew Tagg on the Canadian SAFER Trial [1]. This trial suggested that a 5-day course of antibiotics was not non-inferior to the traditional 10-day course of antibiotics for children with CAP treated as outpatients.

Things were much simpler when I started my pediatric training. I learned that a well-appearing child presenting to clinic with fever, slight tachypnea, and focal lung exam findings could be diagnosed with pneumonia by history and physical exam alone and go home with 10 days of amoxicillin BID. But now for some reason, this topic feels more complicated...maybe because there are so many different ways people go about diagnosing pneumonia and such variability in the reliability of physical exam findings [2,3].

Background:

Since we covered the SAFER trial, we have also had the CAP-IT [4] trial from the United Kingdom and Ireland which evaluated both high and low-dose amoxicillin for the treatment of CAP over three or seven days. They found that both a lower dose and a shorter duration of antibiotic therapy was non-inferior to higher dose, longer duration antibiotic therapy. They did find that cough persisted longer with the group that received a shorter duration of antibiotic therapy but overall adherence to medication was better in the group receiving a shorter duration of antibiotics.

Why so many pneumonia studies? Ultimately, we want to find that balance of treating an infection but avoiding antibiotic-associated adverse effects and antibiotic resistance.

So where is that sweet spot?

Reference: Williams et al. Short- vs standard-course outpatient antibiotic therapy for community-acquired pneumonia in children: the scout-cap randomized clinical trial. JAMA Pediatrics 2022

P

Population: Children 6 to 71 months of age from 8 US cities diagnosed with uncomplicated CAP demonstrating early clinical improvement (no fever, tachypnea, severe cough) on day 3 to 6 of their initially prescribed oral beta-lactam therapy.

- **Excluded:** Severe pneumonia (Hospitalization, radiographic evidence of parapneumonic effusion, empyema, lung abscess, pneumatocele or Microbiologically confirmed Staph aureus or Strep pyogenes pneumonia. Parenteral or combination antibiotic therapy. Undergoing surgery or invasive airway procedures 7 days prior to diagnosis of CAP. Beta-lactam allergy. Concurrent bacterial infection necessitating >5 days of antibiotics. Aspiration pneumonia, bronchiolitis, bronchitis, acute asthma exacerbation. Chronic medical conditions. History of pneumonia within prior 6 months

I

Intervention: Short 5 days course of previously prescribed antibiotic therapy (amoxicillin, amoxicillin with clavulanate, cefdinir) with 5 days of placebo

C

Comparison: Standard course of 10 days of previously prescribed antibiotic therapy

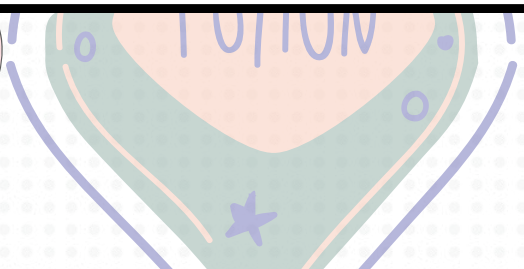
- **Primary Outcome:** End of treatment response adjusted for duration of antibiotic risk (RADAR) at the first outcome assessment visit (OAV1) which occurred on study days 6 to 10. This was a 2-step process: Desirability of outcome ranking (DOOR) based on adequate clinical response, resolution of symptoms, presence, and severity of antibiotic-associated adverse effects. Ranked overall experience based on actual reported treatment duration
- **Secondary Outcomes:** RADAR at the second outcome assessment visit (OAV2) on study days 19 to 25. A portion of participants also consented to throat swab collection at the second outcome assessment visit to evaluate antibiotic resistance genes in oropharyngeal flora.
- **Trial:** Prospective, multicenter randomized double-blind placebo-controlled superiority clinical trial.

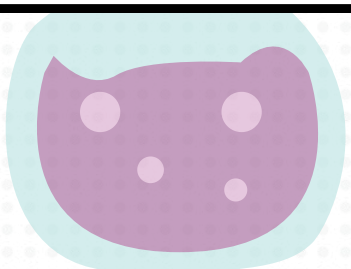
Authors' Conclusions

"In this study, among children responding to initial treatment for outpatient CAP, a 5-day antibiotic strategy was superior to a 10-day strategy. The shortened approach resulted in similar clinical response and antibiotic-associated adverse effects, while reducing antibiotic exposure and resistance."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [?] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [?] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [x] 12. Financial conflicts of interest.





Results

Key Results:

- They included 380 children (189 randomized to short course and 191 randomized to standard course). Mean age was 36 months, 51% male and 91% were treated with amoxicillin.
- **Primary Outcome:** No significant difference in proportions of inadequate clinical response, persistent symptoms, or antibiotic-associated adverse effects between short-course vs standard-course groups.

OAV1

	Short Course	Standard Course	Risk Difference (95% CI)
Inadequate Clinical Response	1%	<1%	0.5 (-2.4 to 3.7)
Persistent Symptoms	7%	8%	-1 (-6.8 to 4.9)
Adverse Effects	40%	37%	3 (-7 to 13)

  - Short course therapy had 69% (95% CI, 63% to 75%) probability of more desirable RADAR outcome compared to standard course.
  - This reflects the probability of a better DOOR (clinical response, resolution of symptoms, and antibiotic-associated adverse effects) for a randomly selected participant from the short course vs the standard course strategy.

- **Secondary Outcomes:**

OAV2

	Short Course	Standard Course	Risk Difference (95% CI)
Inadequate Clinical Response	1%	2%	-0.5 (-3.9 to 2.8)
Persistent Symptoms	6%	6%	0.1 (-5.3 to 5.4)
Adverse Effects	51%	48%	2.6 (-7.7 to 12.9)

Time to Talk Nerdy:

1. Potential Selection Bias: They included 380 patients over a three-year study period. They do not remark on whether patients were enrolled consecutively, but I would assume there were probably quite a few more cases of pneumonia diagnosed across multiple institutions in that study period than were included in the final analysis.

There was also some subjectivity in the enrollment. Patients could not have been included if they had a severe cough. Who decided whether the cough was severe and did they have some objective measure? They also used tachypnea to exclude patients. Measuring tachypnea is well known to be inaccurate and lack inter-rater reliability [5-7]. These factors may lead to some selection bias.

2. Included Patients: Patients included in this study were relatively healthy from 6 months to 71 months of age. We need to be cautious when extrapolating the results to children with underlying conditions or outside those age ranges.

3. Outcomes: We need to say a few things about the outcomes in this trial

- **Complicated:** Their primary outcome was a composite outcome which can make a fuzzier target. It was also a little hard to interpret.
- **ClinicalTrials.gov Data** – We should applaud the authors of this study for reporting the primary and secondary outcomes that they originally proposed. It is still surprising the number of published research trials in which the reported outcomes differ from the proposed outcomes.

Time to Talk Nerdy:

- **DOOR Score:** The DOOR score evaluated patient-oriented outcomes, specifically clinical response, persistence of symptoms, and adverse effects from antibiotic therapy. We acknowledge that these have a degree of subjectivity including grading of cough severity and adverse effects of antibiotic therapy.
- **Resistomes:** A subgroup of the patients had throat swabs to assess for antibiotic resistance genes (ARGs) expressed as resistance genes per prokaryotic cell (RGPC). The authors reported that there were significantly lower RGPCs in the group that had short-course therapy in comparison to standard therapy. This is a lab-oriented outcome that brings up a few questions: Does this assessment of respiratory flora from a throat swab really correlate with what is happening in the lungs? What does a difference of 1.17 vs 1.33 mean clinically if anything? Is this going to be a persistent change?

4. Diagnosis of Pneumonia: All the patients included in this study were previously diagnosed with CAP in an outpatient clinic, urgent care centre, or emergency department. Unfortunately, we do not know how the diagnosis of pneumonia was made. Was it by clinical exam findings? Chest radiograph? Respiratory cultures? How accurate were these diagnoses? However, it is a practical approach and does probably reflect clinical practice.

5. Bacterial vs. Viral Pneumonia: Currently, we do not have a reliable way to discriminate between bacterial and viral pneumonia. It is quite possible that a portion of the patients included in this study did not have a bacterial etiology for their pneumonia, so patients may have recovered completely without any antibiotic therapy.

Time to Talk Nerdy:

I am all for antibiotic stewardship and look forward to a study that includes a group receiving zero days of antibiotics. We have been informed by Dr. Nathan Kupperman (Dr. PECARN) that they are conducting an RCT comparing 7 days to 0 days of out-patient antibiotics in pediatric patients with CAP and low procalcitonin.

Comment on Authors' Conclusion Compared to SGEM Conclusion: This superiority study suggests that a 5-day course of antibiotic therapy for non-severe CAP is superior to a standard 10-day course. However, it is possible that a portion of participants did not have a bacterial etiology for their pneumonia to begin with.

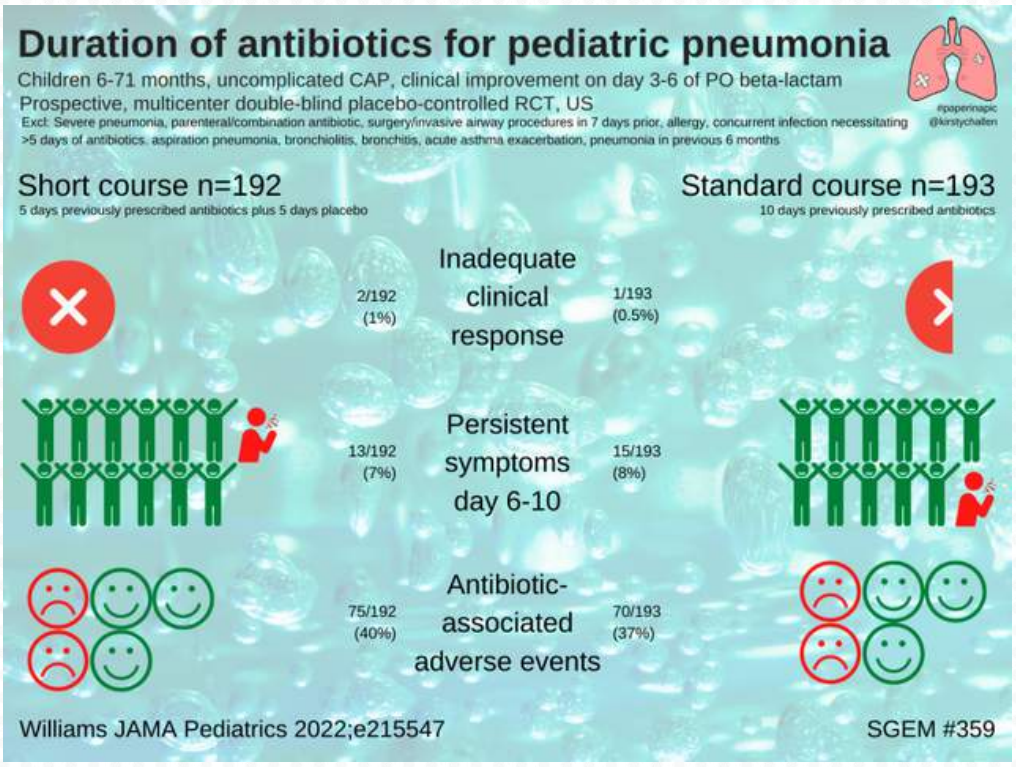
Clinical Application: For well-appearing children diagnosed with CAP and treated with outpatient antibiotics, we may consider a shorter course treatment of antibiotics with close follow up. We look forward to future research that may help us identify low-risk children with CAP who may not need antibiotics at all.

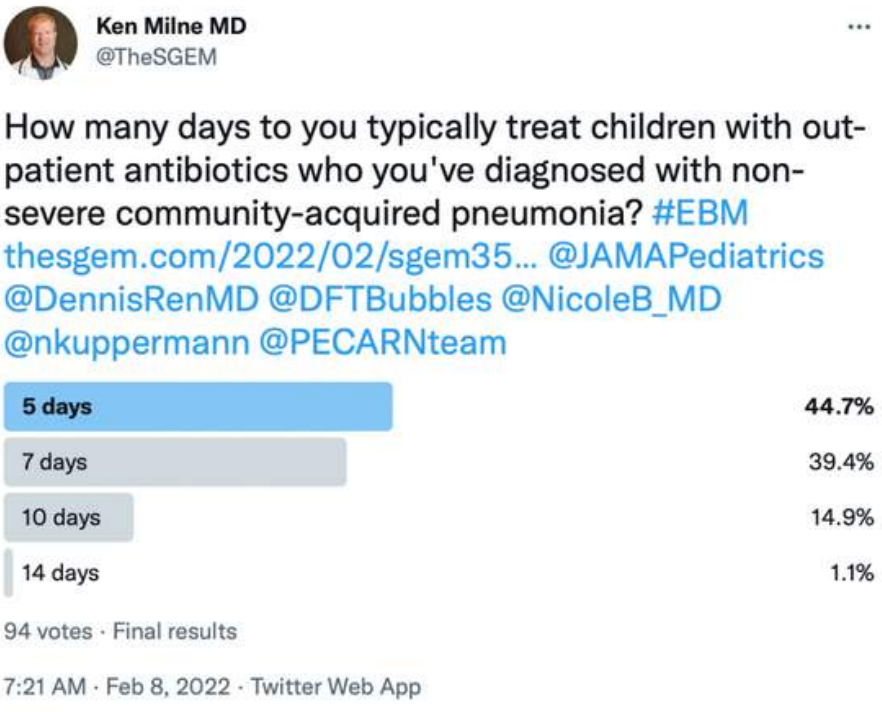
What Do I Tell My Patient? You reply to the mother, "I understand your concern. I believe we share the same goal in making sure your child's pneumonia is treated while minimizing any possible side effects. There is evidence to suggest that a 5-day course of antibiotics may be just as effective with fewer side effects. I feel comfortable doing that as long as you follow up closely with your son's pediatrician or primary care clinician. Please return to the emergency department if you feel like his symptoms are getting worse."

Case Resolution: You consider the mother's question for a moment and agree to a shorter course of antibiotics and counsel her to follow up closely with her child's pediatrician or primary care clinician.

FOAMed Resources:

- Don’t Forget the Bubbles: How long should we treat children with pneumonia for?- the results of CAP-IT,
- REBEL EM: The CAP-IT Trial: Amoxicillin Dose and Duration in Children with Community-Acquired Pneumonia
- REBEL EM: The SAFER Trial: Pediatric CAP-Amoxicillin 5 days vs 10 days
- CHOP PEM: Episode 13: Pneumonia
- Pediatric EM Morsels: Pediatric Pneumonia





360

WE CARE A LOT – THE EMPATH STUDY

Clinical Question:

Does the implementation of a dedicated interdisciplinary unit for mental health patients ppresenting to an ED with suicidal ideation or a suicide attempt reduce inpatient admissions and ED boarding time?

Bottom Line:

The emPATH unit has been helpful in this setting in Iowa but generalisability will depend on how similar other centers are to the one studied

Guest:

Dr. Kirsty Challen (@KirstyChallen) is a Consultant in Emergency Medicine and Emergency Medicine Research Lead at Lancashire Teaching Hospitals Trust (North West England). She is Chair of the Royal College of Emergency Medicine Women in Emergency Medicine group and involved with the RCEM Public Health and Informatics groups. Kirsty is also the creator of the wonderful infographics called #PaperinaPic.

Case Overview:

You are in discussion with your emergency department (ED) manager about the number of patients boarding for hours to days and you are both aware that many of these patients are attending with mental health crises. You wonder whether a model of care involving a specifically designed unit would improve their patient experience and ED boarding times.

Background:

We have covered mental health issues only a few times on the SGEM. The latest SGEM Xtra was a very powerful episode with Dr. Tim Graham sharing his story of burnout, anxiety, and depression. This was based upon his article published in the Canadian Medical Association Journal (CMAJ). We also had Dr. Tyler Black on that episode to provide his expertise as a suicidologist.

ED visits in the US for mental health conditions has increased by 44% from 2006 to 2014. Inadequately resourced provision for emergency mental health care is familiar to health care professionals in multiple jurisdictions and patients can spend days in the ED waiting for inpatient admission.

We've talked about mental health issues in SGEM #252 in 2019. In that episode we concluded that clinician gestalt was likely to be as accurate and efficient in screening for suicidality as a specific tool (Convergent Functional Information for Suicidality screening tool). Also, in SGEM #313 we recognised that three or more ED attendances for alcohol-related issues was associated with a 1-year mortality risk of over 6%.

Background:

Reference: Kim et al. Emergency psychiatric assessment, treatment, and healing (EmPATH) unit decreases hospital admission for patients presenting with suicidal ideation in rural America. AEM February 2022.

P

Population: Adults presenting to a single academic tertiary referral ED in Iowa with suicidal ideation or after a suicide attempt – determined using administrative data..

- **Excluded:** Patients that were medically unstable, needed co-management of a medical condition, were incarcerated, actively violent or judged by the provider to be intoxicated. Also, patients with mental health conditions other than suicidal ideation or attempt.

I

Intervention: Post-establishment of EmPATH unit Nov 2018 – May 2019.

C

Comparison: Pre-establishment of EmPATH unit Nov 2017 – May 2018.

- **Primary Outcome:** Proportion of patients admitted to inpatient psychiatric unit (direct from ED, via EmPATH Unit or by transfer).
- **Secondary Outcomes:** Any admission including psychiatry, intensive care, or medicine; complete vs incomplete psychiatric admission; hospital length of stay in those with a bed requested; ED length of stay; use of restraints in ED, scheduled follow-up, 30-day ED return; restraint use; code green

This is an SGEMHOP episode which means we have the lead author on the show (Dr. Kim). And as a special treat we also have the senior author (Dr. Lee).

Dr. Allie Kim graduated from emergency medicine residency at the University of Iowa last July and now works as an attending physician at Unity Point Health hospitals in Des Moines, Iowa. We also have senior author Dr. Sangil Lee who is a Clinical Associate Professor of Emergency Medicine at the University of Iowa.

The state of Iowa has only a handful of inpatient psychiatric units. The University of Iowa, where the EmPATH unit was implemented, is one of them. We see patients from all over the state, plus even out of state, and with the increase in numbers of mental health presenting to our emergency department, the sheer percentage of our patients needing inpatient psychiatric care was high. And, as many of us have seen, patients may wait in their ER bed for days until an inpatient bed became available. This "boarding" of patients delayed their psychiatric care and left less room for us to see other patients.

The EmPATH program we created, in conjunction with the Department of Psychiatry, is an open concept unit with the capacity to treat 12 adults. Patients must be medically cleared first in the ED, and also be behaviorally appropriate, to enter the EmPATH unit. Once in the unit, there are psychiatrists, nurses, and social workers to help patients. Average stay is about two days and most patients go home after stabilization there; however, if they need additional time, they can be transferred to the inpatient psychiatry unit.

Authors' Conclusions

"The introduction of the EmPATH unit has improved management of patients presenting to the ED with suicidal attempts/ideation by reducing ED boarding and unnecessary admissions and establishing post-ED follow-up care."

Quality Checklist for Observational Study

- [x] 1. Did the study address a clearly focused issue?
- [x] 2. Did the authors use an appropriate method to answer their question?
- [x] 3. Was the cohort recruited in an acceptable way?
- [x] 4. Was the exposure accurately measured to minimize bias?
- [x] 5. Was the outcome accurately measured to minimize bias?
- [ ] 6. Have the authors identified all-important confounding factors?
- [x] 7. Was the follow up of subjects complete enough?
- [ ] 8. How precise are the results? Fairly precise for the primary outcome
- [x] 9. Do you believe the results?
- [?] 10. Can the results be applied to the local population?
- [x] 11. Do the results of this study fit with other available evidence?
- [ ] 12. Funding of the study? Department seed grant

Results

Key Results:

- There were 435 patients included in the pre-EmPATH stage and 527 patients included in the post-EmPATH stage. This gives a total cohort size of 962 patients presenting to the ED with suicidality. The median age was 32 years, it was close to a 50/50 male/female split, almost two-thirds arrived as walk-ins with the rest being by EMS or police, and 13% were identified as homeless.

- **Primary Outcome:** Proportion of patients admitted to inpatient psychiatric unit (direct from ED, via EmPath Unit or by transfer).
  - 57.1% in the pre-EmPATH stage vs 27.3% in the post-EmPATH stage
  - Absolute difference of 29.8% and RR = 0.48 (95% CI = 0.40 to 0.56)
- **Secondary Outcomes:**
- ED boarding time was reduced from a mean of 16 hours to a mean of 5 hours

TABLE 2 Outcomes before and after EmPATH implementation

Outcomes	Pre-EmPATH implementation	Post-EmPATH implementation	Relative risk/β[a]	95% CI
Primary outcome: psychiatric admission	248 (57.1)	144 (27.3)	0.48	0.40 to 0.56
Primary outcome: any admission[b]	282 (65.0)	223 (42.3)	0.65	0.58 to 0.73
Secondary outcome: hospital LOS (days)				
Overall	21.2 (±81.2)	7.3 (±21.3)	−0.12	−0.29 to 0.06
Completed admission[c]	29.8 (±98.1)	8.0 (±22.1)	−0.21	−0.40 to −0.02
Incomplete admission[c]	6.8 (±24.0)	0.6 (±0.7)	−0.78	−1.96 to 0.40
Secondary outcome				
ED boarding time (h)				
Overall	16.2 (±15.6)	4.9 (±7.8)	−1.11	−1.23 to −0.99
Completed admission[c]	15.2 (±14.8)	4.7 (±7.6)	−1.08	−1.20 to −0.95
Incomplete admission[c]	20.4 (±18.5)	8.4 (±12.2)	−0.99	−1.48 to −0.50
Incomplete admission[c]	64 (14.7)	19 (3.6)	0.22	0.11 to 0.43
Restraint use in the ED	12 (2.8)	20 (3.8)	1.37	0.66 to 2.85
Code green in the ED	17 (3.9)	24 (4.6)	1.00	0.98 to 1.01
30-day return to ED	88 (20.3)	80 (15.2)	0.75	0.57 to 0.99
30-day follow-up scheduled	171 (39.4)	333 (63.2)	1.60	1.40 to 1.83

Time to Talk Nerdy:

1. **Retrospective Observational Study –** You acknowledge this as your first limitation. Why do you think it is important to caution readers about this type of study design?
2. **Administrative Data –** You used administrative data (admitting diagnosis) to identify the patients to include in this study. Particularly with patients presenting after suicide attempt, who may have a diagnosis involving injury or poisoning, how sure are you that you can capture all these?
3. **Before and After Study –** This was an uncontrolled before and after observational study. An editorial in the EBM_BMJ by Goodacre cautions against these types of studies.
4. **Stepped Wedge Design –** One way to address this limitation of uncontrolled before and after study design would be to perform a stepped wedge design. A multi-centred cluster RCT would provide more robust information. Have you considered this as a future project?
5. **Single Centre –** That is a great Segway into another nerdy point. This was a single center study. How representative is your center of US EDs in general and academic EDs in particular?
6. **Confounders –** We mentioned in the quality checklist that you haven't presented rates of substance misuse or previous psychiatric diagnosis in the paper. Do you think they have changed or might have had an effect on the EmPATH unit?
7. **Washout –** You had a washout period from May – Nov 2018. Can you explain to listeners why this was important for your study design and what was happening in the ED and EmPATH units during that time?

Time to Talk Nerdy:

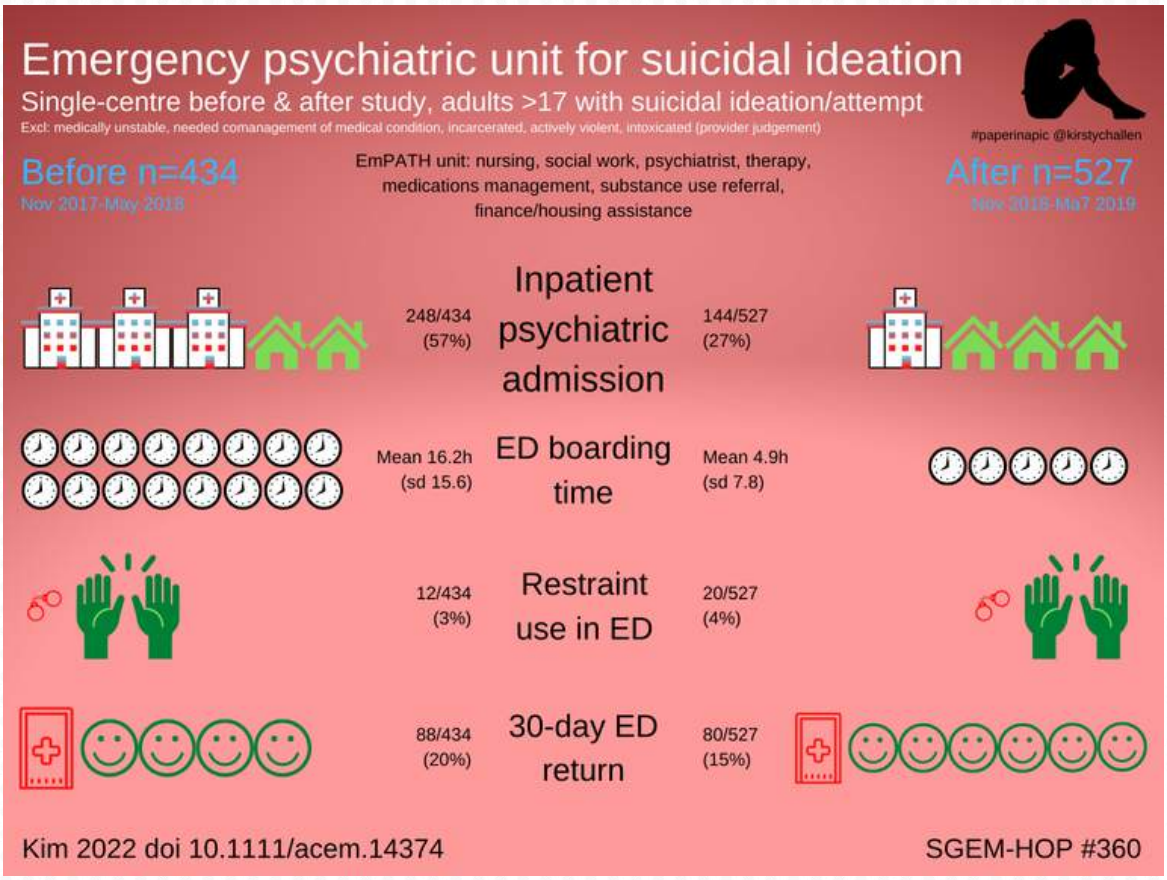
8. Length of Stay – In the United Kingdom they have a goal to try to disposition emergency department patients within 4 hours. The decrease ED length of stay (LOS) decreased from 16 hours down to 5 hours. If confirmed, this could make a significant impact on ED flow. However, the total hospital LOS for patients who had a psychiatric bed request placed did not change with the implementation of EmPATH. Might you just be shifting the boarding problem from the ED to EmPATH, or do you think patients still benefit from the wider scope of care provided in the EmPATH unit?

9. **Long-Term Data –** Why did you not follow-up on the long-term patient outcome such as suicide related using national data as you had done in previous studies?

10. **Anything Else –** Is there anything else you would want the SGEM listeners to know about your research that we have not asked or was not published in the manuscript?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree that in this case the EmPATH unit has been associated with a reduction in psychiatric admissions and ED boarding times.

Clinical Resolution and Clinical Application: You agree with your manager that you need to look more closely at your local data to work out what are the rate-limiting steps locally, and then to address them with your psychiatric and social work teams.



@TheSGEM

Would your ER benefit from an EmPATH Unit?
thesgem.com/2022/02/sgem36... #SGEMHOP
@SAEMonline @KirstyChallen @AcademicEmerMed
@AliRaja_MD @meganranney

Yes	19.5%
No	3.8%
What's an EmPATH Unit?	**76.7%**

159 votes · Final results

361

UNDER MY UMBRELLA, ELLA, ELLA – REVIEW OF META-ANALYSES IN EMERGENCY MEDICINE

Clinical Question:

What is the effect of faults such as underpowered studies ,flawe studies (i.e. methodological and statistical errors, poorly designed studies) and biases in the field of therapeutic interventions in the emergency medicine literature?

Bottom Line:

Many interventions in Emergency Medicine are not supported by high-quality, unbiased evidence

Guest:

Professor Daniel Fatovich is an emergency physician and clinical researcher based at Royal Perth Hospital, Western Australia. He is Head of the Centre for Clinical Research in Emergency Medicine, Harry Perkins Institute of Medical Research; Professor of Emergency Medicine, University of Western Australia; and Director of Research for East Metropolitan Health Service.

Case Overview:

A resident has been following the literature over their four years of training. They have already seen several things come into fashion and go out of fashion during this short time. This includes therapeutic hypothermia for out-of-hospital cardiac arrest (OHCA), tranexamic acid (TXA) for epistaxis and electrolyte solutions for mild pediatric gastroenteritis. They wonder how strong the evidence is for much of what we do in emergency medicine.

Background:

There are many things in medicine that could be considered myth or dogma. We have covered some of these over the 10 years.

- Topical anesthetic uses of 24-48 hours for mild cornea abrasions will cause blindness- No (SGEM# 315)
- Epinephrine for adult out-of-hospital cardiac arrests (OHCAs) results in better neurologic outcomes – No (SGEM#238)
- TXA for intracranial hemorrhage, isolated traumatic brain injury, post-partum hemorrhage or gastrointestinal bleed results in better primary outcomes – No (SGEM#236, SGEM#270, SGEM#214, and SGEM#301)
- Therapeutic hypothermia in adult OHCA saves lives – No (SGEM#336)
- Electrolyte solutions are needed in mild pediatric gastroenteritis – No (SGEM#158)

A lot of medical practice is based on low quality research. Tricoci et al. JAMA Feb 2009 looked at the ACC/AHA guidelines from 1984 to 2008. They found 53 guidelines with 7,196 recommendations. The results were only 11% of recommendations were considered Level A, 39% were Level B and 50% were Level C.

Background:

The definitions used for each level of evidence are as follows:

Level of Evidence	Description
Level A	Supported by data from multiple RCTs or a single, large RCT
Level B	Supported by data from observational studies or a single RCT
Level C	Supported by expert opinion only

An update was published by Fanaroff et al in JAMA 2019. The level of high-quality evidence had not changed much when looking at the ACC/AHA guidelines from 2008-2018. There were 26 guidelines with 2,930 recommendations. Now Level A recommendations were down to 9%, Level B 50% and Level C 41%.

This lack of evidence is not isolated to cardiology. A recent study looked at the top ten elective orthopaedic procedures. It was an umbrella review of meta-analyses of randomized control trials (RTCs) or other study designs if no RCTs existed (Blom et al BMJ 2021). The comparison was the clinical efficacy of the most common orthopaedic procedures with no treatment, placebo, or non-operative care. The primary outcome was the quality of the evidence for each procedure. Only two out of ten common procedures, carpal tunnel decompression and total knee replacement, showed superiority over non-operative care.

Common elective orthopaedic procedures and indications	
Procedure	Main indication
Arthroscopic anterior cruciate ligament reconstruction	Anterior cruciate ligament rupture
Arthroscopic meniscal repair of the knee	Traumatic meniscal tears
Arthroscopic partial meniscectomy of the knee	Degenerative meniscal tears
Arthroscopic rotator cuff repair	Acute rotator cuff tears
Arthroscopic subacromial decompression	Subacromial impingement syndrome
Carpal tunnel decompression	Carpal tunnel syndrome
Lumbar spine decompression	Spinal canal stenosis
Lumbar spine fusion	Degenerative disc disease
Total hip replacement	End stage osteoarthritis
Total knee replacement	End stage osteoarthritis

Background:

Reference: Parish et al. An umbrella review of effect size, bias, and power across meta-analyses in emergency medicine. AEM 2021

P

Population: SRMAs 1990-2020 in the top 20 journals under the google scholar subcategory: emergency medicine; emergency medicine meta-analyses from JAMA, NEJM, BMJ, The Lancet, and the Cochrane Database of Systematic Reviews; emergency medicine topics across all PubMed journals; and an extraction of all studies from the Annals of Emergency Medicine Systematic Review Snapshots (SRS) series.

- **Exclusions:** Articles were excluded if they did not include a quantitative synthesis (meta-analysis); did not contain at least two summarized studies; did not make a comparison between two groups to assess an effect size; did not report an effect size as at least one of mean difference or standardized mean difference (SMD; Cohen's d), odds ratio (OR), risk ratio (RR), hazard ratio (HR), or transformations of these effect sizes; were meta-analyses of diagnostic accuracy studies; or were not related to the practice of emergency medicine.

I

Intervention: Data supplement 1 lists all 431 MAs derived from 332 published SRMAs.

C

Comparison: Includes placebo, usual care, nothing.

Identify broad patterns in study parameters (effect size, power, mortality benefit and potential bias).

We are fortunate to have the lead author on this episode even though it is not an SGEMHOP. Dr. Austin Parish is the Chief Resident in Emergency Medicine at the Lincoln Medical Center, Bronx NY. He is also a researcher for the Meta Research Innovation Center at Stanford (METRICS)

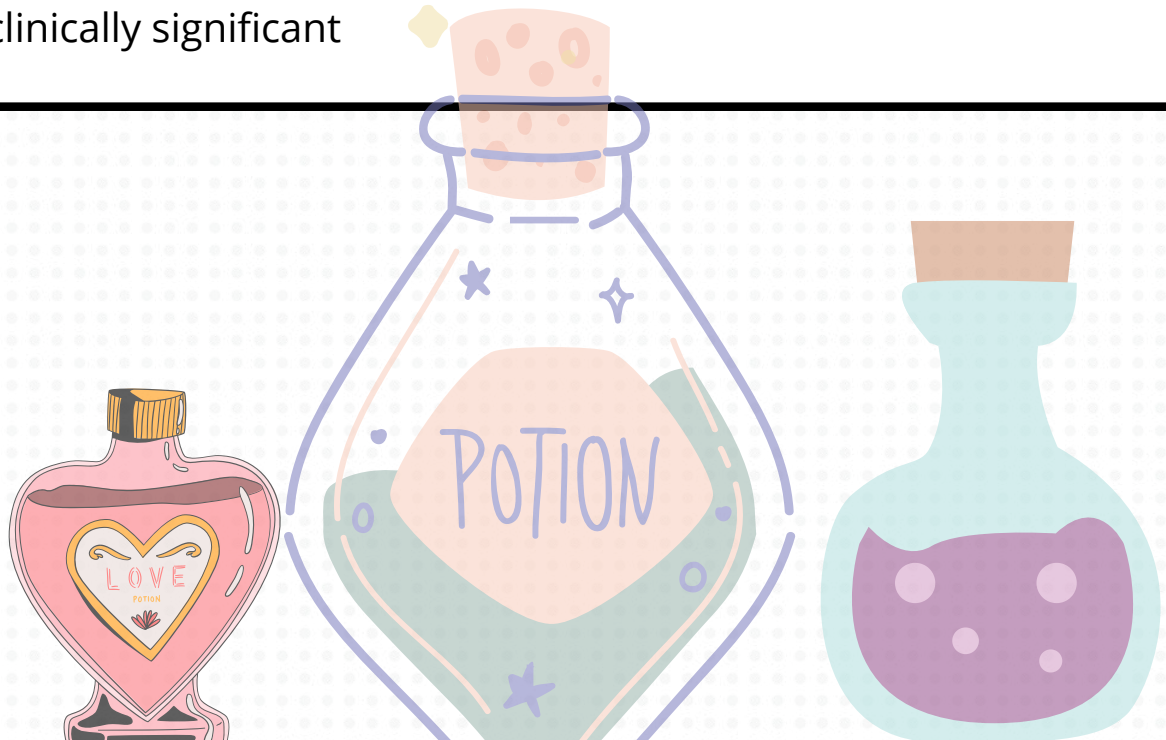
Authors' Conclusions

"Few interventions studied within SRMAs relevant to emergency medicine seem to have strong and unbiased evidence for improving outcomes. The field would benefit from more optimally powered trials."

Quality Checklist for Therapeutic Systematic Reviews

- ☑ 1. The clinical question is sensible and answerable
- ☑ 2. The search for studies was detailed and exhaustive
- ☒ 3. The primary studies were of high methodological quality
- ☑ 4. The assessment of studies were reproducible
- ☑ 5. The outcomes were clinically relevant
- ☒ 6. There was low statistical heterogeneity for the primary outcomes
- ☐ 7. The treatment effected was large enough and precise enough to be clinically significant

Sometimes



Results

Key Results:

- The systematic review identified 431 eligible meta-analyses (MAs) relevant to emergency medicine. The MAs included a total of 3,129 individual study outcomes of which 2,593 (83%) were from randomized controlled trials.

- **Primary Outcome:** Broad patterns in study parameters
  - Effect Size: The median Odds Ratio (OR) across all studies was 0.70. Within each MA, the earliest study effect on average demonstrated larger benefit compared to the overall summary effect. Only 57 of 431 meta-analyses (13%) both favored the experimental intervention and did not show any signal of small study effects or excess significance.
  - Power: Only 12 of 431 MAs had at least one study with 80% or higher power to detect an OR of 0.70
  - Mortality: Zero out of 431 MAs reported the interventions significantly decreased mortality in well-powered trials. Although the power of studies increased somewhat over time, most studies were underpowered.
  - Biases: 92 of the SRMAs included 10 or more studies that could be analyzed with a funnel plot for asymmetry. 25% (23/92) showed evidence of asymmetry suggesting excess significance. 85 (20%) of the SRMAs reported statistical significance in favor of the intervention. Of these, 1/3 showed a signal of small study effect and/or excess significance while 2/3 (57/85) did not. Of the 57, only 36 (63%) had a GRADE assessment reported. Half were rated as low-quality evidence and only 11% rated as high-quality evidence.

Time to Talk Nerdy:

1. How Good is the Evidence? I've often posed the question: what proportion of our EM clinical practice is backed up by high level evidence? After speaking with thought leaders the answer I got to was less than 10%. This umbrella review quantifies the answer in more detail: 12/431 = 2.8%. There is not a large amount of high-level evidence supporting most EM practices. The results demonstrate that very few interventions meet the highest evidence standards, and most of the SRMAs are significantly flawed and may overstate true treatment effects. So, we need to advance our knowledge and practice through never ending questioning of it, via a research culture, whereby clinical trials and clinical research are a routine part of everyday EM work, research that engages clinicians and patients with clinically useful questions – to be a learning health system. What is the proportion of our EM clinical practice is backed up by high level evidence?

2. The Best Evidence: Table 1 in the paper lists the 12 MAs in EM that have statistically significant results ($p < 0.05$ by random effects), based on data with no signal for small study effects or excess significance and at least one RCT and at least one study with 80% power to detect a small effect ($d = 0.2$). The biggest effect of an intervention was the rate of haemolysis using straight needle venepuncture vs an IV; OR 0.11(95%CI; 0.05-0.23).

Of the 12 MAs, only another three had a 95% confidence intervals that did not cross 1 (the line of no statistical difference), for well powered studies (fixed effect): senior doctor vs no senior doctor in triage for preventing patient left without being seen (OR 0.74, 95% CI; 0.70-0.77); clopidogrel pre-treatment vs no clopidogrel pre-treatment in acute coronary syndrome patients to receive percutaneous intervention (OR 0.79, 95% CI; 0.73-0.85) for a major coronary event; glucocorticoids and usual care vs usual care for croup (OR 0.44, 95% CI; 0.27-0.72) on

on rate of return visits.

While there were no mortality benefits listed under fixed effect, well powered studies, under the heading of random effects, all studies – there were some mortality benefits for mechanical CPR, transfer for angioplasty, thrombolysis for PE and vasopressin + catecholamines. The details will be listed in the blog.

- Mechanical CPR vs manual CPR for OHCA on mortality by arrival to hospital (OR 0.80, 95% CI; 0.68-0.94);
- Transfer for angioplasty vs on site thrombolysis for ST elevated myocardial infarction on 30-day mortality (OR 0.78, 95% CI; 0.61-0.99);
- Thrombolysis vs conventional anticoagulation for pulmonary embolism (OR 0.42, 95% CI; 0.19-0.93);
- Vasopressin and catecholamines vs catecholamines alone on 30-day mortality (OR 0.74, 95% CI; 0.58-0.).

What should we make of the lack of high-quality evidence for what we do in EM?

3. Robust: The statistical results were not robust: most of the statistically significant results were near the $P < 0.05$ threshold and using a more stringent type 1 error acceptance rate of $P < 0.005$ would make <10% of all MAs "*positive*". Among studies with lower risk of bias, the effect sizes further decreased and/or disappeared. Furthermore, most of these MAs were grossly underpowered, thus leading to continued ambiguity.

We would expect the p-values to cluster just below 0.05 due to publication bias. Those studies reaching this low bar are more likely be published than those that do not reach statistical significance

(Hopewell et al 2008, Sune et al 2013 and Dwan et al 2013). How do you think we could make results in EM research more "robust"?

4. Thrombolysis: One of our "*favourite*" topics is thrombolysis for stroke, so I was interested to see what was reported in the umbrella review. Appendix S2 lists the topics of redundant MAs found in the EM literature. The total number of MAs on this subject was 3. The data supplement 1 on this subject only lists the Donaldson et al 2016 SRMA.

The conclusion from that SRMA was: *"The available data are unlikely to resolve the controversy regarding the use of intravenous thrombolysis in this population, and further randomised controlled trials are urgently required."* This topic of thrombolysis vs no thrombolysis for stroke did not make it into table 1 (the adequately powered studies). What are your thoughts on thrombolysis for AIS?

5. Philosophical Approach to the Literature: While we think the methods and results are the most important elements of a paper, sometimes we come across a discussion that articulates the subject so emphatically well that it's worth highlighting. Many of these concepts have been promoted by our mentor Dr. Jerry Hoffman for years.

Here are some of the concepts mentioned in your paper that we would like you do comment further upon:

Time to Talk Nerdy:

"early results need to be seen with caution, as the postulated treatment benefits may diminish with additional evidence."
"given that some harms are also recognised only after substantial time has elapsed, a vigilant approach to early evidence about new interventions is warranted."

"Claims of significance dependent on statistical thresholds depend on what threshold is chosen and it should be remembered that statistical and clinical significance have some overlap but may be different entities."

"Few emergency medicine interventions seem to have convincingly strong evidence and interventions that save lives in randomized trials. Some interventions apparently save lives and have such dramatic effects that they are never subjected to randomized trials. (These interventions may include in the acute setting insulin for diabetic ketoacidosis, blood transfusion for severe hemorrhagic shock, defibrillation for ventricular fibrillation, neostigmine for myasthenia gravis, tracheostomy for tracheal obstruction, suturing for repair of large wounds, pressure or suturing for stopping hemorrhage, and one-way valve or underwater seal drainage for pneumothorax and hemothorax). However, these interventions are very few and the vast majority of emergency medicine interventions do require randomized trial evaluations."

Time to Talk Nerdy:

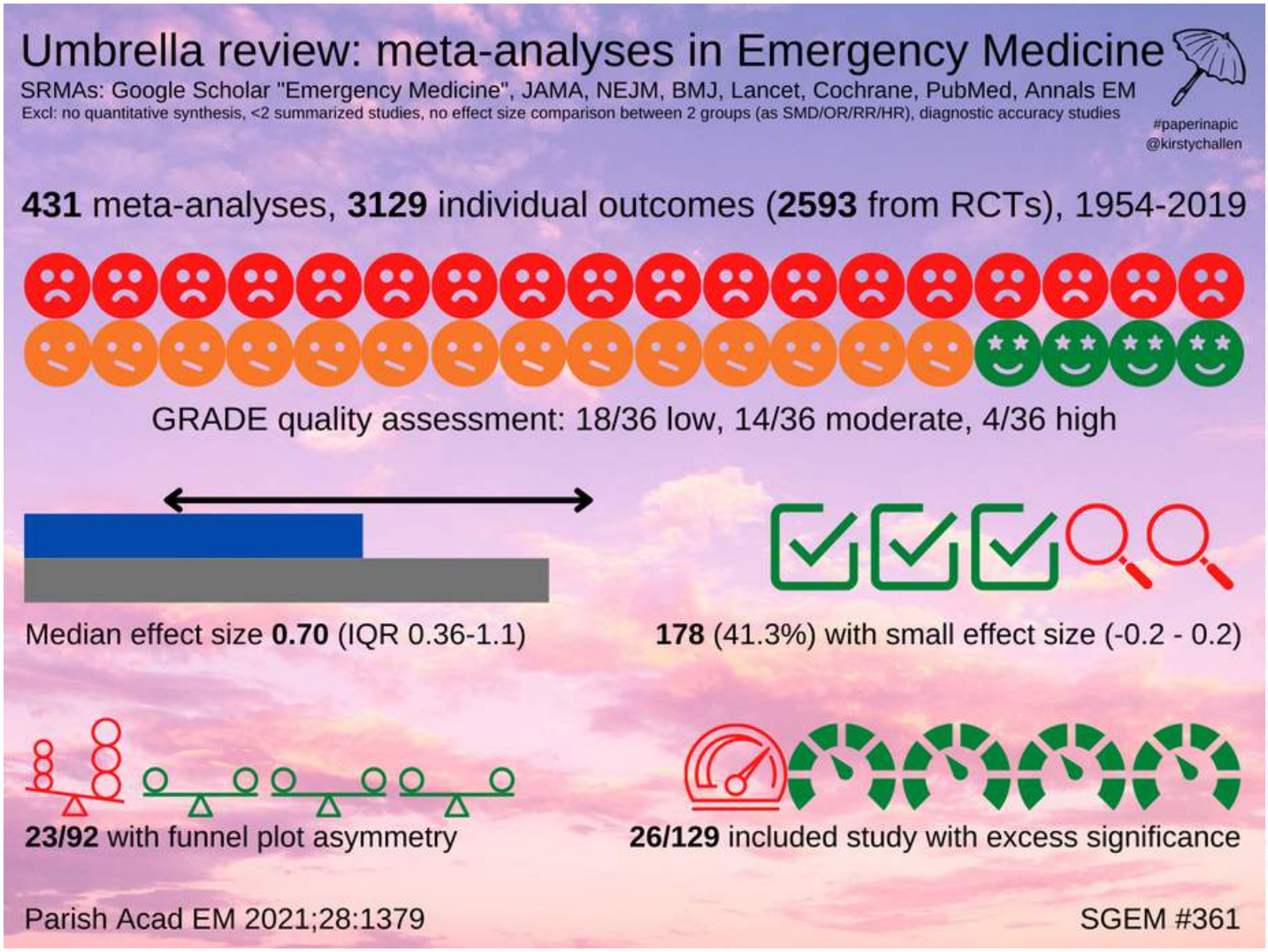
Most medical interventions are not parachutes (Hayes et al CMAJ 2018). It is ethical to perform proper RCTs to ensure patients get the best care, based on the best evidence. Remember that bloodletting used to be the standard of care until an RCT in 1809 challenged that practice and demonstrated an NNT for death with bloodletting of 4 (SGEM#200).

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors of the paper that we need to promote further research on interventions in EM.

Clinical Application: The literature guides and informs our care but should not dictate are care. There are few interventions in EM with high-quality, unbiased evidence. We still need to apply our clinical judgement and ask the patients about their values and preferences. “It is instructive to note that most people make patient-centred decisions every day without high-quality (eg RCT) evidence, and these decisions are not always wrong. Furthermore, foundational papers in EBM make it explicitly clear that EBM was never meant to exclude information derived from experience and intuition.” (Braithwaite RS. JAMA 2013).

What Do I Tell the Resident? Much of what we do in emergency medicine based upon low-quality biased evidence. We are often standing on pillars of salt and sand. Stay skeptical, develop your critical appraisal skills and try to avoid nihilism.

Case Resolution: You discuss scientific skepticism with the resident. Remind them that each claim needs to be supported by evidence and logical arguments. Without high-quality evidence we should usually accept the null hypothesis. That does not mean an intervention could not work. Rather, we do not have good evidence that it does work. This is an important distinction.



Ken Milne MD
@TheSGEM

What proportion of EM clinical practice do you think is backed up by high level evidence? #EBM thesgem.com/2022/03/sgem36... @CCREM2 @srrezaie @KirstyChallen @EMManchester @richardbody @SAEMEBM @MDaware @AliRaja_MD @LWestafer @broomedocs @EMSwami

<10%	33%
10-30%	**43.7%**
31-50%	15.3%
>50%	7.9%

215 votes · Final results

362

SCREEN TIME – CAN'T TAKE MY EYES OFF OF YOU – BUT SHOULD I POST-CONCUSSION?

Clinical Question:

Does screen time in the first 48 hours after concussionhave an impact on the duration of concussive symptoms?

Bottom Line:

We do not know what impact screen times has on post-concussion symptoms.

Guest:

Dr. Catherine Varner is an Assistant Professor and Clinician Investigator in the Department of Family and Community Medicine at the University of Toronto. She is an emergency physician at Mount Sinai Hospital and a Clinician Scientist and the Deputy Director of the Schwartz-Reisman Emergency Medicine Institute. Dr. Varner's research interests are in concussion and pregnancy care in the ED.

Case Overview:

An 18-year-old female presents to the emergency department (ED) after falling off a moving snowmobile and hitting her head on the ground. It was a witnessed fall; she was wearing a helmet at the time and there was no loss of consciousness. There were no other injuries reported and she is found to have a GCS score of 15 after the injury. The Acute Concussion Evaluation–Emergency Department (ACE-ED) Tool is used, and she scores a 2 for headache and feeling foggy. She knows about taking it easy physically for the next couple of days but wonders if she must stay off her computer as well?

Background:

Concussions or mild traumatic brain injury (mTBI) are commonly diagnosed in the Emergency Department (ED). Most patients recover within the first week; however, 15-30% of patients develop persistent post-concussive symptoms.

An issue that often comes up with minor head injuries is do we need to get advanced imaging. A paper by Dr. Ian Stiell and his group gave us a tool to help us decide who to scan with the now infamous clinical decision instrument called the Canadian CT Head Rule [1]. This classic paper was published in Lancet 2001 and reviewed on SGEM#106.

Another issue that comes up is whether children need strict rest after a concussion. SGEM#112 reviewed a small study by Thomas et al published in Pediatrics 2015 asking if there was a benefit to recommending strict rest after a child has a concussion [2]. The bottom line from that episode was that in children with concussion, two days of rest followed by a

Background:

gradual return to activity is preferred over five days of rest followed by a gradual return to activity. The longer strict rest period appears to cause more post-concussive symptoms.

Canadian CT Head Rule

CT head is only required for minor head injury patients with any one of these findings:

High Risk (for Neurological Intervention)

1. GCS score < 15 at 2 hrs after injury
2. Suspected open or depressed skull fracture
3. Any sign of basal skull fracture*
4. Vomiting ≥ 2 episodes
5. Age ≥ 65 years

Medium Risk (for Brain Injury on CT)

6. Amnesia before impact ≥ 30 min
7. Dangerous mechanism ** *(pedestrian, occupant ejected, fall from elevation)*

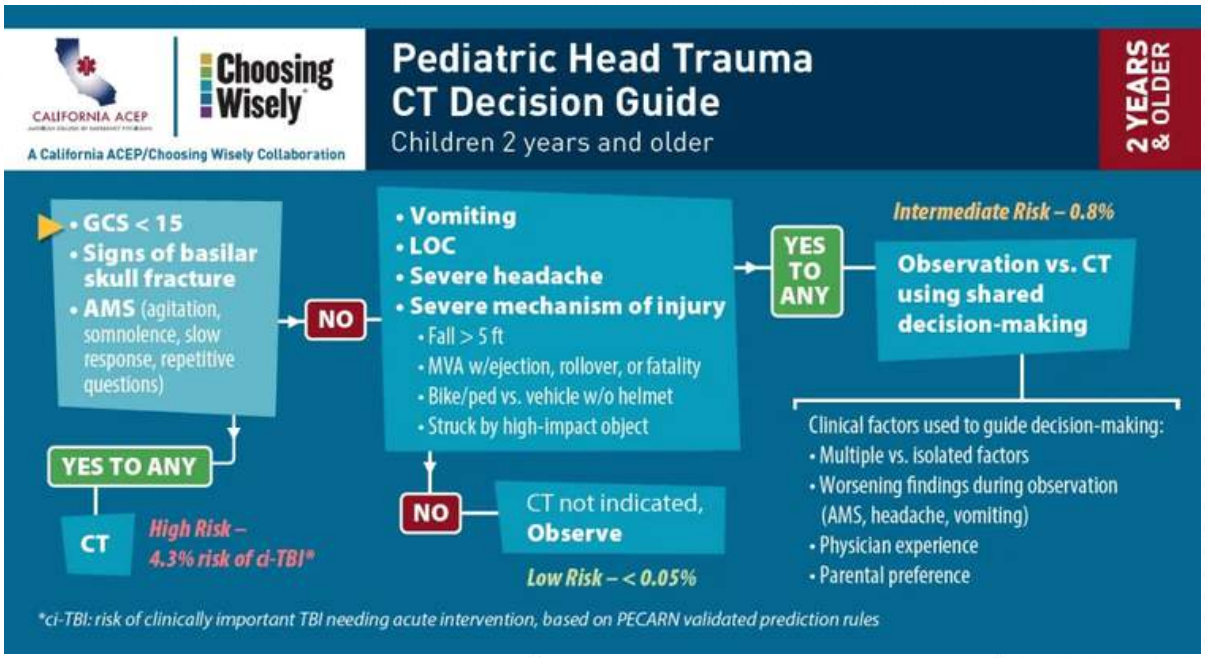
*Signs of Basal Skull Fracture
- hemotympanum, 'racoon' eyes, CSF otorrhea/ rhinorrhea, Battle's sign

** Dangerous Mechanism
- pedestrian struck by vehicle
- occupant ejected from motor vehicle
- fall from elevation ≥ 3 feet or 5 stairs

Rule Not Applicable If:
- Non-trauma cases
- GCS < 13
- Age < 16 years
- Coumadin or bleeding disorder
- Obvious open skull fracture

Stiell IG, et al. The Canadian CT Head Rule for Patients with Minor Head Injury. Lancet 2001;357:1391-96.

Background:



ACUTE CONCUSSION EVALUATION (ACE)

Emergency Department (ED) Version v1.4

Gerard Gioia, PhD[1] & Micky Collins, PhD[2]
[1]Children's National Medical Center
[2] University of Pittsburgh Medical Center

Patient Name_____
DOB: _____ Age:_____
Date:_____ ID/MR#_____

A. Injury Characteristics Date/Time of Injury_____ Reporter: __Patient __Parent __Spouse __Other_____

1. Injury Description _____

1a. Is there evidence of a forcible blow to the head (direct or indirect)? __Yes __No __Unknown
1b. Is there evidence of intracranial injury or skull fracture? __Yes __No __Unknown
1c. Location of Impact: __Frontal __Lft Temporal __Rt Temporal __Lft Parietal __Rt Parietal __Occipital __Neck __Indirect Force
2. **Cause**: __MVC __Pedestrian-MVC __Fall __Assault __Sports (specify)_____ Other_____
3. **Amnesia Before (Retrograde)** Are there any events just BEFORE the injury that you/ person has no memory of (even brief)? __Yes __No Duration_____
4. **Amnesia After (Anterograde)** Are there any events just AFTER the injury that you/ person has no memory of (even brief)? __Yes __No Duration_____
5. **Loss of Consciousness**: Did you/ person lose consciousness? __Yes __No Duration_____
6. **EARLY SIGNS:** __Appears dazed or stunned __Is confused about events __Answers questions slowly __Repeats Questions __Forgetful (recent info)
7. **Seizures**: Were seizures observed? No__ Yes___ Detail_____

B. Symptom Check List* Since the injury, has the person experienced any of these symptoms any more than usual today or in the past day?
Indicate presence of each symptom (0=No, 1=Yes). **Lovell & Collins, 1998 JHTR*

PHYSICAL (10)		COGNITIVE (4)		SLEEP (4)		
Headache	0 1	Feeling mentally foggy	0 1	Drowsiness	0 1	
Nausea	0 1	Feeling slowed down	0 1	Sleeping less than usual	0 1	N/A
Vomiting	0 1	Difficulty concentrating	0 1	Sleeping more than usual	0 1	N/A
Balance problems	0 1	Difficulty remembering	0 1	Trouble falling asleep	0 1	N/A
Dizziness	0 1	COGNITIVE Total (0-4)	____	SLEEP Total (0-4)	____	
Visual problems	0 1	EMOTIONAL (4)				
Fatigue	0 1	Irritability	0 1			
Sensitivity to light	0 1	Sadness	0 1			
Sensitivity to noise	0 1	More emotional	0 1			
Numbness/Tingling	0 1	Nervousness	0 1			
PHYSICAL Total (0-10) ____		EMOTIONAL Total (0-4)	____			
(Add Physical, Cognitive, Emotion, Sleep totals) Total Symptom Score (0-22)			____			

Other Observations
_____
_____
_____
_____
_____
_____
_____
_____

Patient Participation: Full__ Partial __ None __
Reason for Partial/None: Young Age__ Confused__ Inattentive__ Low arousal__ Emotional Upset__ In Pain__ Other_____

C. Concussion History: *Previous# 0 1 2 3 4 5 Date(s)*_____
Headache History: *Prior treatment for headache N___ Y___ Details*_____

D. Diagnosis (ICD): __Concussion w/o LOC 850.0 __Concussion w/ LOC 850.1 __Concussion (Unspecified) 850.9 __Other (854)_____
__No diagnosis

E. Follow-Up Action Plan _√_ **Referral to PCP for Office Monitoring** **MD Name**_____
___ Neuropsychological Testing (recommended for Return to Sport decisions and academic/ behavioral management)
___ Physician: Neurosurgery____ Neurology____ Sports Medicine____ Physiatry____ Psychiatry____
Other_____

Background:

Our episode together looked at the impact of light exercise in adults with mild concussions on the likelihood of developing persistent symptoms up to 30 days following their injury (SGEM#331). We found there was not a statistical difference between light activities like walking and 48 hours of rest with gradual return to activity as tolerated. Our conclusions were that early light exercise may be encouraged as tolerated at ED discharge following mTBI, but this guidance is not sufficient to prevent persistent concussion symptoms [3].

The Acute Concussion Evaluation–Emergency Department (ACE-ED) tool is an instrument used by ED clinicians to diagnose a concussion and identify risk factors for prolonged recovery. It is both helpful for diagnosis and future management of symptoms. When a patient is recovering from a concussion, whether you are using ACE or another symptom scoring tool like the Postconcussion Symptom Scale or the Rivermead Post-concussion Symptom Questionnaire, future health care providers caring for the concussion patient may refer to the quantitative assessment of the patient's symptoms in the acute phase of the injury.

Reference: Macnow et al. Effect of Screen Time on Recovery From Concussion: A Randomized Clinical Trial. JAMA Pediatrics 2021

P

Population: Patients aged 12 to 25 years presenting to the emergency department within 24 hours of sustaining a concussion according to the Acute Concussion Evaluation–Emergency Department (ACE-ED) tool (Giola et al 2008)

- Exclusions: Attending physician declined participation; their guardian was not present; the patient was younger than 18 years, or they (or their parent or guardian) were not fluent in English; intoxication; had a GCS score < 15; had intracranial abnormalities identified on imaging; had pre-existing intellectual disability, severe psychiatric illness, severe neurological conditions, or substantial previous neurological surgery; or required neurosurgical intervention, intubation, or hospital admission

I

Intervention: Patients were asked to abstain from screen time for 48 hours after injury. This was the screen time abstinent group.

C

Comparison: Patients were permitted to engage in screen time in the first 48 hours after injury. This was the screen time permitted group.

- **Primary Outcome:** Number of days until functional resolution of concussive symptoms, which was defined as the first day with a total score of three points or lower on the Post-Concussive Symptom Scale (PCSS)
- **Secondary Outcomes:** Amount of screen and sleep time during the intervention period, the day of return to school or work after the intervention period, the day of return to exercise after the intervention period, and daily PCSS scores.
- **Trial: S**ingle-centre, unblinded, randomized clinical trial

Authors' Conclusions

"The findings of this study indicated that avoiding screen time during acute concussion recovery may shorten the duration of symptoms. A multicenter study would help to further assess the effect of screen time exposure."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [?] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [ ] 12. Funding.

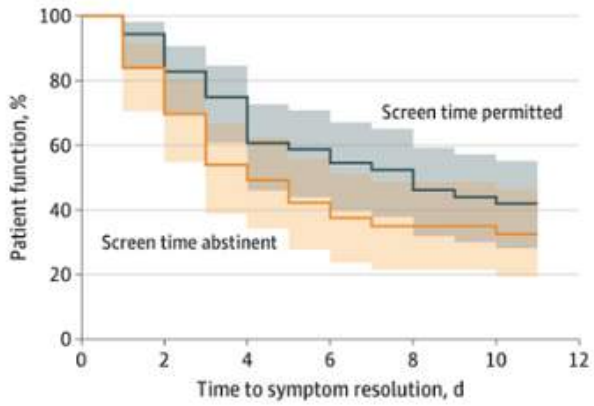
The stated conflicts of interests by the authors would not likely influence the conclusions of this trial.

Results

Key Results:

- They enrolled 125 patients into the study. The mean age was 17 years and 49% were female.
- **Primary Outcome:** Median number of days until functional resolution of concussive symptoms, which was defined as the first day with a total score of 3 points or lower on the Post-Concussive Symptom Scale (PCSS)
  - Abstained 3.5 days vs permitted 8.0 days
  - Hazard ratio [HR], 0.51 (95% CI; 0.29-0.90)

Figure 2. Kaplan-Meier Survival Curve Comparing Days Until Concussion Recovery of Screen Time Abstinent vs Screen Time Permitted Groups



No. at risk

Screen time permitted	53	49	37	28	25	21
Screen time abstinent	50	41	23	18	14	14

Days until concussion recovery defined as a daily Post-Concussive Symptom Scale score of 3 points or lower. Shading represents 95% CIs.

- **Secondary Outcomes:**

	Abstained	Permitted
Screen Time	130min (IQR 61-275)	630min (IQR 415-995)
Sleep Time	29 hours [IQR 24-34)	29 hours [IQR 22-32)
Return to School/Work	6.0 days (IQR 4.0-9.5)	7.0 days (IQR 5.0 to >10.0)
Return to Exercise	7.0 days (IQR 5.0 to >10.0)	8.0 days (IQR 4.0 to >10.0)

- Sensitivity analysis using different PCSS thresholds for recovery

Table 2. Comparison of Median Days to Recovery Between Patient Groups Based on Different Cutoff Scores on the PCSS

	Screen time permitted group		Screen time abstinent group	
PCSS cutoff score	Patients, No.	Median (IQR) d to recovery	Patients, No.	Median (IQR) d to recovery
≤1	48	9.5 (4.0 to >10.0)	42	6.5 (3.0 to >10.0)
≤3	47	8.0 (3.0 to >10.0)	44	3.5 (2.0 to >10.0)
≤6	42	8.0 (3.0 to >10.0)	41	4.0 (2.0 to >10.0)
≤7	38	8.0 (3.0 to >10.0)	38	3.5 (2.0 to >10.0)

Time to Talk Nerdy:

1. Recruitment of Patients – This was a convenience sample when study staff was available. It is very difficult to enroll consecutive patients in the ED 24/7/365. However, we would have liked to know how many people were not approached, why and their characteristics. This would help us know if the patient population included is similar to those being seen at our own centres (tertiary, community or rural). Patients could also be excluded if the physician did not wish to participate. These factors could have introduced an element of selection bias.

2. Who Were These Patients – Let's talk about generalizability? This study took place in a large volume, tertiary care level 1 trauma centre. They enrolled patients ages 12 to 25 years old, so a population in whom concussions are common. In that regard, this study can be generalized to many of the centres where we work and many of the patients whom we commonly see.

However, just like in nerdy point #1, I want to know more about the clinical characteristics of the included patients. What happened to them in the ED? Did they undergo head CT? Did they need analgesics or antiemetics? Were they at risk of prolonged symptoms based on their pre-injury risk factors such as having anxiety or depression? These are some aspects of generalizability that I can't answer when I read this trial.

Our group completed a randomized trial in 241 patients with mild traumatic brain injury, published in Academic Emergency Medicine last year, and when we did a secondary analysis to identify risk factors associated with prolonged symptoms, we found, having a history of anxiety or depression increased the risk of persistent symptoms.

Time to Talk Nerdy:

Consistently studies looking at predictors of persistent symptoms have identified pre-injury depression or anxiety as risk factors. It would have been helpful to know what proportion of participants in this trial previously identified pre-injury risk factors for prolonged symptoms.

3. Blinding – This is an important aspect of RCTs but not always possible. Patients knew what group they were assigned. Were they aware of the hypothesis and did they have pre-conceived notion of the impact of screen time on concussions? This is important because they self-reported their amount of screen. This reporting could have been biased in the intervention control group. It is unclear if this would have biased the results towards or away from the null hypothesis.

4, Primary Outcome – Ensuring the primary outcome and a priori sample size calculation reflect what has already been published in the preceding literature is, in my opinion, the most important aspect to designing a randomized trial. I found this undertaking a bit confusing. The primary outcome definition was the number of days until functional resolution of concussive symptoms was achieved, which meant a score of 3 or less on the PCSS. This made a few assumptions that were a bit unclear when I went back to the original papers:

- Screen time avoidance would decrease the PCSS by 12 points.
- This would result in 2 fewer days to symptom recovery.
- A previously published study compared days to recovery defined by a PCSS threshold, which was not, as far as I can tell, less than 3.

With those assumptions, the a priori sample size calculation for the primary outcome was 106 patients (53 in each group). However, the authors later decided to do a survival curve analysis rather that simply compare median days to recovery. It does make me worry this study is underpowered to reject the null hypothesis.

Time to Talk Nerdy:

5. Attrition – Enrolling patients in the ED is often a challenge. However, following them up after an ED discharge is even more challenging.

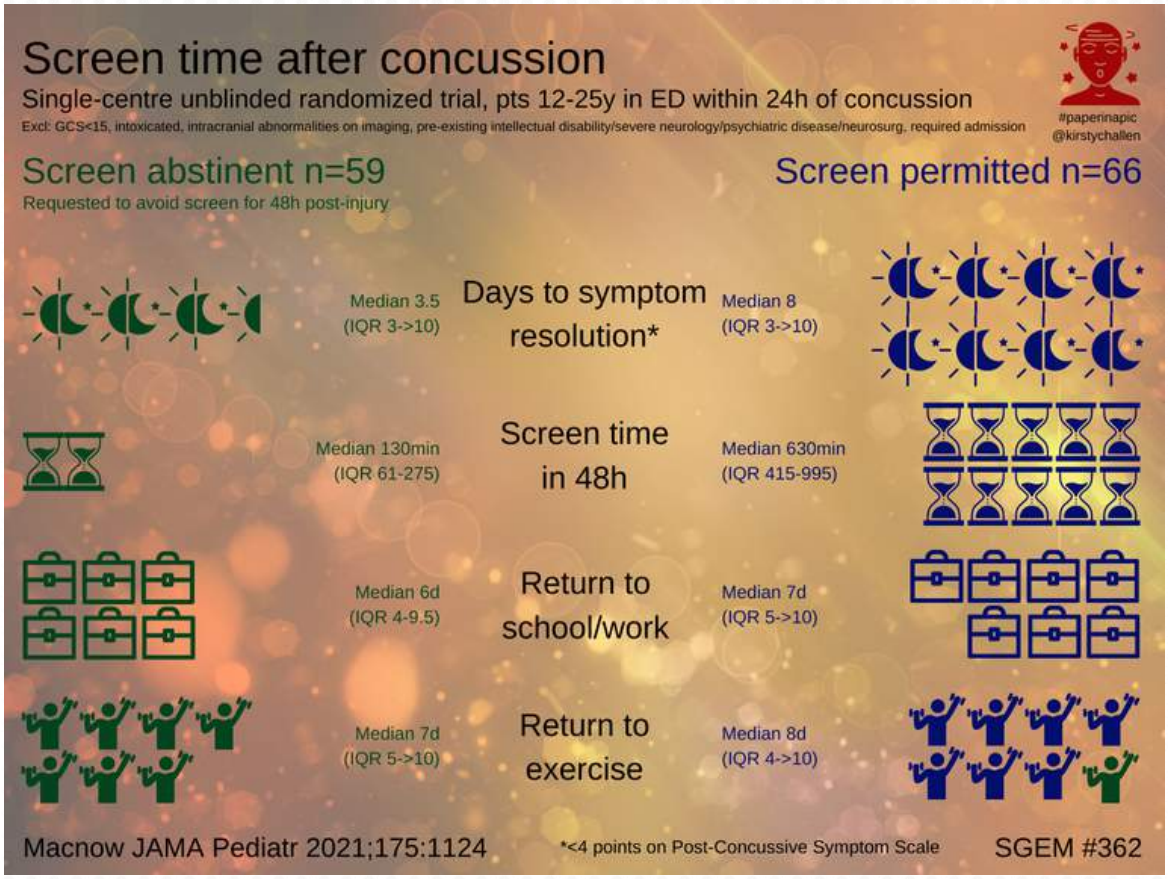
Kudos to this team for taking on an RCT in the ED! As someone who does research in this patient population, it did not surprise me at all that this study had a hard time with attrition. Ideally, attrition can be anticipated and included in the sample size calculation of the study. In fact, we almost always include about 20% loss to follow-up in the design of trials taking place in the ED. Another kudos to the authors for using creative follow-up methods for these patients, including text messaging.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors that abstaining from screen time in the acute period after concussion may or MAY NOT be associated with a shorter duration of symptoms, which supports clinical recommendations to limit screen time in the acute period after concussion.

Clinical Application: Based on the limitations we have discussed for this study and the paucity of research in this area, we cannot make screen time recommendations at this point.

What Do I Tell My Patient? You have a mild concussion. In the vast majority of patients, your symptoms should resolve with 7 days if not sooner. Light activity seems ok after a concussion. We do not have good information to tell you to stay off your computer, but in my practice I tell patients to limit screen time as much as possible, take breaks if you are unable to limit screen time, and if screentime is making symptoms worse, take a break.

Case Resolution: Patient is given standard discharge instructions for a concussion which does not include a recommendation about screen time.



Ken Milne MD
@TheSGEM

How long should you advice people to abstain from screen time post concussion based on this trial in @JAMAPediatrics? thesgem.com/2022/03/sgem36... @CVarnerEmerg @nkuppermann @drsaminaali @KirstyChallen @NicoleB_MD @AAPNews

No abstaining	18.1%
24 hours	12%
48 hours	**38.6%**
> 48 hours	31.3%

83 votes · Final results

7:56 AM · Mar 15, 2022 · Twitter Web App

363

VIEW MASTER – VIRTUAL REALITY IMMERSION TOOL TO REDUCE PEDIATRIC ANXIETY

Clinical Question:

Does a 5-minute virtual reality program reduce situational anxiety in the pediatric ED?

Bottom Line:

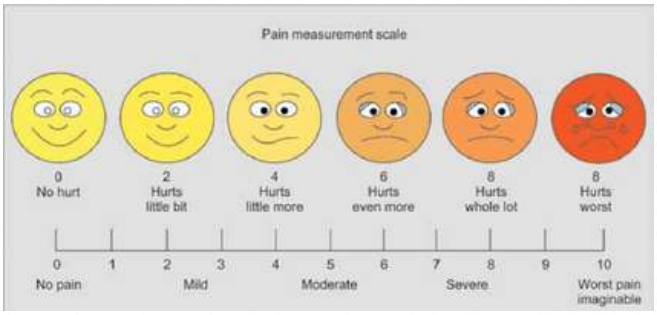
The virtual reality "tale aise" immersion tool is another possible non-pharmaceutical intervention to reduce anxiety of pediatric patients in the ED.

Guest:

Dr. Lauren Westafer is an Assistant Professor in the Department of Emergency Medicine at the University of Massachusetts Medical School – Baystate. She is the cofounder of FOAMcast and is a pulmonary embolism and implementation science researcher. Lauren won the 2021 SAEM FOAMed Excellence in Education Award.

Case Overview:

A 15-year-old male presents to the pediatric emergency department (ED) with right ankle pain sustained while twisting his ankle during dance practice. The right ankle is swollen and tender. He rates his pain a 5 on the FACES scale and is awaiting examination by the treating clinician.



Background:

Pediatric emergency department (ED) visits and related procedures can invoke pain and anxiety among children. Patients who experience adequate pain relief during their ED stay have significant reductions in distress, improved rapport with their physician, improved intent to comply with discharge instructions and higher levels of personal and caregiver satisfaction.

Children represent one group of patients that are less likely to receive adequate analgesia (Brown et al, Selbst and Clark). This phenomenon is known as oligoanalgesia or poor pain management through the underuse of analgesia.

We have covered pediatric pain with PEM super hero Dr. Anthony Crocco on SGEM#78 who did a RANThony on this issue. Dr. Samina Ali is a PEM super (s)hero who was on SGEM#242 looking at intranasal (IN) ketamine vs fentanyl on pain reduction for extremity injuries in children.

Background:

The bottom line from that trial was IN ketamine appears to be non-inferior to IN fentanyl for efficacy, but with more adverse events.

Many clinicians utilize distraction techniques to reduce pain and anxiety in children during their ED visits [4]. However, there are no prospective randomized trials using virtual reality (VR) as a distraction technique while awaiting physician evaluation.

Reference: Butt et al. Take-Pause: Efficacy of mindfulness-based virtual reality as an intervention in the pediatric emergency department. AEM March 2022

P

Population: Patients ages 13-17 years who presented to the pediatric ED with mild to moderate acute pain (pain score 2-6 on FACES pain scale)

- **Exclusions:** Patients with developmental delays, inability to speak English, prone to motion sickness, significant visual/hearing impairment, pregnancy, parental refusal, received analgesic ≤4 hours prior to ED arrival, or inability to use the pain scale.

I

Intervention: Virtual reality "Take Pause" program for 5 minutes

C

Comparison: Passive distraction technique with hospital-owned iPad with pre-downloaded age-appropriate games for 5 minutes

- **Primary Outcome:** Difference in the change in situational anxiety level between groups 15 minutes after intervention using the Spielberger State – Trait Anxiety Inventory (STAI: Y-6 item)
- **Secondary Outcomes:** Mean difference in pain score on the FACES scale, heart rate, respiration rate from baseline to 15 minutes after intervention
- **Trial:** Prospective, randomized, single-blind trial

This is an SGEMHOP episode which means we have the lead author on the show. Mahlaqa Butt, MPH is a third-year medical student at New York Institute of Technology-College of Osteopathic Medicine and a clinical research associate at the Department of Emergency Medicine at Maimonides Medical Center, Brooklyn NY. She has co-authored 11 peer-reviewed emergency medicine research publications primarily focused on opioid-free pain management in the ED. She will be pursuing a residency in emergency medicine this fall.

Spielberger State – Trait Anxiety Inventory (STAI: Y-6 item)

Published:

Marteau TM and Bekker H. The development of a six-item short-form of the state scale of the Spielberger State – Trait Anxiety Inventory (STAI). *British Journal of Clinical Psychology*. 1992;31:301-306.

Measure:

Name ..... *Date* .....

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the most appropriate number to the right of the statement to indicate how you ***feel right now, at this moment****. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.*

	Not at all	Somewhat	Moderately	Very much
1. **I feel calm**	1	2	3	4
2. **I am tense**	1	2	3	4
3. I feel upset	1	2	3	4
4. I am relaxed	1	2	3	4
5. **I feel content**	1	2	3	4
6. I am worried	1	2	3	4

Authors' Conclusions

"Take-Pause, offering an active and immersive distraction technique, is more effective than a passive distraction approach to lower anxiety levels in adolescent ED patients."

Quality Checklist for Randomized Clinical Trials

- ☑ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ☒ 5. The study teams were recruited consecutively (i.e. no selection bias).
- ? 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☒ 10. All patient-important outcomes were considered.
- ? 11. The treatment effect was large enough and precise enough to be clinically significant.
- ☑ 12. Was the study without any financial conflicts of interest.

Results

Key Results:

- They enrolled 110 teenagers into the trial with 55 participants in each group. The mean age was 15 years, 60% were male and the mean pain score was 4.1/10.
- **Primary Outcome:** Mean anxiety score on the Spielberger State – Trait Anxiety Inventory (STAI: Y-6 item)
  - VR group improved by 10 points vs. 6 points in the iPad group (95% CI: 0.44 to 7.6) $p < 0.001$
- **Secondary Outcomes:** At 15 minutes, there was no difference in mean pain scores (3.6 vs 3.6), heart rate (intervention 81 bpm vs control 83 bpm), or respiratory rate (intervention 18 vs control 20)

Time to Talk Nerdy:

Listen to the SGEM podcast to hear Mahlaqa answer our five nerdy questions.

1. Patient Characteristics – Very little information is given regarding patient characteristics. For example, we have no information on traumatic vs nontraumatic pain, location of pain, race/ethnicity, or other potentially important variables. Although randomization should theoretically balance out any differences, it is helpful to have patient characteristics reported so we can gauge – are these patients like my patients?

2. Virtual Reality (VR) for Mindfulness – We have looked at mindfulness to help relieve the stress of interns on their EM rotation on SGEM#178. In this other small study, it seemed to be effective. However, that study had 10 weeks of mindfulness training sessions as the intervention. Can you describe this Take Pause VR immersion tool in more detail?

3. Effect Size – Effect size is a quantitative measurement of the magnitude of the difference between groups. In this study, the authors set out to find a difference of ≥3 on the STAI Y-6 from baseline to post-intervention. They felt this would be statistically significant as a 1999 study that looked at music before bronchoscopy had a 3.6 reduction on the anxiety score (but did not meet the arbitrary 5 points set out by those authors). It often takes more participants to detect a smaller effect size.

4. Comparison Group – You compared the VR Take Pause immersion tool to standard distraction techniques using an iPad. This could have introduced a bias towards lower anxiety because some teenagers desire to use some cool new technology. Why not use another VR headset intervention?

Time to Talk Nerdy:

Patients knew they were going to be randomized into the VR or iPad group. You mentioned in your publication this could have led to optimism bias. Could you explain that type of bias further?

Did you consider other techniques not involving technology like animal therapy? On SGEM#289 we looked at having a dog to play with to relieve stress on the staff. The intervention looked promising, and I wonder how it would have compared to using a VR device.

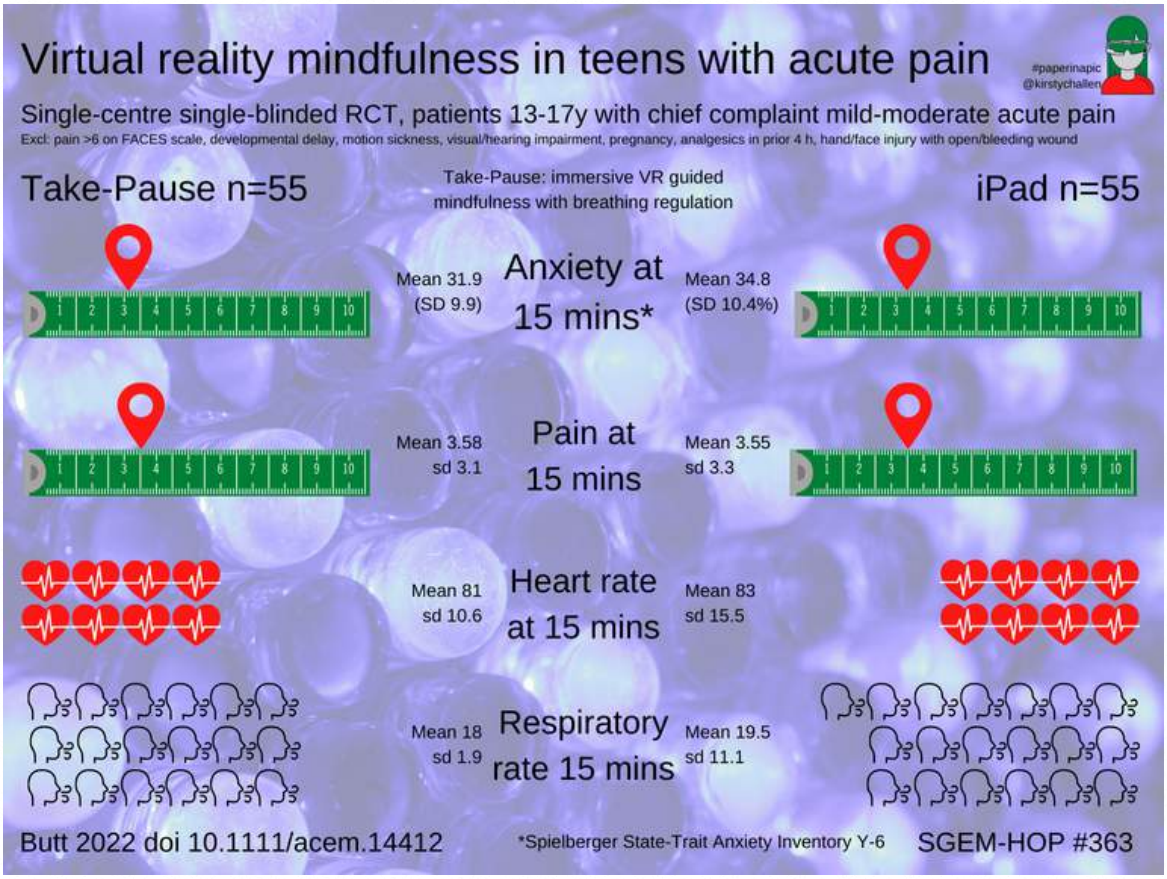
5. Statistical Significance vs Clinical Significance – The mean baseline anxiety score (STAI Y-6 score) placed nearly the same proportion of patients in the mild anxiety group (score 20-40) ~82-94% and in the moderate anxiety group (score 41-60) – 16% of patients in both groups. The virtual reality arm had a 10-point reduction from baseline while the iPad group had a 6-point reduction. However, the post-intervention score was only 2.9 points different between groups. Overall, it's not clear that the statistically significant difference between groups is clinically significant.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We disagree with the authors conclusion and believe that this trial shows both Take-Pause and passive distraction with an iPad reduce self-reported anxiety levels in adolescent ED patients.

Clinical Application: Reducing anxiety is important in the emergency department. There are several non-pharmacologic techniques that can be used. This small study suggests the VR Take Pause immersion tool can be one of those techniques.

What Do I Tell My Patient? There are several ways to reduce anxiety in the pediatric emergency department. Both a mindfulness based virtual reality program and playing games on an iPad may help reduce your anxiety.

Case Resolution: The patient is offered either a mindfulness-based virtual reality program or an iPad with preprogrammed games while awaiting clinician evaluation.



Ken Milne MD
@TheSGEM

Does your emergency department use virtual reality in caring for patients? thesgem.com/2022/04/sgem36... #SGEMhop @LWestafer @mahlaqabee @SAEMonline @AcademicEmerMed

Yes	14.5%
No	**85.5%**

62 votes · Final results

8:57 AM · Apr 5, 2022 · Twitter for iPhone

364

DON'T YOU FORGET ABOUT ME – DW:MRI SENSITIVITY FOR TRANSIENT GLOBAL AMNESIA

Clinical Question:

What is the sensitivity of diffusion-weighted magnetic resonance imaging (DW-MRI) as a function of time from symptom onset compared to clinical diagnosis of TGA?

Bottom Line:

Urgent DW-MRI for patients meeting standard diagnostic criteria for TGA is a low yield intervention.

Guest:

Dr. Chris Bond is an emergency medicine physician and assistant Professor at the University of Calgary.

Case Overview:

A 65-year-old man presents to your emergency department with his wife. She tells you that he woke up normally this morning, but after breakfast he began asking the same questions repetitively and was amnestic to the answer, seemingly unable to form new memories. He remained completely awake and alert and otherwise appeared well. There was no history of recent trauma, infectious symptoms, or any other illness.

Background:

Transient global amnesia (TGA) is an idiopathic acute neurological disorder that presents with sudden onset anterograde memory loss. It was first described as a syndrome in 1956 by Courjon and Guyotat and also by Bender [1,2]. Fisher and Adams formally described as TGA in 1964 [3].

The usual presentation is a patient between 50 and 70 years of age who are cognitively and neurologically intact but asking repetitive questions, unable to form new memory. Symptoms do not last very long and resolve within 24 hours. The incidence has been reported as 23.5 per 100,000 people per year [4] and is more common in people who get migraine headaches [5].

TGA is often precipitated by physical or emotional stressors, pain, the Valsalva maneuver, hot or cold-water immersion or sexual intercourse [6] Diagnosing TGA combines items put forward by Hodges and Warlow and Caplan [7-9]. This results in seven diagnostic criteria for TGA.

Background:

1. Attack is witnessed
2. Clear-cut anterograde amnesia during the attack
3. No neurologic symptoms or signs during the attack other than amnesia (no clouding of consciousness or loss of personal identity)
4. No neurologic physical examination findings others than anterograde amnesia
5. Memory loss is transient (resolution within 24 h)
6. No epileptic features and no active epilepsy (defined as no seizure within 2 years or on antiepileptic medication)
7. No recent head injury

A diagnostic algorithm has been published for patients with sudden onset of anterograde amnesia [6]. Included in this differential is transient epileptic amnesia, transient ischemic attack, stroke, metabolic disorders, psychogenic disorders, and post traumatic amnesia. The workup can include laboratory testing, EEGs, ECGs, echocardiogram and advanced neuroimaging.

Background:

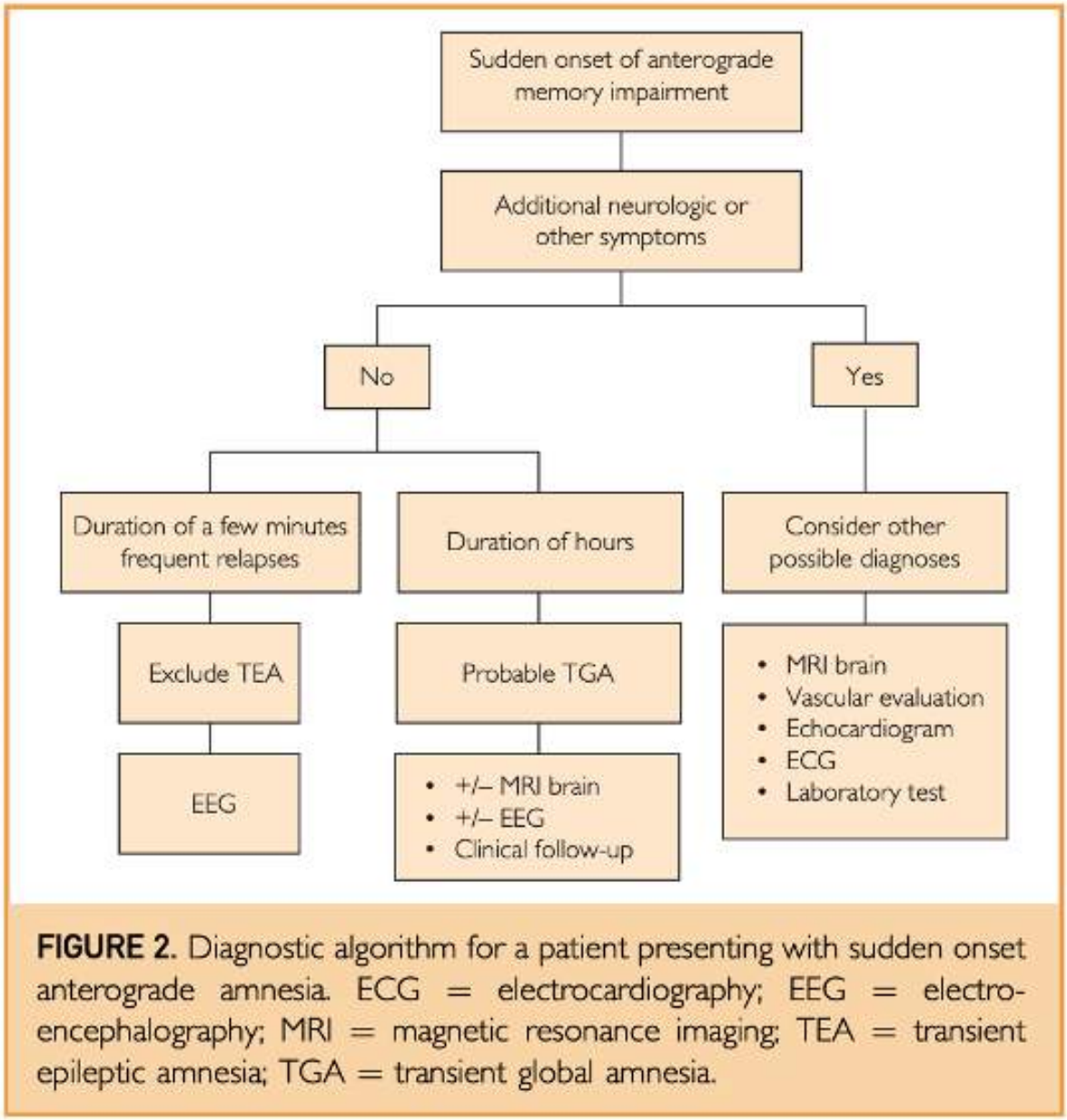


FIGURE 2. Diagnostic algorithm for a patient presenting with sudden onset anterograde amnesia. ECG = electrocardiography; EEG = electroencephalography; MRI = magnetic resonance imaging; TEA = transient epileptic amnesia; TGA = transient global amnesia.

Reference: Wong et al. Sensitivity of diffusion-weighted magnetic resonance imaging in transient global amnesia as a function of time from symptom onset. AEM April 2022

P **Population:** Adult patients 16 years of age and older with a diagnosis of TGA based on the existing clinical criteria

I **Intervention:** Evaluation with DW-MRI at varying time intervals post symptom onset

C **Comparison:** No comparison as no studies of patients without DW-MRI were included

O Sensitivity of DW-MRI in diagnosis of TGA

This is a back-to-back SGEMHOP episode. We did the March episode at the end of last month and the April episode is the first week of this month.

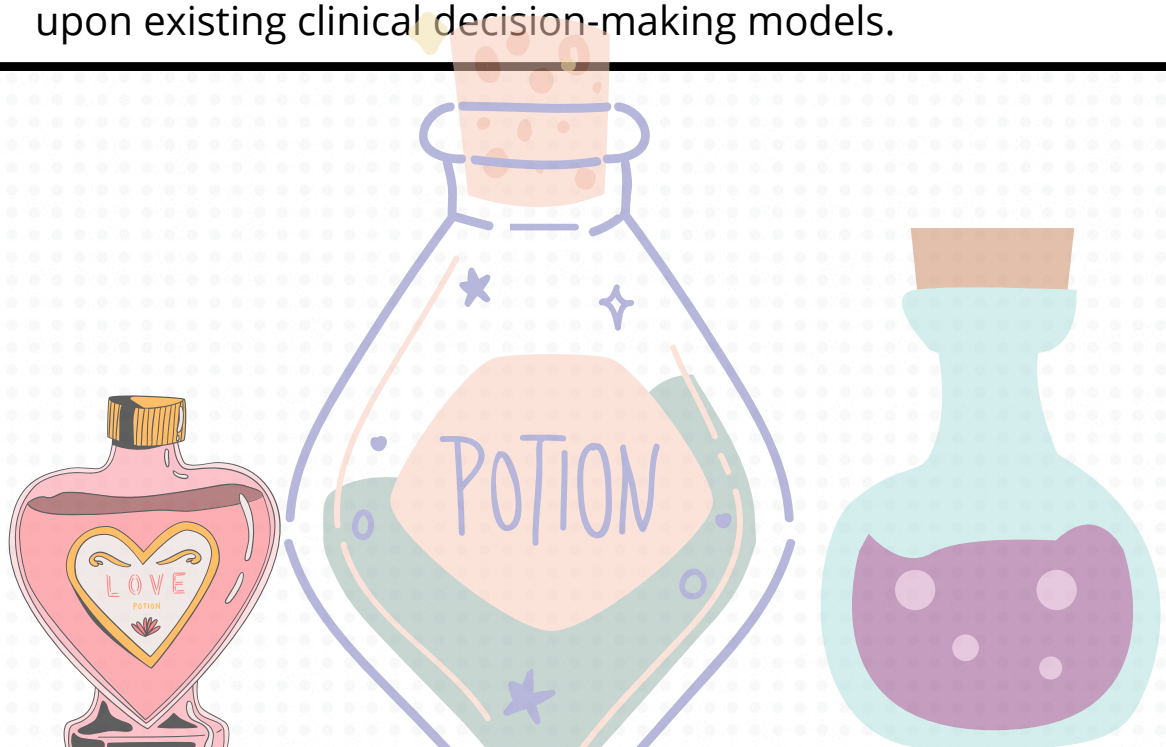
We are pleased to have the lead author on the show. Dr. Matthew Wong is an emergency physician and educator at Beth Israel Deaconess Medical Center, and an Assistant Professor at Harvard Medical School.

Authors' Conclusions

"DW-MRI lesions are uncommon in patients with TGA early after symptom onset, but the sensitivity (i.e., positivity rate) of DW-MRI increases with time. Despite the limited quality of existing evidence, obtaining an early DW-MRI in patients with clinical diagnosis of TGA in the acute setting is likely a low-yield test."

Quality Checklist for Randomized Clinical Trials

- ☑ 1. The diagnostic question is clinically relevant with an established criterion standard.
- ☑ 2. The search for studies was detailed and exhaustive.
- ☑ 3. The methodological quality of primary studies were assessed for common forms of diagnostic research bias.
- ☑ 4. The assessment of studies were reproducible.
- ☒ 5. There was low heterogeneity for estimates of sensitivity or specificity.
- ☒ 6. The summary diagnostic accuracy is sufficiently precise to improve upon existing clinical decision-making models.



Results

Key Results:

- They identified 23 studies in their search with a total of 1,688 patients who met inclusion criteria. All studies were case series of adult patients clinically diagnosed with TGA who underwent DW-MRI.

Time interval (h) from symptom onset to MRI	Number of studies (number of patients)	Pooled DW-MRI sensitivity, % (95% CI)	I^2, %
0–12	8 (325)	15.6 (2.6–35.0)	90
0–24	10 (539)	23.1 (6.1–45.7)	96
12–24	4 (71)	72.8 (40.8–96.3)	84
24–36	2 (59)	68.8 (44.8–88.8)	70
36–48	2 (55)	72.4 (59.8–83.5)	0
48–60	3 (57)	82.8 (54.7–99.6)	72
60–72	3 (25)	66.9 (47.5–83.9)	0
72–96	2 (41)	72.0 (30.1–100.0)	86

In the first 12 hours from symptom onset, sensitivity of DW-MRI is 15.6%. It improves thereafter to sensitivities between 66 and 83%, with very wide confidence intervals for all point estimates. There is also significant heterogeneity between studies.

Time to Talk Nerdy:

Listen to the SGEM podcast to hear Matt answer our ten nerdy questions.

1. Number of Studies: It's unfortunate that there was a paucity of data to inform our care on TGA. While you identified 23 studies with almost 1,700 patients there were only 2 studies for some time frames with a few dozen patients. The largest time frame only had 10 studies containing 539 patients.

2. Observational Studies: All the studies were observational in nature. There were no randomized trials allocating patients to any time frame (early or late). This limits conclusions to time being associated with better sensitivity for diagnosis TGA with DW-MRI. There could have been reasons why some patients go an MRI sooner while others receive an MRI later.

3. Heterogeneity: The heterogeneity measured by the I2 test was very high (72%-96%) for all time points besides 36-48 hours and 60-72 hours. Why did you decide to meta-analyze the data rather than just providing a narrative report?

4. Table 3: This has 0-12, 0-24 and 12-24 hour groups for time interval from onset. Why did you use three-time groupings here?

5. Partial Verification Bias (Referral Bias, Work-up Bias) – This happens when only a certain set of patients who underwent the index test is verified by the reference standard. Only those who met the clinical criteria for TGA got a DW-MRI. What about all those patients who did not meet clinical criteria and therefore did not get an MRI? This could increase sensitivity.

6. Spectrum Bias – Sensitivity depends on the spectrum of disease, while specificity depends on the spectrum of non-disease. So, you can falsely raise sensitivity if the clinical practice has lots of people with TGA. Do you know what the prevalence of TGA was in the included studies? Responds

Time to Talk Nerdy:

7. Imperfect Gold Standard Bias (Copper Standard Bias): This is what can happen if the "gold' standard is not that good of a test. False positives and false negatives can really mess up results. What is the diagnostic accuracy of the clinical criteria for diagnosing TGA? Responds

8. Serial MRIs: Some of the studies included in the SRMA used serial MRIs. Can you comment if the results were aligned with the entire group within the meta-analysis?

9. Future Studies: You know this area well after having looked at all these studies. How would you design a study using DW-MRI to evaluate for TGA based upon what you know now?

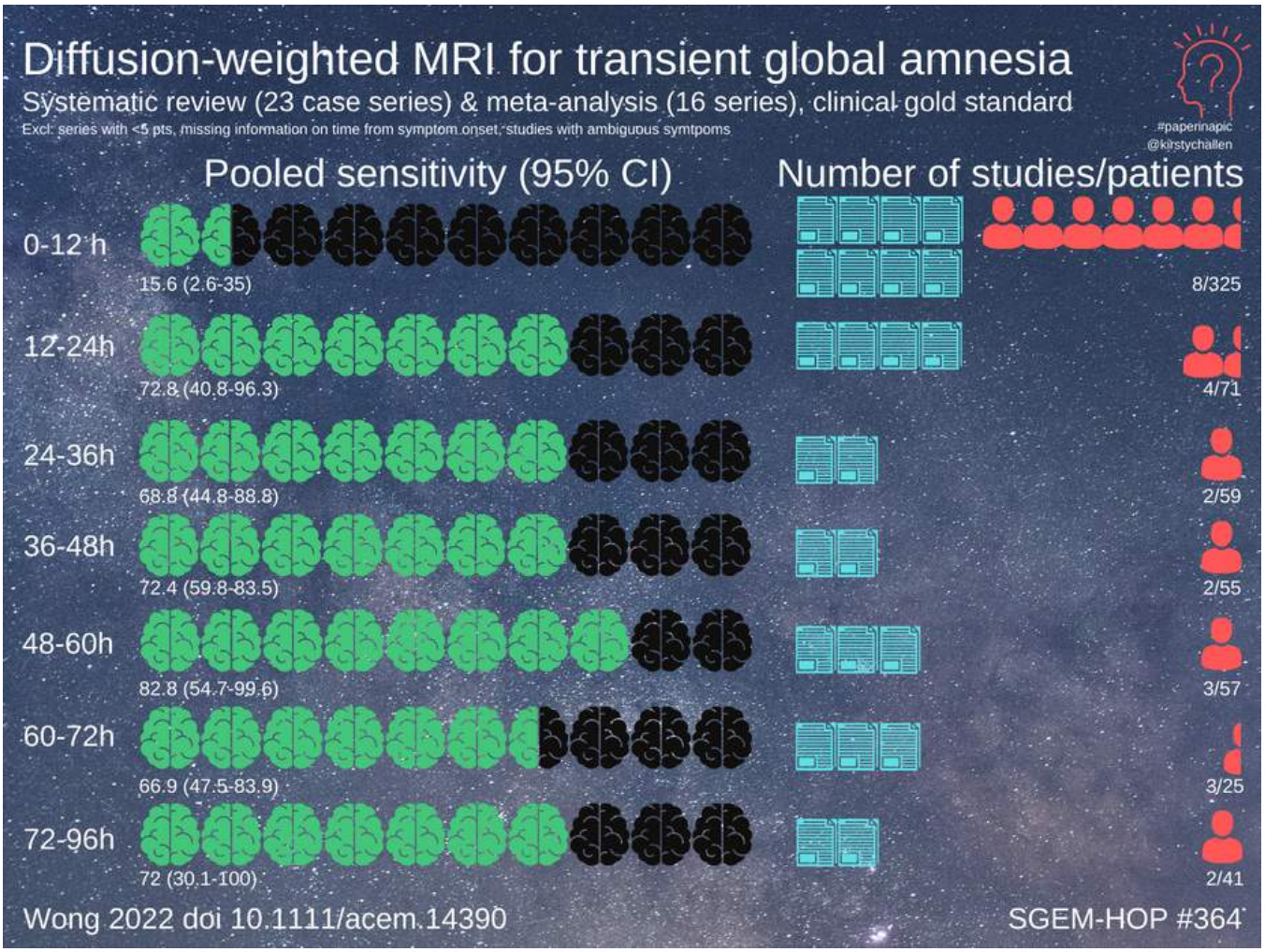
10. Open Question: Is there anything else you would like the SGEMer to know about TGA in general or your study specifically?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors conclusions.

Clinical Application: We do not need to request an urgent DW-MRIs in patients who meet clinical diagnostic criteria for TGA.

What Do I Tell My Patient? You have something called transient global amnesia or TGA. This condition is not a stroke or seizure or other dangerous disease and will mostly likely resolve over 24 hours. You should have no long-lasting effects from this. You also explain this to the patient's caregiver and provide a written handout from the Mayo Clinic explaining the same. Should you develop any other neurologic symptoms such as weakness, sensory changes, speech abnormalities or confusion, or are worried you should return to the emergency department immediately.

Case Resolution: You perform a good history, followed by a directed physical examination. You then observe him over a period of hours in the emergency department and he slowly begins to form new memories. You perform an unenhanced CT head and basic bloodwork which is normal. He is discharged home with his wife and will follow up with a neurologist as an outpatient.



Ken Milne MD
@TheSGEM

What time frame can you usually get a DW-MRI in a patient suspected of transient global amnesia? thesgem.com/2022/04/sgem36... @EM_phile @socmobem @LWestafer @First10EM @KirstyChallen @CHeitzMD #SGEMHOP

<12hr	26.8%
12hrs - 24hrs	19.5%
24hrs - 48hrs	11%
>48hrs	**42.7%**

82 votes · Final results

9:29 AM · Apr 12, 2022 · Twitter Web App

365

STOP! IT'S NOT ALWAYS HAMMER TIME

Clinical Question:

What is the effectiveness of common elective orthopaedic procedures compared with no treatment, placebo, or non-operative care?

Bottom Line:

There is a lack of high-quality evidence to support all but two out of the ten most common elective orthopedic procedures.

Guest:

Dr. Matt Schmitz, Pediatric Orthopedics, Adolescent Sports Medicine and Young Adult Hip Preservation Surgeon at San Antonio Military Medical Center in Texas.

Case Overview:

A 55-year-old man comes into the emergency department (ED) for increasing knee pain and decrease in function. He's had an anterior cruciate ligament (ACL) repair and used to run marathons. However, he is finding it more difficult to even put his socks on. Physical exam shows varus deformity at the knee, decreased range of motion, crepitus, no locking and neurovascularly intact distal. X-rays show severe, tri-compartment arthritis.

Background:

Musculoskeletal complaints are one of the most common presentations to emergency departments. Often emergency physicians are assessing, treating, and answering patients question about orthopedic surgical procedures. How good is the evidence for the most common elective procedures?

Before we answer that question, let's remind everyone that only a small number (2.8%) of interventions published in SRMA and relevant to emergency medicine have unbiased and strong evidence for improved outcomes (SGEM#361).

This is a broader problem in medicine. Tricoci et al. JAMA Feb 2009 looked at the ACC/AHA guidelines from 1984 to 2008. They found 53 guidelines with 7,196 recommendations. Only 11% of recommendations were considered Level A, 39% were Level B and 50% were Level C.

An update was published by Fanaroff et al in JAMA 2019. The level of high-quality evidence had not changed much when looking at the ACC/AHA guidelines from 2008-2018.

Background:

There were 26 guidelines with 2,930 recommendations. Now Level A recommendations were down to 9%, Level B 50% and Level C 41%.

Time to turn our skeptical eye to the evidence for elective orthopaedic procedures.

Reference: Blom et al. Common elective orthopaedic procedures and their clinical effectiveness: umbrella review of level 1 evidence. BMJ 2021

P

Population: Meta-analyses of randomised controlled trials

- **Exclusions:** Network meta-analyses (when pairwise meta-analyses were available), narrative reviews, systematic reviews that did not pool data or do a meta-analysis, and meeting abstracts

I

Intervention: Surgery

C

Comparison: No treatment, placebo, or non-operative care

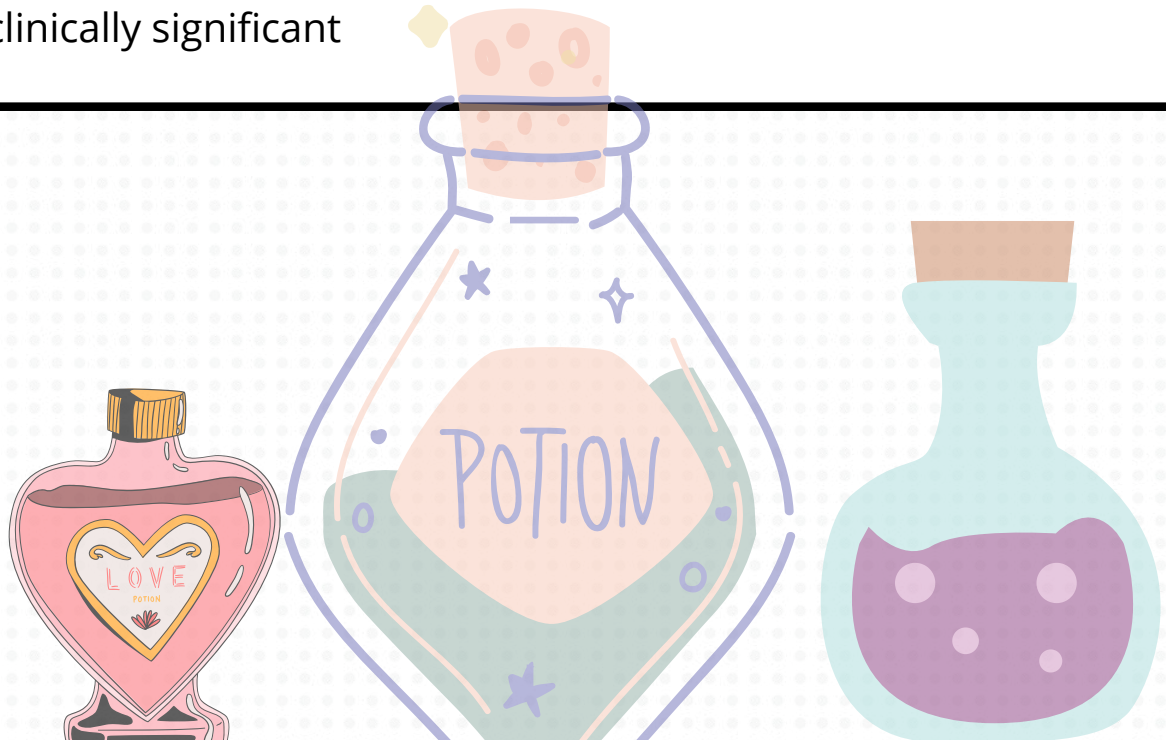
Quality and quantity of evidence behind the ten most common elective orthopaedic surgeries and comparisons with the strength of recommendations in relevant national clinical guidelines.

Authors' Conclusions

"Although they may be effective overall or in certain subgroups, no strong, high quality evidence base shows that many commonly performed elective orthopaedic procedures are more effective than non-operative alternatives. Despite the lack of strong evidence, some of these procedures are still recommended by national guidelines in certain situations."

Quality Checklist for Therapeutic Systematic Reviews

- [x] 1. The clinical question is sensible and answerable
- [x] 2. The search for studies was detailed and exhaustive
- [x] 3. The primary studies were of high methodological quality
- [x] 4. The assessment of studies were reproducible
- [x] 5. The outcomes were clinically relevant
- [ ] 6. There was low statistical heterogeneity for the primary outcomes
- [ ] 7. The treatment effected was large enough and precise enough to be clinically significant



Results

Key Results:

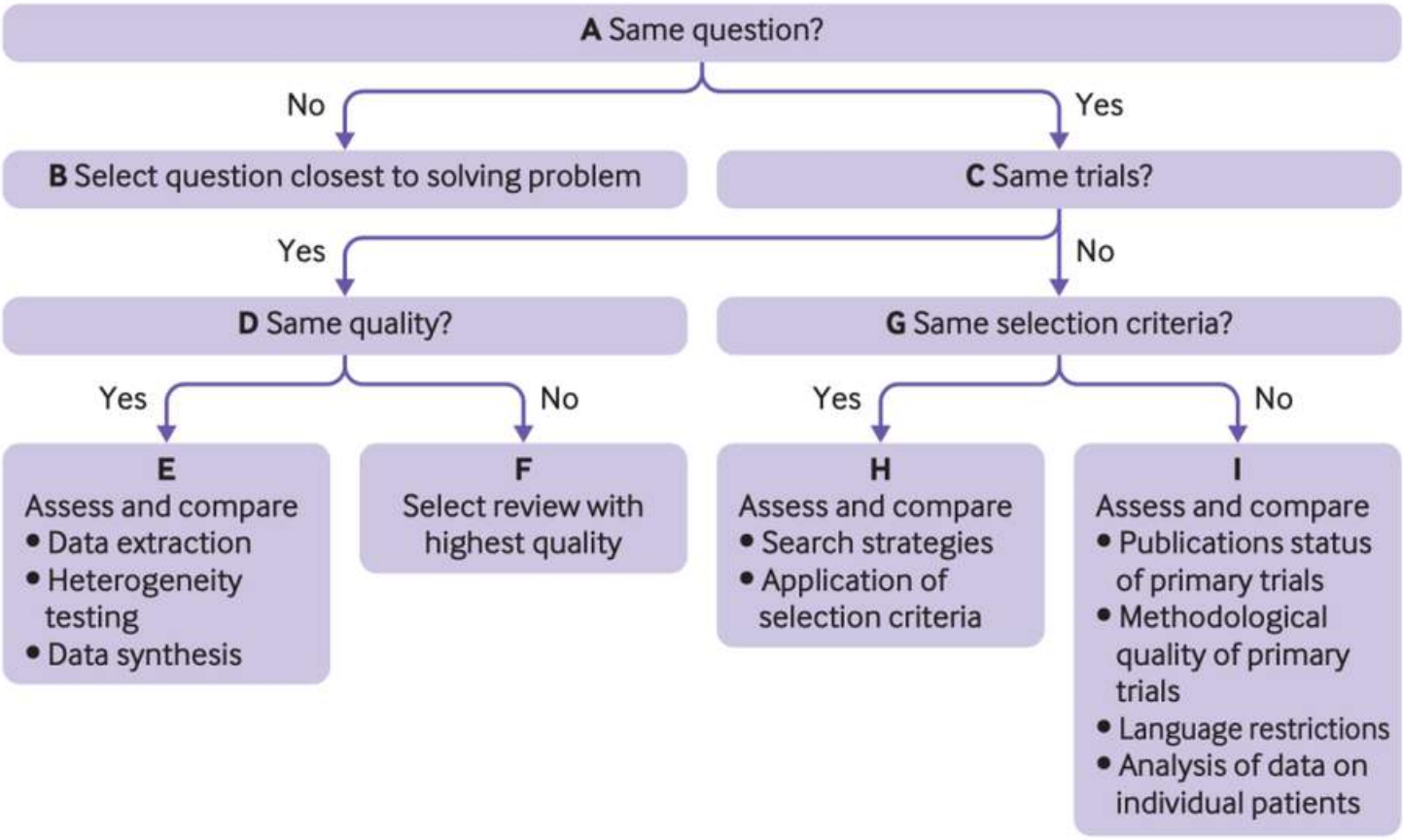
- The ten most common elective orthopaedic procedures were identified using a literature search, an assessment of Hospital Episode Statistics procedure frequency counts, and discussions with expert orthopaedic surgeons.
    - arthroscopic anterior cruciate ligament reconstruction
    - arthroscopic meniscal repair of the knee
    - arthroscopic partial meniscectomy of the knee
    - arthroscopic rotator cuff repair
    - arthroscopic subacromial decompression
    - carpal tunnel decompression
    - lumbar spine decompression
    - lumbar spine fusion
    - total hip replacement
    - total knee replacement
- Only two out of ten common procedures, carpal tunnel decompression and total knee replacement, showed superiority over non-operative care.

Common elective orthopaedic procedures and indications	
Procedure	Main indication
Arthroscopic anterior cruciate ligament reconstruction	Anterior cruciate ligament rupture
Arthroscopic meniscal repair of the knee	Traumatic meniscal tears
Arthroscopic partial meniscectomy of the knee	Degenerative meniscal tears
Arthroscopic rotator cuff repair	Acute rotator cuff tears
Arthroscopic subacromial decompression	Subacromial impingement syndrome
Carpal tunnel decompression	Carpal tunnel syndrome
Lumbar spine decompression	Spinal canal stenosis
Lumbar spine fusion	Degenerative disc disease
Total hip replacement	End stage osteoarthritis
Total knee replacement	End stage osteoarthritis

- They identified no RCTs that specifically compared total hip replacement or meniscal repair with non-operative care.
- The six other common orthopaedic procedures showed no benefit over non-operative care.

Time to Talk Nerdy:

1. Jadad Decision Algorithm: This is probably an unfamiliar process to most SGEM listeners. It is a process proposed in the late 1990's to help decision-makers select from among discordant reviews [1]. Since its publication, the Jadad decisions algorithm is now commonly used to interpret between SRMA with discordant results [2,3].



2) Absence of Evidence: Just because we do not have high-quality RCTs does not mean we can conclude the procedures do not work. Total hip arthroplasty is one of the most successful surgical procedures in all of orthopedics.

Time to Talk Nerdy:

3) Arthroscopic ACL Repair: The overall evidence does not support the routine reconstruction of a patients ACL. That does not mean a certain individual does not need their ACL repaired.

There as a landmark study called KANON (Knee Anterior cruciate ligament NON operative vs operative treatment) published over a decade ago (NEJM 2010). KANON was an RCT of 121 young active adults with an acute ACL injury. The primary outcome was the change from baseline to two years in the average score on four subscales of the Knee Injury and Osteoarthritis Outcome Score (KOOS) and knee-related quality of life. They found that rehabilitation plus early ACL reconstruction was not superior to rehabilitation plus optional delayed ACL reconstruction.

A secondary analysis was just published that looked at the incidence of spontaneous healing of the ruptured ACL in the KANON trial (BMJ Sport and Ex Med 2022). They found there was a high rate of ACL healing in patients managed without surgery and only rehabilitation (56% at two years and 58% at five years). In addition, these individuals reported better patient-reported outcomes compared to the non-healed and reconstructed groups.

So, like most things in medicine the answer is it all depends. Decision to perform surgery depends on many factors including the patients' values and preferences. What are their current activities, and do they want to continue those activities?

I had both my ACLs repaired well before the KANON trial. One repair went well while the other injured my common peroneal nerve, leaving me with foot drop for months and permanent decrease in sensation.

Time to Talk Nerdy:

4) Possible Parachute: One of the other 10 common procedures lacking RCTs was arthroscopic meniscus repair. I don't need an RCT to verify that it is not safe to jump out of an airplane without a parachute and I don't need an RCT to inform my decision to repair a meniscus.

I would caution you that most medical procedures are not parachutes and an RCT could be conducted [4]. In fact, even parachutes were tested in a RCT, but the plane was on the ground and not moving (SGEM#284).

5) Potential Harms: We have been discussing the lack of superiority for efficacy in six out of ten common orthopedic procedures. It is important to also consider the potential harms. While modern surgery is very safe, there is increased morbidity and mortality with surgical interventions.

There is always a risk with surgical intervention. Higher risks with things like joint arthroplasty or spine surgery so it is important to exhaust conservative measures. However, when there is nerve impingement causing weakness (carpal tunnel, herniated disk, etc) delaying surgical decompression can lead to permanent weakness (different then neurogenic pain).

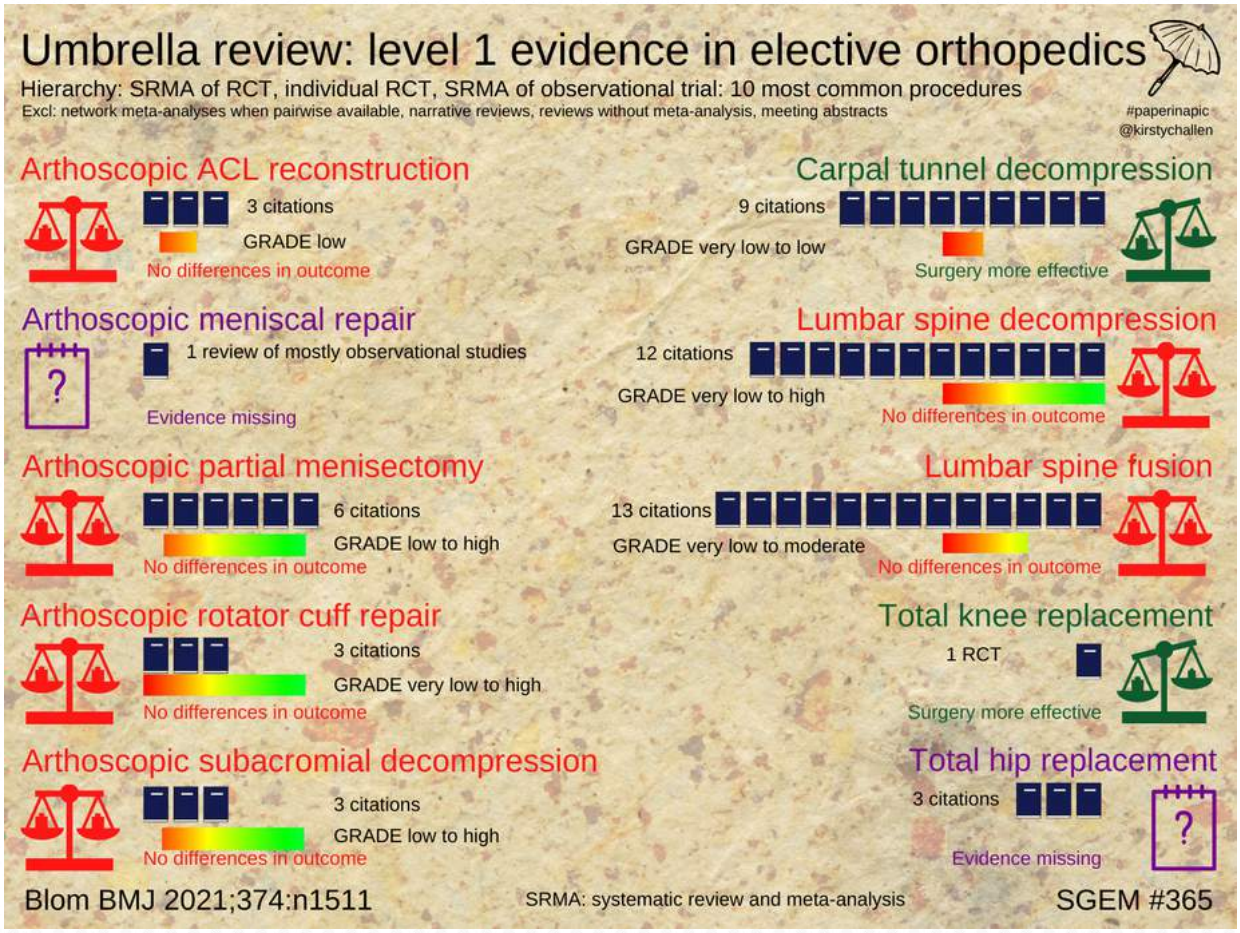
Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors conclusions.

Clinical Application: This information can help patients and physicians in their decision-making process. In their supplemental material they compare their results to the American Academy of Orthopaedic Surgeons (AAOS) guidelines in Appendix 11.

AAOS clinical practice guidelines (CPGs) use similar methodology with work groups analyzing the best available evidence and grading it. They look at not only surgical options but also non-surgical options (orthobiologics, steroids, physiotherapy for knee osteoarthritis, etc). As is highlighted in this review, there is frequently a lack of high-level studies to support any intervention (operative or nonoperative) and that is reflected in the grading of CPG.

What Do I Tell My Patient? I recommend exhausting all conservative measures before considering joint replacement surgery. Although the technology is getting better (implants lasting longer), you will want to delay as long as possible because we know primary joint replacements have better outcomes than originals. So, if you have it replaced, you only want it replaced once. There is little downside to trying conservative management (therapy, injections, etc).

Case Resolution: The patient with his progressively worse knee is referred to an orthopedic surgeon to discuss his options.



Ken Milne MD
@TheSGEM

Which orthopaedic procedure has level 1 evidence showing it's superior to non-operative treatment? #orthotwitter (AS=ArthroScopic) thesgem.com/2022/04/sgem36... @RugbyMD @AAOS1 @OrthopodReg @BMJ_Open

AS ACL Reconstruction	32.9%
Lumbar Spine Fusion	3%
Carpal Tunnel Release	**57.3%**
AS Rotator Cuff Repair	6.7%

164 votes · Final results

2:11 AM · Apr 19, 2022 · Twitter for iPhone

366

RELAX, DON'T DO IT – SKELETAL MUSCLE RELAXANTS FOR LOW BACK PAIN

Clinical Question:

What is the efficacy of skeletal muscle relaxant administration in addition to an NSAID in treating acute low back pain?

Bottom Line:

We cannot recommend the routine use of SMR in adult patients presenting to the ED with acute, non-traumatic, non-radicular low back pain who have already received an NSAID.

Guest:

Dr. Sergey Motov is an Emergency Physician in the Department of Emergency Medicine, Maimonides Medical Center in New York City. He is also one of the world's leading researchers on pain management in the emergency department and specifically the use of ketamine. His twitter handle is @PainFreeED.

Case Overview:

A 45-year-old man without a significant past medical history presents to your emergency department (ED) with two days of severe lower back pain after shoveling some dirt. The pain is 10/10 in intensity, gets worse with bending, turning, and prolonged walking. He denies numbness or paresthesia in both lower extremities, as well as bowel or bladder dysfunctions. A heating pad and acetaminophen has not helped with the pain. On examination, he is in moderate distress and has prominent tenderness to palpation at the bilateral paralumbar region and intact neurovascular examination. You diagnose him with a lumbar muscle strain and plan to prescribe him a non-steroidal anti-inflammatory (NSAID) while setting expectations. However, the patient wonders if you can give him something that can relax his back muscles and take his pain away.

Background:

Low back pain (LBP) is one of the most encountered ailments in clinical practice and is responsible for 2.6 million visits to U.S. EDs annually (1). Many patients with acute LBP experience substantial improvement in the first month, but up to one third report persistent back pain, and 1 in 5 report some limitations in activity. These persistent symptoms are associated with high costs, including those related to health care, and indirect costs from missed work or reduced productivity (2).

Many pharmaceutical treatments besides opioids have been tried to address acute LBP pain with limited success (SGEM#87 and SGEM#173). These include: acetaminophen (Williams et al Lancet 2014), steroids (Balakrishnamoorthy et al Emerg Med J 2014) and benzodiazepines (Friedman et al Ann Emerg Med 2017).

Background:

Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended as first-line medication therapy for patients with LBP despite a lack of evidence of efficacy (Machado et al Ann Rheum Dis 2017),

There are several non-pharmaceutical treatments that have also been tried to treat LBP. They include: CBT and mindfulness (Cherkin et al JAMA 2016), chiropractic (Paige et al JAMA 2017), physical therapy (Paolucci et al J Pain Research 2018) and acupuncture (Colquhoun and Novella Anesthesia and Analgesia 2013). Unfortunately, none of these other treatment modalities has high-quality evidence supporting their use.

Skeletal muscle relaxants (SMRs) are a frequently used in the ED and at discharge for acute back pain management and include methocarbamol, cyclobenzaprine, orphenadrine, carisoprodol, tizanidine, metaxalone, and baclofen. Estimates suggest up to 35% of patients with nonspecific low back pain are prescribed SMRs, with orphenadrine, and methocarbamol being used in more than 250,000 U.S. ED visits for low back pain annually (3-5). Despite their branding as muscle relaxants, the anti-spasmodic and analgesic effects of SMRs are predominantly due to unknown mechanism of action.

Reference: Abril et al. The Relative Efficacy of Seven Skeletal Muscle Relaxants. An Analysis of Data From Randomized Studies. J Emerg Med 2022

P

Population: Patients were considered for inclusion if they were 18– 69 years of age and presented to the ED primarily for management of acute LBP. This was defined as pain of two weeks' duration or less originating between the lower border of the scapulae and the upper gluteal folds, and received a diagnosis consistent with nontraumatic, non-radicular, musculoskeletal LBP, as determined by the attending emergency physician. All patients had already received a dose of an NSAID.

- Exclusions: Radicular pain, pain duration for greater than two weeks, direct trauma to the back within the previous month, or a history of experiencing LBP on average more than several times per year, pregnancy, breastfeeding, allergy to study medications.

I

Intervention: One of seven skeletal muscle relaxants (metaxalone, tizanidine, baclofen, diazepam, orphenadrine, methocarbamol, or cyclobenzaprine)

C

Comparison: Placebo

- **Primary Outcome:** Improvement in the Roland-Morris Disability Questionnaire (RMDQ) between ED discharge and the 1-week follow-up. The RMDQ goes from 0 to 24 with a 5-point improvement on this scale generally considered clinically significant.
- **Secondary Outcomes:** Moderate or severe LBP 1 week after the ED visit and medication adverse effects, assessed by asking patients to report any symptoms from the medications and dichotomizing their responses (yes/no).

Authors' Conclusions

"Among patients in the ED with acute LBP treated with a nonsteroidal anti-inflammatory drug, SMRs do not improve outcomes more than placebo. Neither age, sex, nor baseline impairment impacts these results."

Quality Checklist for Therapeutic Systematic Reviews

- [?] 1. The clinical question is sensible and answerable.
- [x] 2. The primary studies were of high methodological quality.
- [ ] 3. The assessment of studies were reproducible.
- [x] 4. The outcomes were clinically relevant.
- [ ] 5. There was low statistical heterogeneity for the primary outcomes.
- [x] 6. The treatment effect was large enough and precise enough to be clinically significant.

Results

Key Results:

- There were four RCTs conducted between 2012 and 2018 by the same research group with a combined total of 887 patients. The mean age was 39 years, 56% were male, median RMDQ score was 18 and 67% had a history of LBP.

- **Primary Outcome:** The seven SMRs and placebo group reported a decrease in their RMDQ score by about 10 points. The between-group differences were not statistically significantly different. We will put a table in the show notes with the point estimates and the 95% confidence intervals.
- Results were similar regardless of age, sex, and baseline severity. Higher baseline RMDQ was associated with greater clinical improvement (B coefficient 5.7 < 0.01).

Table 3. One Week Outcomes

Skeletal Muscle Relaxant	Mean Improvement in RMDQ (95% CI)
Placebo	10.5 (9.5–11.5)
Baclofen	10.6 (8.6–12.7)
Metaxalone	10.3 (8.1–12.4)
Tizanidine	11.5 (9.5–13.4)
Diazepam	11.1 (9.0–13.2)
Orphenadrine	9.5 (7.4–11.5)
Methocarbamol	8.1 (6.1–10.1)
Cyclobenzaprine	10.1 (8.3–12.0)

- **Secondary Outcomes:** Regarding pain intensity at 1 week, there was also no statistically significant differences among the groups (p = 0.93). Adverse medication effects were more common with cyclobenzaprine than with placebo (p < 0.01).

Time to Talk Nerdy:

1. Not a SRMA – This publication was a planned analysis of four RCTs looking at seven different SMRs with a total of 887 patients. All four of the RCTs had the same principal investigator, Dr. Friedman, and he was the senior author on this manuscript. Dr. Friedman has contributed greatly to the area of pain management.

The analysis was not a SRMA nor was it claimed to be one. The team presented the results of their four RCTs. A more comprehensive study would been to conduct a systematic review using the PRISMA guidelines. This would have included an exhaustive search of the world's literature without language restrictions and of the grey literature. Some of these RCTs may have been captured in the search depending on the inclusion and exclusion criteria.

2. Statistical Analysis – They performed a reasonably robust statistical analysis of their data. This was beyond the baseline characteristics of age, sex, RMDQ score and type of SMR recorded as a mean with a standard deviation, median with interquartile range or frequency with a precent when appropriate.

Their analysis included an ANOVA to determine if the between group differences measured on the RMDQ were statistically significant. There was no statistical or clinical (5-point change) difference between the seven SMR or placebo. They conducted a linear regression model to determine if there was an association of age, sex, baseline RMDQ severity, and history of back pain with the primary outcome. They also performed two logistic regression models with detailed explanation of variables.

3. Age Restriction – None of the four RCTs included patients over the age of 69 years. This is important to remember because this older cohort of patients is generally at greater risk of adverse events from medications with sedative side effects.

Time to Talk Nerdy:

Any potential benefit from the treatment, which was not demonstrated in this publication, would need to be weighed against the potential harms. The harms in a geriatric age group could be more serious. As an example, SMR could lead to more falls. Falls are the most common cause of traumatic injury resulting in older adults presenting to the ED [6]. Approximately 20% of falls result in injuries, and falls are the leading cause of traumatic mortality in this age group [7-9].

4. Placebo Effect – This study provides more evidence that the placebo effect is real and can be clinically significant. The mean improvement on the RMDQ score was 10.5 which is more than double what is considered clinically important. It demonstrates how easily it could patients can be fooled and how we can fool ourselves thinking the treatment provided "works". SMR were just as effective in lowing RMDQ scores as a placebo. We also need to consider the ethical considerations of knowingly prescribing a placebo in clinical practice (10).

5. Nihilism – It is hard not to become nihilistic when reviewing the evidence for LBP. There is a serious lack of high-quality evidence demonstrating clinical improvement to inform our care. This includes both pharmacologic (steroids, NSAIDS, and acetaminophen), and non-pharmacologic therapies (chiropractic, acupuncture, message therapy and physical therapy).

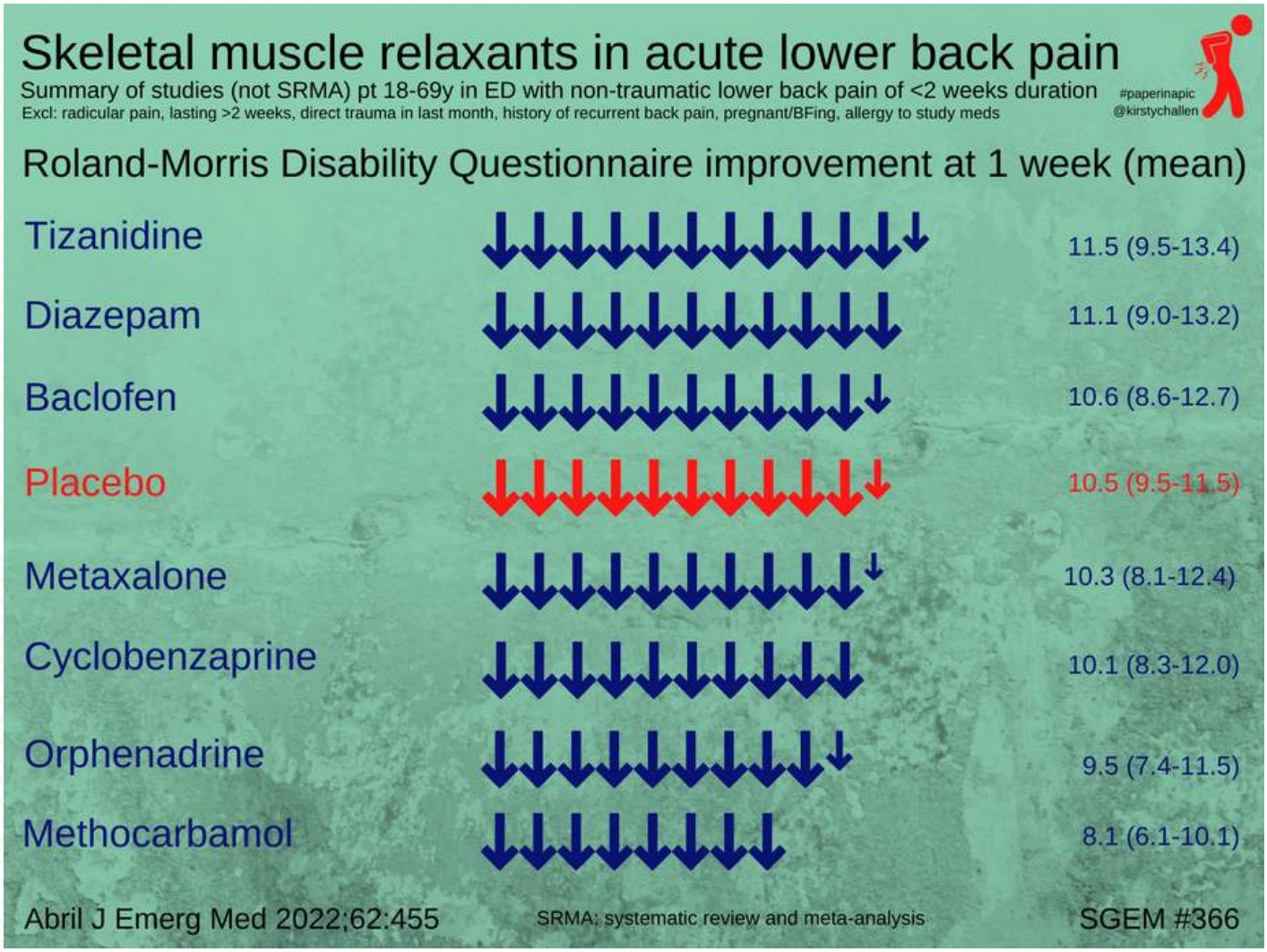
Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusion that combination of an NSAID and a SMR does not improve acute LBP outcomes more than an NSAID plus placebo, regardless of age, sex, baseline functional impairment, or history of LBP.

Clinical Application: There still appears to be no great treatment options for patients presenting with acute low back pain. Evidence for individual pharmaceutical therapies is limited and this trial provides evidence that a combination therapy of SMR and NSAIDs is not better than NSAIDs alone.

One final thing that is important is to discuss expectations with the patient. They need to know that their pain might not be completely relieved in the ED. It is about limiting suffering not eliminating pain. Most patients will have persistent symptoms a week after presentation and many will have continued pain and functional impairment months after symptom onset [11-13]. We need to be supportive and realistic when discussing the natural history of acute low back pain with patients.

What Do I Tell My Patient? You have a muscle strain in your back. This is a very common problem and can be very painful. Ibuprofen may help lower your pain, but it is unlikely get rid of your pain completely. Adding medications like a muscle relaxant has not shown to be more effective. In addition, muscle relaxants can cause some very bothersome and potentially dangerous side effects, such as dizziness, drowsiness that may lead to loss of balance and/or coordination and falls. Unfortunately, you may have pain over the next few weeks or months. Try to stay active and if your pain is getting worse, you can't function or are otherwise worried please return to the ED for re-assessment.

Case Resolution: You recommend an oral dose of ibuprofen 400mg as a first line agent and try to set reasonable expectations.



Ken Milne MD
@TheSGEM

What skeletal muscle relaxant (SMR) do you routinely prescribe for ED patients with non-traumatic acute low back pain? thesgem.com/2022/05/sgem36... @painfreeED @ACEPNow #EBM #FOAMed

Baclofen	4.7%
Cyclobenzaprine	22%
Other (specify)	9.7%
Don't routinely Rx SMR	**63.6%**

341 votes · Final results

367

GRACE2 – LOW-RISK, RECURRENT ABDOMINAL PAIN

Clinical Question:

What are the recommendations for managing patients with low-risk, recurrent, previously undifferentiated abdominal pain in the ED?

Bottom Line:

Given the lack of evidence available to guide us, there is tremendous uncertainty in the most appropriate management plan for these patietns. We should be open about that uncertainty without our patients and involve them in shared decision-making to ensure that the chosen management plan matches their personal values.

Guest:

Dr. Justin Morgenstern is an emergency physician and the creator of the #FOAMed project called First10EM.com

Case Overview:

A 33-year-old male presents to the emergency department (ED) complaining of abdominal pain. He states he has had the same pain for more than 10 years, and no one has ever been able to figure out what is going on. He doesn't have any specific symptoms today, including no fever, vomiting, diarrhea, or urinary symptoms. His vital signs are normal. His abdomen is diffusely tender, but without any surgical findings. You review his chart and note that he has had five CTs performed in the last year at your hospital alone, all of which were negative. You are worried about the cumulative radiation dose he has received but find it hard to exclude significant pathology on history and physical. After all, even patients with chronic abdominal pain can develop a new acute issue like appendicitis.

Background:

The Society of Academic Emergency Medicine (SAEM) has launched an initiative called GRACE which stands for Guidelines for Reasonable and Appropriate Care in the Emergency Department.

The first GRACE publication looked at low risk chest pain, and in my opinion, they filled a very valuable role. Most guidelines focus on a single emergency visit in isolation, but a patient who presents to the emergency department recurrently with the same symptoms may require a different approach. In the context of recurrent chest pain, they made eight key recommendations. The SGEM bottom line was there is moderate level of evidence that ACS can be excluded in adult patients with recurrent, low-risk chest pain using a single hs-troponin below a

Background:

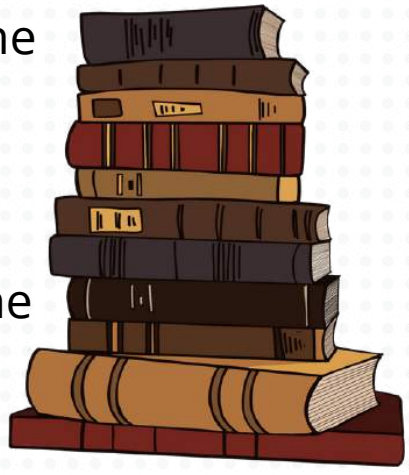
validated threshold without further diagnostic testing in patients who have a CCTA within the past two years showing no coronary stenosis.

The writing group of GRACE-2 wanted to look at clinically relevant questions to address the care of adult patients with low-risk, recurrent, previously undifferentiated abdominal pain in the ED. Through consensus, four questions were developed and then a systematic review of the literature was performed. This literature was then synthesized to come up with recommendations, following GRADE methodology.

GRADE stands for Grading of Recommendations, Assessment, Development, and Evaluation, it was pioneered at McMaster University, in creating rigorous, transparent, and trustworthy guidelines on common clinical problems for EM physicians that are not always directly studied in EM research activities.

There can be many presentations for low-risk abdominal pain. We have covered cannabis hyperemesis on SGEM#318 and SGEM#46 and pediatric gastroenteritis on SGEM#254.

Reference: Broder et al. Guidelines for Reasonable and Appropriate Care in the Emergency Department (GRACE) 2: Low-Risk, Recurrent Abdominal Pain in the Emergency Department. AEM May 2022



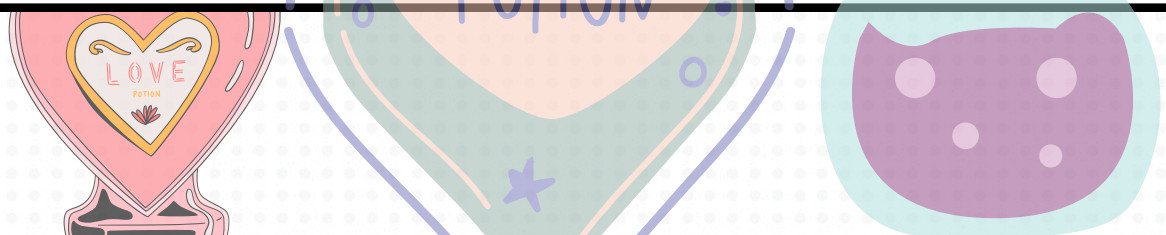
This is an SGEMHOP episode which means we have the lead author on the show. Dr. Joshua Broder is the Residency Program Director and Vice Chief for Education In the Division of Emergency Medicine Duke University School of Medicine.

Authors' Conclusions

"No direct evidence exists to direct the care of patients with low-risk recurrent undifferentiated abdominal pain in the ED. Improved definitions are required to better define this population, and clinically relevant outcomes of interest should be described and studied with rigorous research methodology to inform future clinical guidelines."

Quality Checklist for a Guideline

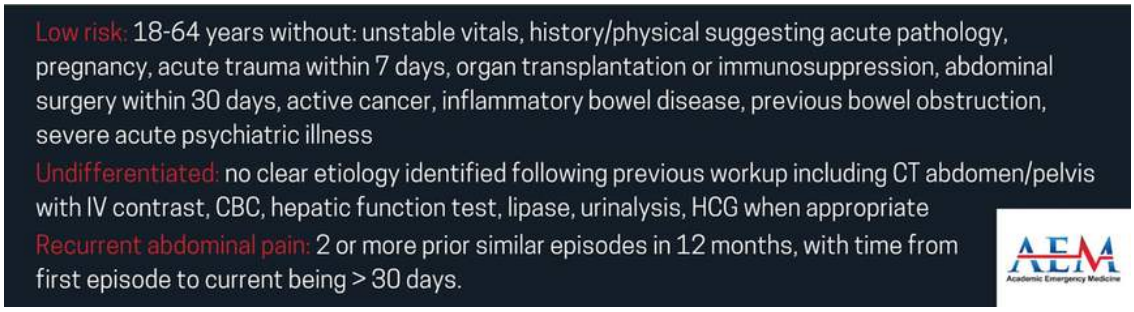
- [x] 1. The study population included or focused on those in the emergency department?
- [x] 2. An explicit and sensible process was used to identify, select and combine evidence?
- [x] 3. The quality of the evidence was explicitly assessed using a validated instrument?
- [x] 4. An explicit and sensible process was used to the relative value of different outcomes?
- [x] 5. The guideline thoughtfully balances desirable and undesirable effects?
- [x] 6. The guideline accounts for important recent developments?
- [x] 7. The guidelines has been peer-reviewed and tested?
- [x] 8. Practical, actionable and clinically important recommendations are made?
- [x] 9. The guideline authors' conflicts of interest are fully reported, transparent and unlikely to sway the recommendations of the guidelines?



Results

Key Results:

- We don't have a key result section but what we do have is the key recommendations. It is important to understand the definitions created by the guideline committee for terms "low-risk, undifferentiated and recurrent".



- **Listen to the SGEM podcast to hear Josh comment on each of these four recommendations.**
- **Recommendation #1:** In adult ED patients with low-risk, recurrent, undifferentiated abdominal pain and prior negative 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. [Consensus, no evidence]

Time to Talk Nerdy:

Listen to the podcast to hear Josh answer our five nerdy questions.

1. Scope of the Review: There are thousands of questions I could imagine asking for this guideline. What is the role of observation and repeat exams instead of imaging? When is blood work required? What chronic therapeutic options should the emergency physician consider? Obviously, this guideline was a massive undertaking as it stands. How did you decide which questions were the most important to ask?

2. Pediatric Patients: This guideline only applies to adult patients. Those of us who work community ED or as Pediatric Emergency Medicine know many children present with abdominal pain. Are there any plans for the GRACE group to look at this issue?

3. Patient Representative: In the recommendation to screen for depression, you lean heavily of the comments of a patient representative in your group. For a scientific guideline, I think that might surprise people. Can you explain the role of the patient representative in the creation of these guidelines? Patients are all unique. I wonder how representative this one patient's views are for the average patient.

4. Gaps in Knowledge: Clearly there are huge gaps in knowledge in this area. That could be looked at as a negative or a positive. It is an opportunity for those listening to design a study with a clinically relevant question and proper methods to answer the question. If could give future researchers one area that you think would have the biggest impact for patients, what would it be?

5. Making Guidelines without Evidence: Personally, I find it very frustrating when guidelines make strong recommendations in the absence of evidence. This guideline does a very good job discussing the absence of evidence, and explaining why recommendations were made, but it is still a difficult task without evidence. I wonder if you

Time to Talk Nerdy:

could comment on what you think is the best approach to writing a guideline when no evidence exists, and the clinical value of such guidelines.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusion that there is no direct evidence to guide our management of patients with low risk, recurrent, undifferentiated abdominal pain.

Clinical Application: Although the current lack of evidence is somewhat disappointing, managing uncertainty is a core skill of emergency physicians. In some ways, the lack of clear science frees us up to use our clinical judgement and talk to our patients to develop individualized treatment plans that suit their values best.

What Do I Tell My Patient? Unfortunately, despite recurrent abdominal pain being a very common presentation, there is very little good science to guide us. You have been through these symptoms many times before, so you know that it is unlikely that a repeat CT scan will provide us with an answer today. However, we never want to miss anything, and there is always a chance that something new is happening today. Let's talk about the specific risks and benefits, and then you can help me decide what is the best management plan for you.

Case Resolution: You discuss the potential harms and the potential benefits of repeat imaging with your patient and opt for repeat exams over a brief period of observation with rapid follow-up with his primary care provider. You treat his pain effectively with non-opioid analgesia. You discuss depression and anxiety with him, and he admits that the recurrent abdominal pain has been causing significant anxiety, but he is already addressing that with his family doctor.

Ken Milne MD
@TheSGEM

Which is a GRACE2 recommendation for adult ED patients with low-risk, recurrent, undifferentiated abdominal pain? thesgem.com/2022/05/sgem36... #sgemhop @KirstyChallen @First10EM @AcademicEmerMed @SAEMonline

No CTAP after neg CT <1yr	23.1%
Get US after neg IV-CTAP	7.7%
May screen for depression	**65.4%**
Maximize opioid use	3.8%

78 votes · Final results

8:25 AM · May 31, 2022 · Twitter for iPhone

GRACE-2: Low-Risk, Recurrent Abdominal Pain in the ED

1 Prior negative CTAP in last 12 months: insufficient evidence to avoid or recommend repeat imaging.

After negative IV contrast CTAP in ED: no ultrasound unless concern for biliary/pelvic pathology. **2**

3 Screening for depression &/or anxiety may be performed during the ED evaluation.

Suggest opioid-minimizing stategy for pain control. **4**

Low risk: 18-64 years without: unstable vitals, history/physical suggesting acute pathology, pregnancy, acute trauma within 7 days, organ transplantation or immunosuppression, abdominal surgery within 30 days, active cancer, inflammatory bowel disease, previous bowel obstruction, severe acute psychiatric illness

Undifferentiated: no clear etiology identified following previous workup including CT abdomen/pelvis with IV contrast, CBC, hepatic function test, lipase, urinalysis, HCG when appropriate

Recurrent abdominal pain: 2 or more prior similar episodes in 12 months, with time from first episode to current being > 30 days.

SGEM-HOP #367

AEM Academic Emergency Medicine

368

JUST A NORMAL SALINE DAY IN THE ICU – THE PLUS STUDY

Clinical Question:

Is the 90-day mortality in critically ill adult patients lower with the use of plasma-lyte 148, a balacned crystalloid solution, for fluid resuscitation and therapy, than the use of normal saline?

Bottom Line:

Plasma-lyte is not routinely necessary for fluid resuscitation in critically ill adults in the ICU.

Guest:

Dr. Aaron Skolnik is an Assistant Professor of Emergency Medicine at the Mayo Clinic Alix School of Medicine and Consultant in the Department of Critical Care Medicine at Mayo Clinic Arizona. He is board certified in Emergency Medicine, Medical Toxicology, Addiction Medicine, Internal Medicine-Critical Care, and Neurocritical Care. Aaron is a full-time multidisciplinary intensivist. He is the Medical Director of Respiratory Care for Mayo Clinic Arizona and is most proud of his position as medical student clerkship director for critical care.

Case Overview:

A 62-year-old man is brought in by EMS from home with lethargy and hypotension. Chest x-ray is clear, labs are remarkable for a leukocytosis of 16,000 with left shift; exam is notable for left flank pain and costovertebral tenderness. Straight catheter urinalysis is grossly cloudy, and pyuria is present on microscopy. Blood pressure is 85/50 mmHg. You wonder which IV fluid should you order?

Background:

There has been a longstanding debate about which intravenous fluid is the best for volume resuscitating critically ill patients. We've known for some time that albumin is bad for injured brains, and that hydroxyethyl starch solutions have been associated with kidney injury and mortality. Since then that debate has broadly centered on the choice between what we will call "abnormal saline" (0.9% sodium chloride), and balanced crystalloid solutions, meaning those with a chloride composition closer to plasma such as lactated ringer's or Plasma Lyte 148.

Early work suggested potential harm from 0.9% saline, that may be partly driven by kidney injury associated with the administration of high-chloride content IV fluids.

In the last few years, the pendulum has swung back and forth. Two large, cluster-randomized trials (SMARTand SALT-ED) showed a small benefit to the use of balanced crystalloids in preventing a composite outcome of Major Adverse Kidney Events within 30 days (aka MAKE-30).

Background:

Then, the BaSICS trial (a multicentred RCT done in 75 Brazilian ICUs) came along and compared saline to Plasma-Lyte at what the authors deemed slow and fast infusion rates. We reviewed that last time on SGEM#347. There was no interaction between fluid type or rate of infusion with the primary outcome of 90-day survival. Among 19 secondary outcomes, which should only be considered hypothesis generating, SOFA scores and neuro SOFA scores at day seven were worse in the balanced crystalloid group.

Now we have the PLUS trial, from Australia and New Zealand to add to the medical literature on this issue.

Reference: Finfer et al. Balanced Multielectrolyte Solution versus Saline in Critically Ill Adults. NEJM 2022.

P

Population: Patients 18 years or older, admitted to 53 ANZ ICUs over 38 months, whom the treating clinician deemed to need fluid resuscitation and were expected to be in the ICU on three consecutive days.

- **Exclusions:** Patients with specific ICU fluid requirements, those who received disqualifying fluid prior to enrollment (> 500 mL in the ICU), those at imminent risk for death or with life expectancy < 90 days, and those at risk for cerebral edema.

I

Intervention: Plasma-Lyte 148 for all resuscitation episodes while in ICU for up to 90 days after the first episode of fluid resuscitation

C

Comparison: 0.9% saline for all resuscitation episodes while in ICU for up to 90 days after the first episode of fluid resuscitation

- **Primary Outcome:** All-cause mortality within 90 days after randomization
- **Secondary Outcomes:** Peak serum creatinine level during the first seven days after randomization, the maximum increase in creatinine level during ICU stay, receipt of new renal-replacement therapy, receipt and duration of treatment with vasoactive drugs, duration of mechanical ventilation in the ICU, length of ICU and hospital stays, and death from any cause during ICU stay, during hospital stay, and within 28 days after randomization.
- **Trial:** Double-blind, parallel-group, randomized, controlled trial.

Authors' Conclusions

"Among adults with out-of-hospital cardiac arrest, treatment with intravenous or intraosseous calcium compared with saline did not significantly improve sustained return of spontaneous circulation. These results do not support the administration of calcium during out-of-hospital cardiac arrest in adults."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [ ] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [x] 12. Financial conflicts of interest.

Results

Key Results:

- They recruited 5,037 patients from 53 ICUs in Australia and New Zealand. The mean age was 62 years, 39% female, 76% had invasive mechanical ventilation, and a median APACHE score of 19.
- **Primary Outcome:** All-cause mortality within 90 days after randomization
  - 21.8% Plasma-Lyte 148 group vs 22.0% saline group
    - Absolute difference of −0.15 percentage points (95% CI, −3.60 to 3.30; P=0.90)
  - Odds Ratio of 0.99 (95% CI, 0.86 to 1.14)
- **Secondary Outcomes:** Over the first seven days after randomization, arterial blood pH was higher, and the serum chloride level was lower in the balanced crystalloid group. Both achieved statistical significance, though the absolute difference was probably not clinically meaningful. Over that same time period, there were no significant differences in mean heart rate, mean arterial pressure, mean central venous pressure, creatinine, hemoglobin, and lactate between groups. Measures of organ failure including rise in creatinine and need for renal replacement therapy were similar between groups. There was also no significant difference in days alive free of the vent, free of renal replacement, outside of the ICU, or outside of the hospital. Adverse events did not differ between groups.

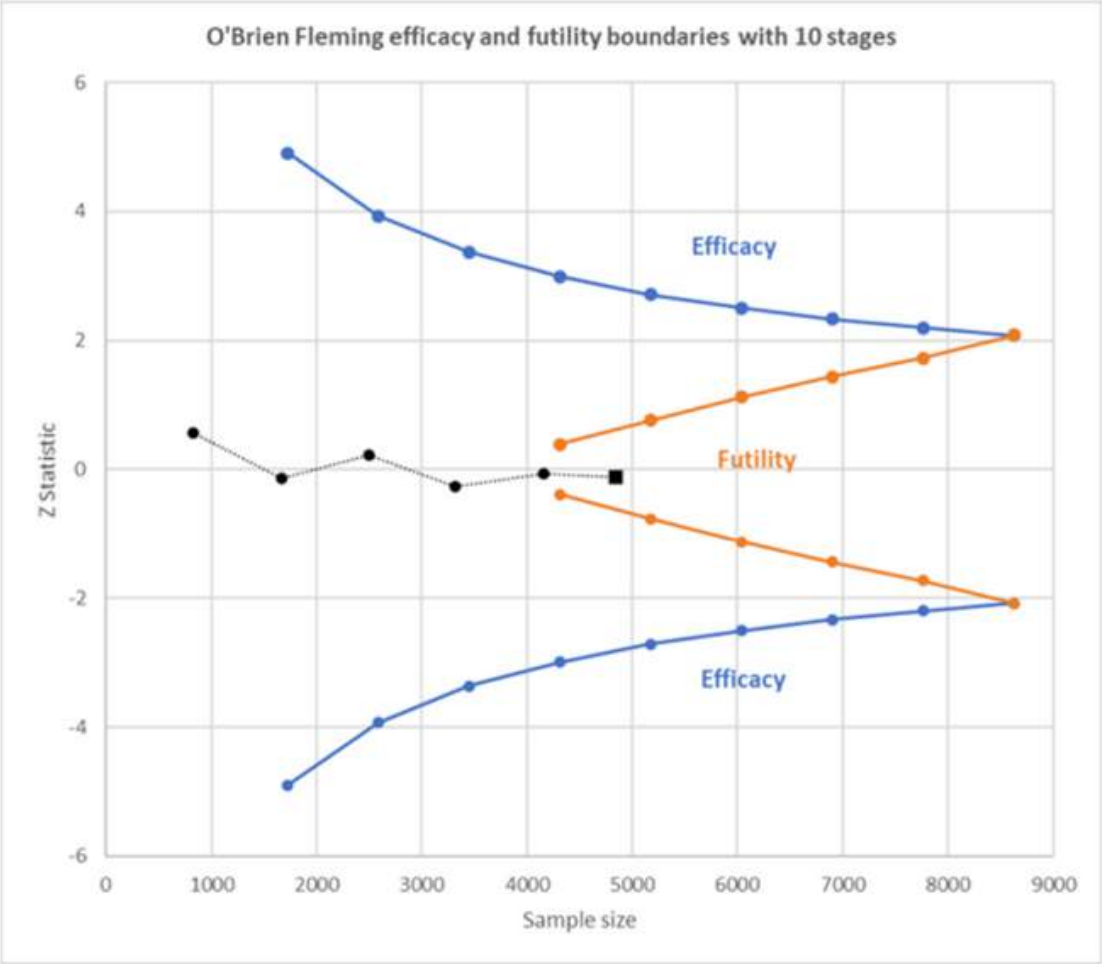
Time to Talk Nerdy:

We reached out to the lead author Dr. Simon Finfer. He was kind enough to send a brief responses to our five nerdy questions.

1) Recruitment: The trial was originally designed to recruit a sample size of 8,800 patients. Due to COVID-19, the recruitment stopped at just over 5,000 patients. Do you think this influenced the trial results in any meaningful way?

- "NO – this was covered in paper and supplementary figure S1**1**

Figure S11. Post-hoc assessment of data in relation to efficacy and futility boundaries



We conducted a post hoc analysis to determine whether our results would have crossed standard futility boundaries. We used an O'Brien Fleming type of spending function,[4] which is one of the most conservative and widely used methods. Regardless of the number of interim analyses conducted, our observed z-value (-0.12) crossed the futility boundaries which lie at approximately -0.57 and +0.57 at 56% of originally proposed information.

Time to Talk Nerdy:

2) Fluids: More than half of the patients in the balanced crystalloid group received more than 500 mL of normal saline, mostly because of medications that could not be mixed in balanced solution. How might this have swayed the trial result and what did the authors do to account for this?

- "We did several secondary analyses that did not alter the results. They are all in table 2 – see attached which is convincing that going on further to 8800 or even more would not have produced a different result"

Table 2. Trial Outcomes.*

Outcome	BMES Group (N=2515)	Saline Group (N=2522)	Odds Ratio (95% CI)	Absolute Difference (95% CI)†
Death from any cause within 90 days after randomization				
Primary analyses				
Unadjusted — no./total no. (%)	530/2433 (21.8)	530/2413 (22.0)	0.99 (0.86 to 1.14)	−0.15 (−3.60 to 3.30)‡
Adjusted§			0.99 (0.86 to 1.14)	−0.17 (−3.51 to 3.16)
Multiple imputation¶			0.99 (0.86 to 1.13)	−0.22 (−3.61 to 3.18)
Secondary analyses‖				
Secondary analysis 1			1.19 (0.96 to 1.46)	2.78 (−1.71 to 7.27)
Secondary analysis 2			0.94 (0.77 to 1.15)	−0.95 (−5.13 to 3.24)
Secondary analysis 3			1.06 (0.79 to 1.42)	0.91 (−4.65 to 6.47)
Inverse probability of treatment weighting — no./total no. (%)	176/858 (20.5)**	298/1574 (18.9)**	1.06 (0.88 to 1.28)	1.01 (−3.49 to 5.51)
Other mortality outcomes				
Death from any cause within 90 days after randomization while in the ICU — no./total no. (%)	395/2433 (16.2)	371/2413 (15.4)	1.07 (0.91 to 1.25)	0.89 (−2.03 to 3.81)
Death from any cause within 90 days after randomization while in the hospital — no./total no. (%)	503/2433 (20.7)	511/2413 (21.2)	0.97 (0.85 to 1.12)	−0.49 (−3.83 to 2.85)
Death from any cause within 28 days after randomization — no./total no. (%)	451/2433 (18.5)	445/2413 (18.4)	1.01 (0.87 to 1.17)	0.12 (−3.31 to 3.56)
Other binary outcomes				
Receipt of new renal-replacement therapy — no./total no. (%)	306/2403 (12.7)	310/2394 (12.9)	0.98 (0.83 to 1.16)	−0.20 (−2.96 to 2.56)
Receipt of vasoactive drugs — no./total no. (%)	2115/2453 (86.2)	2133/2448 (87.1)	0.92 (0.78 to 1.09)	−0.85 (−4.06 to 2.36)
Continuous outcomes				
Maximum creatinine level in the ICU during days 1 to 7 — μmol/liter	155.8±127.4	154.4±126.3		0.89 (−3.50 to 5.28)
Maximum increase in creatinine level in the ICU — μmol/liter	36.6±94.0	36.1±90.0		0.52 (−4.65 to 5.69)
Days alive and free of mechanical ventilation	68.3±33.4	68.2±33.4		0.06 (−1.79 to 1.91)
Days alive and free of vasoactive agents	69.9±32.9	69.9±32.7		0.03 (−1.80 to 1.85)
Days alive outside the ICU	65.3±32.8	65.3±32.8		0.05 (−1.77 to 1.87)
Days alive outside the hospital	52.9±31.7	52.3 ±31.5		0.62 (−1.15 to 2.38)

Time to Talk Nerdy:

23) Brain Injury: The authors didn't test balanced crystalloid solution in TBI patients or others thought to be at risk for cerebral edema. What do you think about balanced versus saline in this group? Is this population the clinical stronghold of normal saline?

- "The BaSICS study validates our decision not to expose patients with TBI to PL148 which has higher tonicity than other balanced fluids but still lower than NS. Patients with TBI should get NS.

4) Small Effect Size: The trial is a "negative" one, but as the authors point out in their discussion, their results also allow for up to a 3% increase or decrease in the risk of death or new renal replacement associated with balanced crystalloid administration. Is that an acceptable level of uncertainty about effect? How do you apply those confidence intervals to patient care?

- "See answer to point 1 and below"

5) Other Evidence: There is a recent systematic review and meta-analysis published in NEJM Evidence examining 13 RCTs and over 35,000 patients comparing balanced crystalloid to saline in critically ill adults. That SRMA concluded "The estimated effect of using balanced crystalloids versus saline in critically ill adults ranges from a 9% relative reduction to a 1% relative increase in the risk of death, with a high probability that the average effect of using balanced crystalloids is to reduce mortality." What do you think of the SRMA and how do you integrate all of this recent evidence into your clinical practice?

- "Well, as I am the corresponding author for that paper, I think it is quite good. The overall message is that balanced solutions are probably better overall, but the effect is small, for patients with a low risk of death the absolute effect is very small indeed. Patient with TBI and possibly other acute brain pathologies should get normal saline or a fluid of equal tonicity. We are conducting a patient level meta-analysis which will allow us to look at subgroups' effects in more detail (I am the senior author for that as well).

Time to Talk Nerdy:

We have all the data and hope to publish by the end of this year."

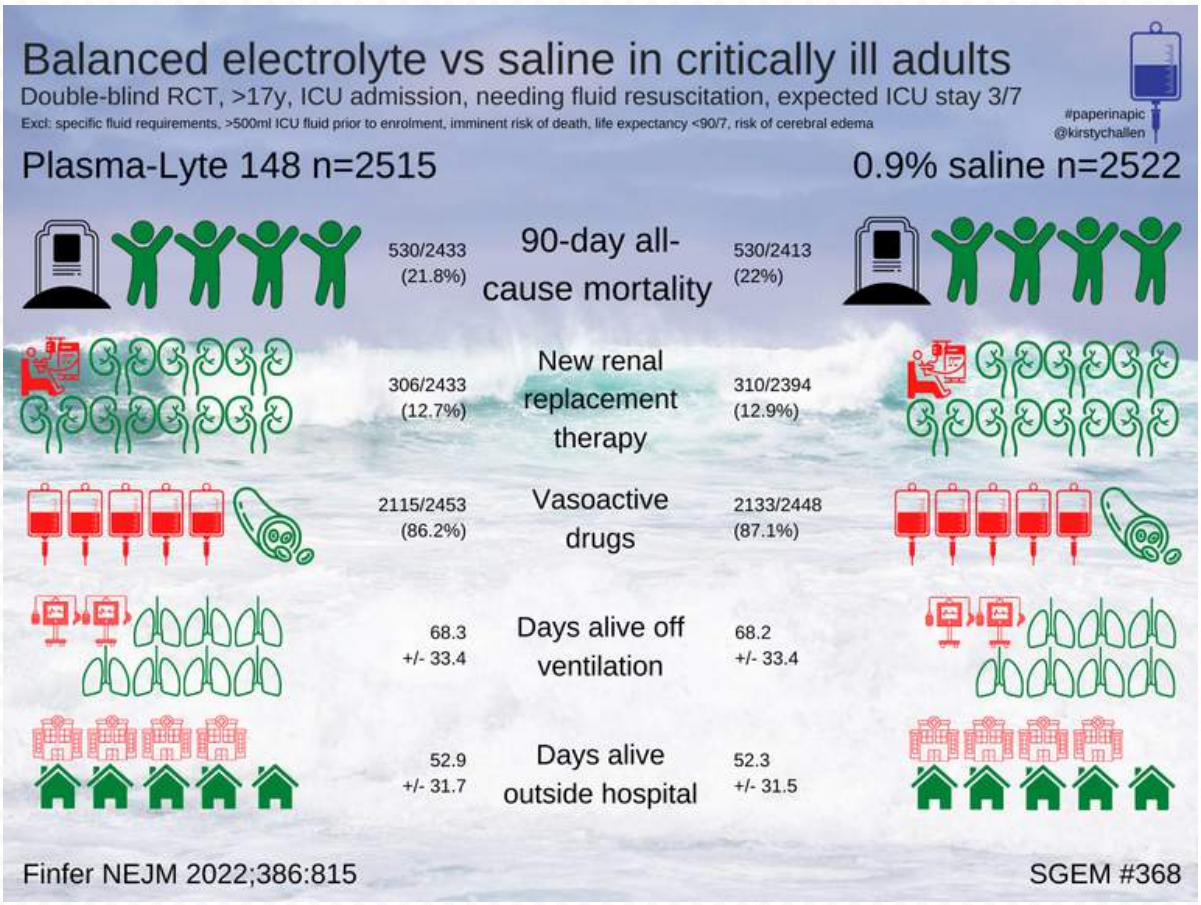
Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: Critically ill emergency department patients without significant brain injury can be safely fluid resuscitated with either balanced crystalloids or normal saline without a large difference in patient-centered outcomes.

What Do I Tell My Patient? You have very low blood pressure caused by your body's response to a bad infection. We are treating your infection with antibiotics. We are going to give you some IV fluids to try to raise your pressure, but we may have to use some medicines to keep it up for some time, and take care of you in the intensive care unit.

Case Resolution: You cover the patient with piperacillin/tazobactam and resuscitate him with a total of 2 liters of normal saline. He remains hypotensive and point of care ultrasound reveals a normal ejection fraction and a plump, adynamic inferior vena cava. He is started on norepinephrine and admitted to the intensive care unit. Urine culture grows pan-sensitive E.coli and antibiotics are narrowed. He is discharged home well on hospital day three.

Other FOAMed: REBEL EM



Ken Milne MD
@TheSGEM

What IV solution do you usually use for resuscitating critically ill patients? #EBM
thesgem.com/2022/06/sgem36...
@NEJM @ACEPNow @stemlyns @srrezaie
@KirstyChallen

"Normal" Saline	26.5%
Ringer's Lactate	**60.1%**
Plasma-Lyte	10.8%
Other (specify)	2.7%

566 votes · Final results

7:31 AM · Jun 14, 2022 · Twitter Web App

369

ROMEO IS BLEEDING – DOES HE NEED A REPHILL?

Clinical Question:

In the resuscitation of pre-hospital trauma patients with hemorrhagic shock is there a patient-oriented benefit to using blood and plasma over 0.9% saline?

Bottom Line:

The results of rephill do not justify the expense and logistical difficulties associated with the use of lyophilised plasma and red cell use in prehospital ambulance services for adult trauma patients.

Guest:

Dr. Casey Parker is a Rural Generalist that includes in his practice emergency medicine, anaesthesia and critical care. He is also now a fully fledged “sonologist”. Casey currently splits his time between Broome, a small rural hospital in the remote Kimberley region of Western Australia, and a large tertiary ED in sunny Perth.

Case Overview:

You are working in the emergency department (ED) and receive a call from the Advanced Care Paramedics who are at the scene of a stabbing. Apparently, two rival gangs (Jets and Sharks) had a rumble. The young man has been stabbed in the abdomen and lost a lot of blood. The patient is tachycardic (120 beats/minute), hypotensive (80/60 mmHg) and looks very pale. They have two large bore intravenous (IV) access and are planning to bring them to your ED as soon as possible. The paramedic asks you, “we have saline, and we also have red-cells and this fancy new lyophilised plasma. Should we give our shocked patient saline or plasma / red cells en route to the ED?” What do you advise him?

Background:

The use of fluids in trauma resuscitation has been studied in a number of trials in recent years. A lot of observational data has been collected from the battlefields of Iraq and Afghanistan.

The Control of Major Bleeding After Trauma (COMBAT) Trial was published in the Lancet in 2018. It was a pragmatic, randomised, single-centre trial done at the Denver looking at the use of plasma in the prehospital setting. This trial did not show a statistical mortality benefit within 28 days of injury. First10EM and REBEL EM both did a review of the COMBAT trial.

The Prehospital Air Medical Plasma (PAMPer) trial was published in NEJM, also in 2018. The goal of this trial was to determine the efficacy and safety of prehospital administration of thawed plasma in injured patients who are at risk for hemorrhagic

Background:

shock. This trial did report that prehospital administration of plasma was safe and resulted in lower 30-day mortality. PAMPer was reviewed by First10EM and The Bottom Line.

The traditional teaching in trauma is to replace blood with blood products, so we would expect that we should see a benefit if we used blood and plasma instead of saline alone for the initial resuscitation.

Reference: Crombie et al. Resuscitation with blood products in patients with trauma-related haemorrhagic shock receiving prehospital care (RePHILL): a multicentre, open-label, randomised, controlled, phase 3 trial. The Lancet Haematology 2022

P

Population: Adult patients 16 years of age or older suffering traumatic injury resulting in shock believed to be due to a traumatic haemorrhage. Shock was defined as a systolic BP less than 90 mmHg or an absent radial pulse.

- **Exclusions:** Patients known to refuse blood produces, those who received transfusion of prehospital blood products before assessment for eligibility, pregnancy (known or apparent), isolated head injury without evidence of major haemorrhage, and prisoners.

I

Intervention: Up to four units of blood products boluses one unit at a time. Units were alternating between units of O-negative packed red cells (PRBC) or or reconstituted lyophilised plasma to a maximum of two units of either.

C

Comparison: Up to four boluses of 0.9% saline (250ml/bolus)

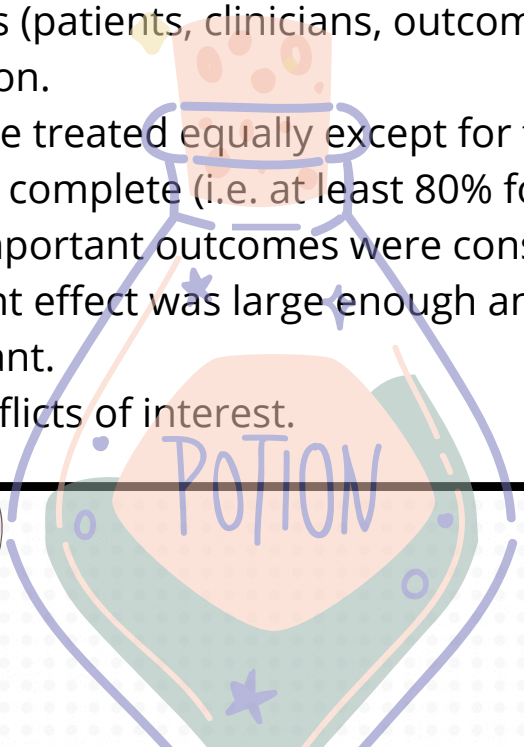
- **Primary Outcome:** Composite outcome of mortality from time of injury to hospital discharge or the failure to clear lactate by 20% within the first two hours after randomisation.
- **Secondary Outcomes:** Individual components of the composite primary outcome, fluid volumes, measures of coagulopathy, 30 day mortality and common side effects of transfusion such as reaction and adult respiratory distress syndrome (ARDS)
- **Trial:** This was a multi-centre, open-label, concealed, single-blinded, randomised controlled trail

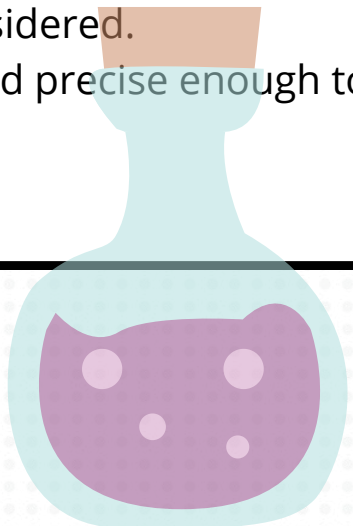
Authors' Conclusions

"The trial did not show that prehospital PRBC–LyoPlas resuscitation was superior to 0.9% sodium chloride for adult patients with trauma related haemorrhagic shock. Further research is required to identify the characteristics of patients who might benefit from prehospital transfusion and to identify the optimal outcomes for transfusion trials in major trauma. The decision to commit to routine prehospital transfusion will require careful consideration by all stakeholders."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [?] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [?] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [x] 12. Financial conflicts of interest.





Results

Key Results:

- The trial randomized 432 participants. Median age was 38 years, 82% were male and 62% of patients had blunt force trauma from a motor vehicle collision.

- **Primary Outcome:** Composite outcome of mortality from time of injury to hospital discharge or the failure to clear lactate by 20% within the first two hours after randomisation.
  - 64% in the blood product group vs 65% of the saline group
  - Adjusted risk difference –0·025% [95% CI –9.0 to 9.0], p=0·996)
  - Adjusted risk ratio 1.01 [95% CI 0.88 to 1.17]
- **Secondary Outcomes:**
  - Mortality: 43% in the blood products group vs 45% in the saline group (Adjusted risk ratio 0.97 [95% CI 0.78 to 1.20]; p=0·75)
  - Failure to clear lactate: 50 vs 55% (Adjusted risk ratio 0.94 [95% CI 0.78 to 1.13]; p=0·52)
  - None of the other secondary outcomes reported were statistically different
  - Serious adverse events were similar between both groups

Time to Talk Nerdy:

1. Mixing POOs and LOOs: Is it appropriate to place LOOs (lab-oriented outcomes) and POOs (patient-oriented outcomes) together in a composite primary? This trial used a composite primary outcome that included mortality (a big POO) with lactate clearance (a lab-oriented outcome that may or may not be a surrogate marker for mortality). Usually one might design a trial with softer LOOs if one were trying to detect a subtle difference in a population where hard patient-oriented outcomes are rare. However, in this trial nearly half of the patients died. Mortality is very objective and important to patients, and it would therefore seem better to stick with a single primary outcome and power the recruitment to that end.

2. Dose: The RePHILL trial participants received less than a litre of fluid in total prior to arriving in hospital. That could either be all saline in the control group or a mixture of saline and blood products in the intervention group. The fact that this was a "negative" trial may mean that there truly is no difference between saline and blood products in pre-hospital resuscitation. Or, it could mean that at this dosage there is no detectable potential benefit or potential harm observable. For example, If we only gave 10 mg of aspirin to patients with ST elevated myocardial infarction and observe no mortality benefit, but also no GI bleeds we could conclude that aspirin has no effect. However, we do have high-quality data showing that there is a benefit to giving 162.5mg of aspirin to STEMI patients with a small increase in harm (TheNNT.com). So is the RePHILL trial telling us there is no benefit, or that the doses are not adequate to give an effect that we can observe? This is why it is good to be cautious not to over or under-interpret the data. The most accurate conclusion is that the intervention provided in this cohort of trauma patients with shock did not demonstrate superiority over the control group. This is different than concluding blood products do not work for trauma patients in the prehospital setting.

Time to Talk Nerdy:

3. External Validity: This trial used a team of pre-hospital physicians and critical care paramedics in the UK. The team traveled by helicopter or land based rapid response vehicles with a blood product that is relatively new and hard to come by (lyophilised plasma). If RePHILL had been a positive trial and shown a clear benefit then we would be stuck with the issue of external validity, especially in rural areas like Canada and Australia which are much larger countries geographically. We do not have the systems or access to this product. It would be very difficult to bring a physical-led plasma wielding team to the roadside in most parts of the world. Rural clinicians know about the tyranny of distance. The goal should be to get the best medical care to rural patients which can be logistically tough at times. However, it should not be the knowledge of the team that results in lesser care.

4. Too Good to Be True: The original power calculation for RePHILL was based on the consensus that a 10% absolute difference in the primary outcome. This is a large difference for a complex disease like trauma using a simple intervention. However, the previous PAMPer trial did show an amazingly high 9.8% mortality reduction. The RePHILL trial was unfortunately interrupted by COVID19 after 432 patients were randomised. It is unlikely that if RePHILL has enrolled 68 more patients for a total of 500 it would have shown a 10% absolute reduction in the primary outcome. We know that science usually iterative and moves in baby steps. In diseases like sepsis or trauma where there are complex interventions and systems involved it is really very unlikely that any single intervention will have such a large mortality impact. This suggests that the PAMPer trial is an outlier and we should remain skeptical as these results seem too good to be true. Trials with results that seem too good to be true are rarely reproduced on subsequent studies. We think RePHILL is such a case. It could be viewed as a partial repeat of the PAMPer trial and is more consistent with the COMBAT trial results demonstrating no superiority.

Time to Talk Nerdy:

5. The Goldilocks Zone of Mortality: When looking at mortality data there are at least three possible populations:

- Mild Traumatic Injuries: Patients who are not too sick and 100% will survive, no matter what intervention. This is why we do not put ankle sprains into trauma trials like RePHILL.
- Severe Traumatic Injuries: These are the super sick patients whom will die no matter what we do. For example if you only studied patients with hypotension due to penetrating heart injury then you would find it difficult to prove any intervention helped them
- Goldilocks Zone: These patients are the ones that are not too sick, but not too well to get a clinically meaningful benefit from an intervention. The patients in the the RePHILL trail seem to be within the Goldilocks zone – high mortality for sure, but with potentially salvageable injuries that need to get to definitive care

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions. This trial does not demonstrate any benefit to the use of small volumes of prehospital blood products over the use of normal saline.

Clinical Application: The choice of pre-hospital fluids remains an open question. We simply do not know if there is a real benefit to early infusion of blood products in the field.
There are certainly some patients who will benefit from the use of blood products – although at this time it seems that we can limit the use of blood products to the ED and hospital phase of care. Further research is needed to define the group patient whom may benefit from earlier blood in the prehospital environment.
Having said that – trauma is a team sport, and having a seamless system of care between the prehospital providers, the ED, and the operating room is crucial.

What Do I Tell My Patient? You have been stabbed and lost a lot of blood. We are going to start some intravenous fluids and get you to the hospital as quick as possible. They will be standing by with a team to help you on arrival.

Case Resolution: I will advise the prehospital team to use whatever fluid they have and feel is necessary to resuscitate the patient whilst expediting transfer to the ED. A trauma call is put out to activate the lab, surgical teams and radiology in order to provide rapid care to this very sick patient.

Other FOAMed:

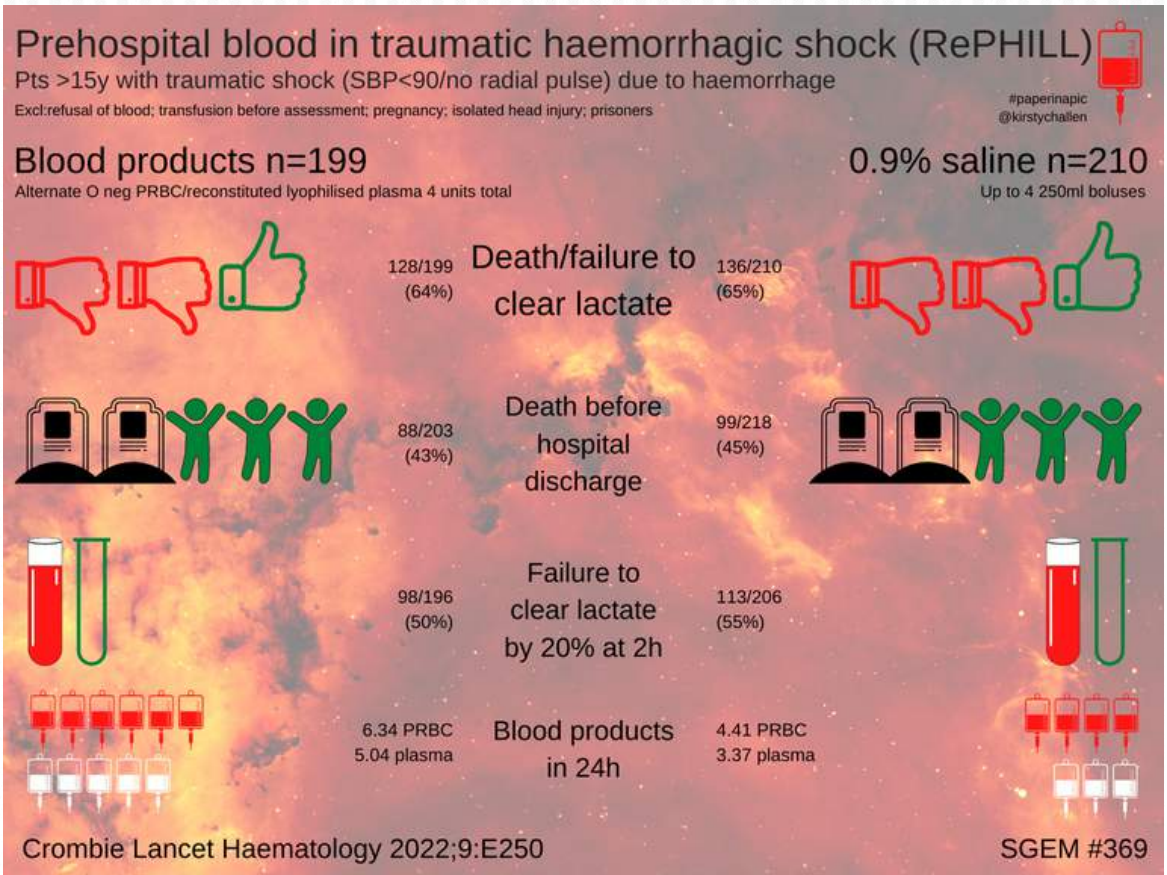
- REBEL EM: The RePHILL Trial
- Critical Care Reviews: RePHILL Trial Results Livestream
- St. Emlyn's Blog: The RePHILL Trial
- The Bottom Line: RePHILL
- First10EM: The RePHILL Study – Is Saline the Fluid of Choice in Trauma?

What is your resuscitation fluid of choice usually in adult hemorrhagic shock patients in the pre-hospital setting? thesgem.com/2022/06/sgem36... @broomedocs @DrHowieMell @hp_ems @EMS1 @EMSWorldOFCL

Saline 0.9%	24.7%
Lactated Ringer's	28.3%
Blood Products	**41.9%**
Other (specify)	5.1%

198 votes · Final results

8:09 AM · Jun 21, 2022 · Twitter for iPhone



370

LISTEN TO YOUR HEART (SCORE)... MACE INCIDENCE IN NON-LOW RISK PATIENTS WITH KNOWN CORONARY ARTERY DISEASE

Clinical Question:

What is the 30-day incidence of MACE in patients who are non-low risk but have known coronary artery disease?

Bottom Line:

It may be reasonable, in patients who are moderate risk by the HEART score but do not have existing known CAD, to pursue outpatient follow up instead of urgent inpatient workup.

Guest:

Dr. Corey Heitz is an emergency physician in Roanoke, Virginia. He is also the CME editor for Academic Emergency Medicine.

Case Overview:

You are working a shift in your local community emergency department (ED) when a 47-year-old male presents with chest pain. His symptoms are moderately suspicious, he has a normal EKG, and a history of hypertension. His father had a minor heart attack at the age of 63. With a negative initial troponin, this gives him a HEART score of 4. He has no history of coronary artery disease. You have been reading about the overuse of objective cardiac testing (OCT) and wonder if this patient really needs admission to the hospital.

Background:

Chest pain is one of the most common presentations to the ED. Much ink has been spilled over the years on trying to find a way to safely rule-out acute coronary syndrome in these patients. Multiple clinical decision instruments have been created to risk stratify patients and guide clinicians (TIMI, GRACE, MAC, T-MAC, HE-MAC, ADAPT, VCPR, EDACS, etc).

The HEART score was originally developed in 122 patients in the Netherlands and published in 2008. Backus and colleagues published their multi-centre validation of the HEART score in 2010. Since then, there have been several studies looking at this clinical decision instrument.

We looked at a HEART Score Pathway that included a HEART Score and 0 and 3 hour cardiac troponin testing on SGEM#151 with our friend Salim Rezaie. The bottom line from that episode was that the HEART Pathway appears to have the potential to safely decrease objective cardiac testing, increase early discharge rates and cut median length of stay in low-risk chest pain patients presenting to the ED with suspicion of ACS.

Background:

In prior decades nearly all patients presenting to EDs with chest pain were admitted to hospital. If we thought about ACS, we brought them in. This would be for objective cardiac testing including stress test, CT-angiography, and/or invasive angiography. However, all this recent research into clinical decision tools and pathways to risk-stratify these patients is reducing admissions and therefore ED and hospital overcrowding [1-5].

Many patients risk stratified as “non-low” risk are admitted, but the benefit of objective cardiac testing in this cohort is unclear in the absence of elevated troponins or abnormal EKGs [6-9]. The study we will be reviewing today seeks asks if the presence of known coronary artery disease is predictive of major adverse cardiac events (MACE) in a previously identified non-low risk group of patients.

Reference: McGinnis et al. Major adverse cardiac event rates in moderate-risk patients: Does prior coronary disease matter? AEM June 2022.

P

Population: Adult patients (age >21 years) with chest pain or suspected ACS, HEAR >4, elevated troponin, ischemic EKG or prior CAD

- **Exclusions:** Patients with evidence of an ST-segment elevated myocardial infarction and patients who were identified as low risk (HEAR < 4) by the HEART Pathway

I

Intervention: Assessment of moderate-risk patients as described in the inclusion/exclusion criteria

C

Comparison: None

- **Primary Outcome:** 30-day MACE defined as the composite of all-cause death, MI, or coronary revascularization.
- **Secondary Outcomes:** Individual components of the MACE composite at the index visit

Study Design: A preplanned subgroup analysis of non–low-risk patients in the HEART Pathway Implementation Study was conducted. The original study was a prospective interrupted time-series of accrued adults with possible ACS from three US sites (November 2013–January 2016).

This is an SGEMHOP episode, which means we have the lead author on the show. Dr. Henderson McGinnis is a Professor in the Dept of Emergency Medicine at Atrium Health Wake Forest Baptist.

Henderson is the Medical Director for AirCare, the system's critical care air and ground transport service. He is also the fellowship director of the Wilderness Medicine Fellowship at the Wake Forest EM Program.

Authors' Conclusions

"MACE rates at 30 days were low among moderate-risk patients but were significantly higher among those with prior CAD."

Quality Checklist for Clinical Decision Tools

- ✓ 1. The study population included or focused on those in the ED.
- ✓ 2. The patients were representative of those with the problem.
- ? 3. All important predictor variables and outcomes were explicitly specified.
- ✗ 4. This is a prospective, multicenter study including a broad spectrum of patients and clinicians (level II).
- ✓ 5. Clinicians interpret individual predictor variables and score the clinical decision rule reliably and accurately.
- ✗ 6. This is an impact analysis of a previously validated CDR (level I).
- ? 7. For Level I studies, impact on clinician behavior and patient-centric outcomes is reported.
- ✓ 8. The follow-up was sufficiently long and complete.
- ✓ 9. The effect was large enough and precise enough to be clinically significant.

Results

Key Results:

- Out of the original cohort of patients, 37.7% (1,715/4,550) were classified as moderate risk with non-ischemic EKGs and negative serial troponins. Mean age was 61 years, 55% were women, and 29.6% had known coronary artery disease..

- **Primary Outcome:** 30-day MACE defined as the composite of all-cause death, MI, or coronary revascularization.
  - Moderate risk patients with known CAD: 7.1% (36/508)
  - Moderate risk patients without CAD: 1.4% (17/1,207)
  - LR- for 30-day MACE among moderate-risk patients without prior CAD was 0.08 (95% CI; 0.05 to 0.12).
- **Secondary Outcomes:** Individual components of the MACE composite at the index visit and 30-day

Component	Moderate Risk with CAD	Moderate Risk no CAD
All-Cause Mortality	3 (0.6%)	4 (0.3%)
Myocardial Infarction	13 (2.2%)	3 (0.2%)
Revascularization	25 (4.9%)	12 (1.0%)

Time to Talk Nerdy:

Listen to the podcast to hear Henderson answer our 10 nerdy questions.

1. Secondary Analysis of a Subgroup – The biggest limitation which you identify up front is that this study is a secondary analysis of a subgroup of patients from the HEART Pathway Implementation Study. How cautious should we be in interpreting these results until a prospective study is done specifically looking at the patient population that could potentially be discharged home from the ED?

2. Prior Coronary Artery Disease (CAD): This study hinges in part on whether the patient had known CAD. In the methods section, there is no definition of prior known CAD. What entities does this encompass?

3. Objective Cardiac Testing (OCT): Often people were admitted to hospital for OCT (stress testing, coronary computed tomography angiography, or invasive coronary angiography). Our friend Dr. Morgenstern at First10EM has written multiple blog posts on why he does not order stress tests. What OCT are you doing at your centre and on whom?

4. HEAR Score: A lot of your discussion centers around what you term the “HEAR” score, or HEART without the “T“. Can you discuss this concept for our listeners, and if and how you suggest using it clinically?

5. Not HS-Troponin: Since we are talking about the “T” in the HEART score this study did not use hs-sensitivity troponins. Many places are now switching over to this assay. What impact do you think it will have on managing these patients with moderate risk?

6. Pre/Post and Wash-In: In the method section you discuss the different phases of the study such as pre-implementation, post-implementation, and a wash-in period. You also excluded patients with another chest pain visit within a year. Can you explain how this influences the study population?

Time to Talk Nerdy:

7. Two Percent Threshold: This gets back to my previous question about OCT. Moderate risk patients with no CAD has a 30-day MACE of 1.4%. This is below the pretest threshold of 2% which has been determined to be a reasonable cut off for getting OCT.

8. Primary Outcome: While the 30-day MACE of 1.4% is below 2% for OCT, it is still above the what most physicians consider acceptable [10-12].

9. MACE Events: There were 17 MACE events that made up the 1.4% in the moderate-risk patients without known CAD. Included four deaths of which at least two were apparently due to noncardiac causes. In addition, two of the three missed MIs were due to serial troponin protocol violations. Recategorizing those patients would result in 12/1,207 (0.99%) that would be below both the 2% and 1% threshold.

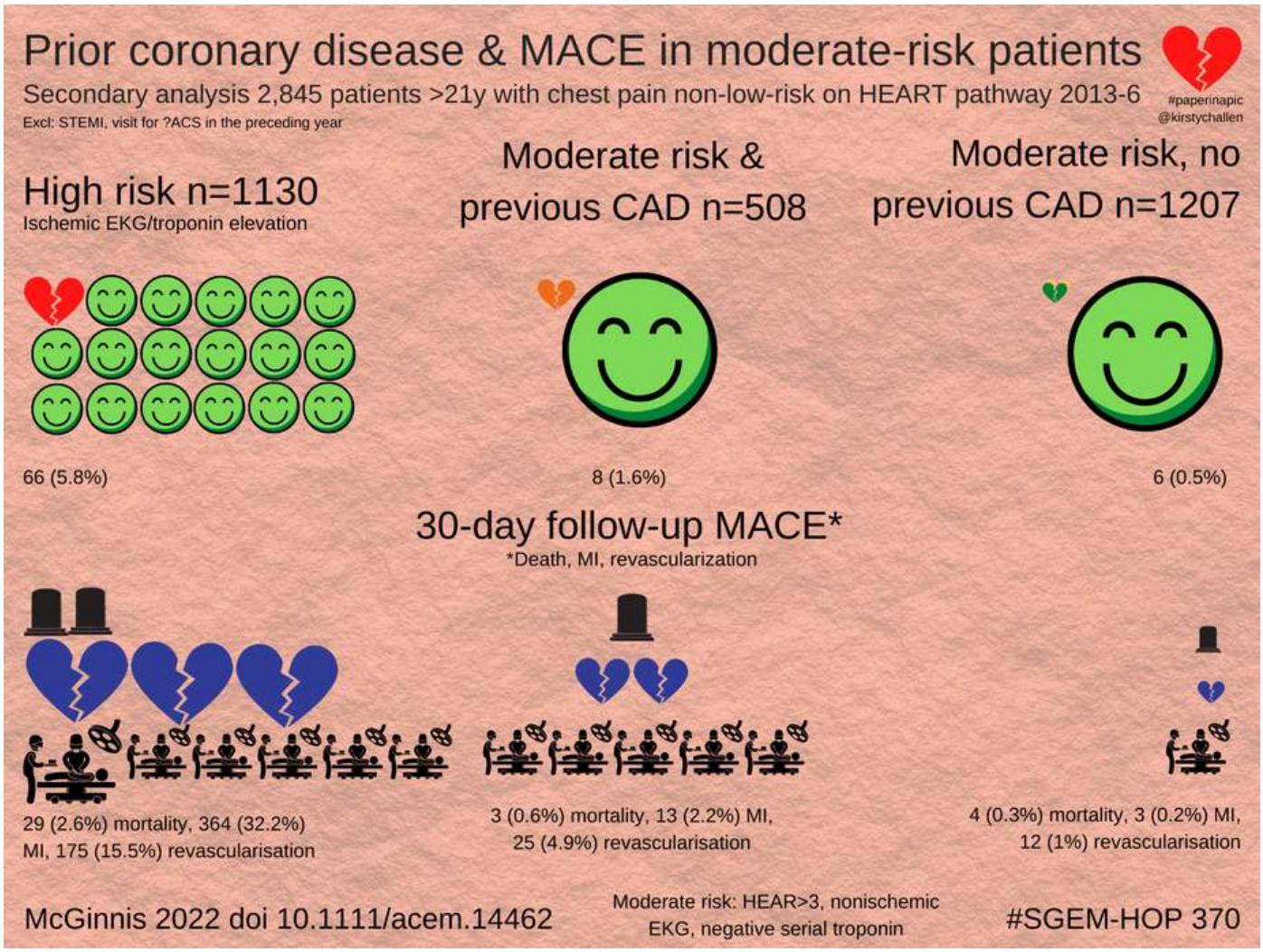
10. Anything Else: Is there any other aspect of the trial that you would like to highlight or discuss in this talk nerdy section?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors conclusions.

Clinical Application: The HEART Pathway Implementation Study is a well-designed study, of which this is a well-done subgroup analysis. The results are somewhat limited by the mis categorizations of the initial HEAR(T) score, but correct categorization would likely have further decreased the incidence of MACE for moderate risk patients without CAD. The LR- for moderate risk patients without CAD, compared to those with CAD and high-risk patients, was 0.08. This means it may be possible to further identify a group of low-risk patients even among those who are initially categorized as moderate risk.

What Do I Tell My Patient? Based on your age, the features of your symptoms, and other risk factors, you are in a group that we consider "moderate" risk for negative outcomes in the coming weeks. However, the fact that you have no prior CAD may allow us to consider you low risk and discharge you home with outpatient follow up.

Case Resolution: You discuss the situation with your patient, and offer him the option of pursuing admission, or close outpatient follow up. He elects discharge after serial troponins and will call his physician in the morning.



Ken Milne MD
@TheSGEM

What was the 30d MACE in moderate risk patients without a history of coronary artery disease in this #SGEMHOP STUDY? thesgem.com/2022/07/sgem37... @CHeitzMD @KirstyChallen

Less than 1%	31%
1% to 2 %	**45.2%**
2% to 5%	19%
Greater than 5%	4.8%

42 votes · Final results

8:56 AM · Jul 5, 2022 · Twitter for iPhone

371

ALL MY LOVIT, VITAMIN C WON'T WORK FOR YOU

Clinical Question:

In adult patients with sepsis, in the ICU, on vasopressor therapy, does vitamin C reduce the risk of death or persistent organ dysfunction at 28 days compared to placebo?

Bottom Line:

We still do not have high-quality evidence to support the routine use of vitamin C in critically ill septic patients.

Guest:

Dr. Salim R. Rezaie completed his medical school training at Texas A&M Health Science Center and continued his medical education with a combined Emergency Medicine/Internal Medicine residency at East Carolina University. Currently, Salim works as a community emergency physician at Greater San Antonio Emergency Physicians (GSEP), where he is the director of clinical education. Salim is also the creator and founder of REBEL EM and REBEL Cast, a free, critical appraisal blog and podcast that try to cut down knowledge translation gaps of research to bedside clinical practice.

Case Overview:

A 59-year-old woman presents to the emergency department (ED) with fever, tachycardia, and hypotension. She is found to have a urinary tract infection. She requires vasopressor therapy, intravenous fluids, and intravenous antibiotics. She is admitted to the intensive care unit (ICU) for septic shock. The ICU team is considering using Vitamin C therapy for this patient.

Background:

Dr. Paul Marik got the critical care world all excited when he claimed a Vitamin C cocktail (Vitamin C, hydrocortisone and thiamine) as a possible cure for sepsis. His position was in part based upon a retrospective before and after study he conducted at his hospital.

The SGEM did a structured critical appraisal of Dr. Marik's observational study on SGEM#174. A dozen top EM skeptics commented about the validity of the study. The SGEM bottom line was that Vitamin C, hydrocortisone and thiamine was associated with lower mortality in severe septic and septic shock patients in this one small, single centred retrospective before-after study but causation has yet to be demonstrated.

We also did an episode looking at a SRMA of using Vitamin C in an adult critically ill ICU patient or cardiac surgery patients (SGEM#268). While there were several limitations to this study the bottom line was there was not enough evidence to support the routine use of Vitamin C in critically ill patients.

Background:

There is a pathophysiologic basis for why Vitamin C may be beneficial in critically ill patients like those with sepsis. Vitamin C can potentially mitigate tissue injury induced by oxidative stress, but it cannot be synthesized by humans. Vitamin C levels are low in many critically ill patients. The reasonable hypothesis would be that by correcting these levels you could have a patient-oriented outcome (POO) of benefit. However, before accepting the claim of net benefit it would need to be demonstrated with high-quality evidence.

Multiple studies have now been conducted and published looking at Vitamin C as a potential treatment. Only one randomized control trial (CITRIS-ALI), using a higher dose of vitamin C (50mg/kg every six hours) reported a lower 28 day risk of death compared to those randomly allocated to placebo. This outcome however was one of 46 secondary outcomes, making it hypothesis generating. No other study reported a statistical difference in the objective outcome of mortality.

	Timing	Mortality	Time Off Pressors
CITRIS-ALI 2019	6hrs	Improved	Not Reported
VITAMINS 2020	9 - 12hrs	No Difference	No Difference
HYVCTTSSS 2020	???	No Difference	No Difference
ORANGES 2020	9.9hrs	No Difference	Improved
ACTS 2020	2hrs	No Difference	No Difference
ATESS 2020	1hr	No Difference	No Difference
VICTAS 2021	15hrs	No Difference	No Difference
LOVIT 2022	13hrs	Increased	No Difference

ORANGES: Primary Outcome Changed to In-Hospital Mortality to Time Off Pressors
CITRIS-ALI: Mortality one of 46 secondary outcomes

Reference: Lamontagne F et al. Intravenous Vitamin C in Adults with Sepsis in the Intensive Care Unit. NEJM 2022.

P

Population: Adult patients 18 years of age and older admitted to the ICU in less than 24 hours with proven or suspected infection as main diagnosis, and receiving vasopressor therapy

- **Exclusions:** Contra-indications to Vitamin C therapy, receipt of open-label Vitamin C, or expected death or withdrawal of life-sustaining therapy within 48 hours.

I

Intervention: 50mg/kg infusion of Vitamin C mixed in 50cc of 5% dextrose solution every six hours for up to 96 hours

C

Comparison: 5% dextrose in water or normal saline infusion every six hours for up to 96 hours

- **Primary Outcome:** Composite of death or persistent organ dysfunction (defined as use of vasopressors, invasive mechanical ventilation, or new renal replacement therapy) on day 28
- **Key Secondary Outcomes:** Number of days without organ dysfunction in the ICU up to day 28 and 6 months
- **Trial:** Phase 3, Multicenter, Randomized, placebo-controlled trial

Authors' Conclusions

"In adults with sepsis receiving vasopressor therapy in the ICU, those who received intravenous vitamin C had a higher risk of death or persistent organ dysfunction at 28 days than those who received placebo."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [?] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [?] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.
- 12. Financial Conflicts of Interest.

Study was funded by the Lotte and John Hecht Memorial Foundation. Nova Biomedical Canada provided glucometers, testing strips, and control solutions to trial sites that requested them

Results

Key Results:
They enrolled and analyzed 863 patients 429 in the vitamin C group and 434 in the placebo group). The mean age was 65 years, almost two-thirds were male, and 83% were medical admissions. Almost all the patients (97%) received at least 90% of the scheduled doses of Vitamin C or placebo. Median length of stay in the ICU was six days and 16 days in the hospital.

- **Primary Outcome:** Composite of death or persistent organ dysfunction on day 28
  - Vitamin C 44.5% vs Placebo 38.5%
  - Risk Ratio 1.21 (95% CI; 1.04 to 1.40) p = 0.01
- **Secondary Outcomes:**
  - Death at 28d: Vitamin C 35.4% vs Placebo: 31.6%
  - Risk Ratio 1.17 (95% CI 0.98 to 1.40)
  - Persistent Organ Dysfunction: Vitamin C 9.1% vs. Placebo: 6.9%
  - Risk Ratio 1.30 (95% CI; 0.83 to 2.05)

Time to Talk Nerdy:

1. Composite Outcome of Unequal Value: We understand why researchers create composite outcomes to help ensure they have a trial that is powered well enough. However, when the outcomes included in the composite outcome are of unequal value, it makes it more difficult from a clinical standpoint to know what to do with that information.

2. Reproducibility of Results: We worry that we have expended so much finite time, money, and effort researching this topic which has been consistently reproduced as not beneficial. This is what we dream of in EBM...reproducibility of results. Perhaps we should have stopped studying this four trials ago. As Professor Altman so eloquently stated years ago, "we need less research, better research and research done for the right reasons" (BMJ 1994). Yes, it is more difficult to prove a negative but at some point, we need to recognize that there may not be any utility in investigating this further. Our time, money and valuable patient volunteers should be utilized to investigate other potential therapies.

3. Consecutive Sample or Convenience Sample: They assessed 2,234 patients were for eligibility, and 872 underwent randomization. However, another 528 patients who were eligible were not enrolled for various reasons. This is over half the sample size included. Additionally, study recruited from 35 ICUs from November 8, 2018 to August 15, 2021). This makes us unsure whether it was a consecutive sample and if some selection bias may have been introduced.

4. Assumptions Made Prior to the Study: The authors state that in the control group there would need to be risk of death at 28 days or persistent organ dysfunction in the control group of approximately

Time to Talk Nerdy:

50% to achieve an 80% power to detect an absolute between group difference of 10%. In the control group the primary outcome only occurred 38.5%. They based this on the retrospective before and after Marik study from 2017 (Link is HERE). This is a flawed assumption as there have since been multiple RCTs that show a 10% difference to be great. Should the difference have been smaller? In a disease that affects thousands world-wide even a 3% decrease could be clinically meaningful.

5. Subgroup Analysis: In the patients with COVID-19 there were trends toward vitamin C having benefit compared to patients without COVID-19. However, the problem with subgroup analysis is they can be misleading. The more subgroups you investigate, the more likely you are to find a statistically significant effect by chance. Rarely are subgroups investigated further to confirm the hypothesis. We've mentioned before the study by Wallach et al JAMA Intern Med 2017. They evaluated how often subgroup claims are corroborated by subsequent RCT and meta-analyses. They concluded that: "Attempts to corroborate statistically significant subgroup differences are rare; when done, the initially observed subgroup differences are not reproduced."

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors conclusion that in adults with sepsis receiving vasopressor therapy in the ICU, those who received vitamin C therapy had a higher risk of death or persistent organ dysfunction at 28 days than those who received placebo

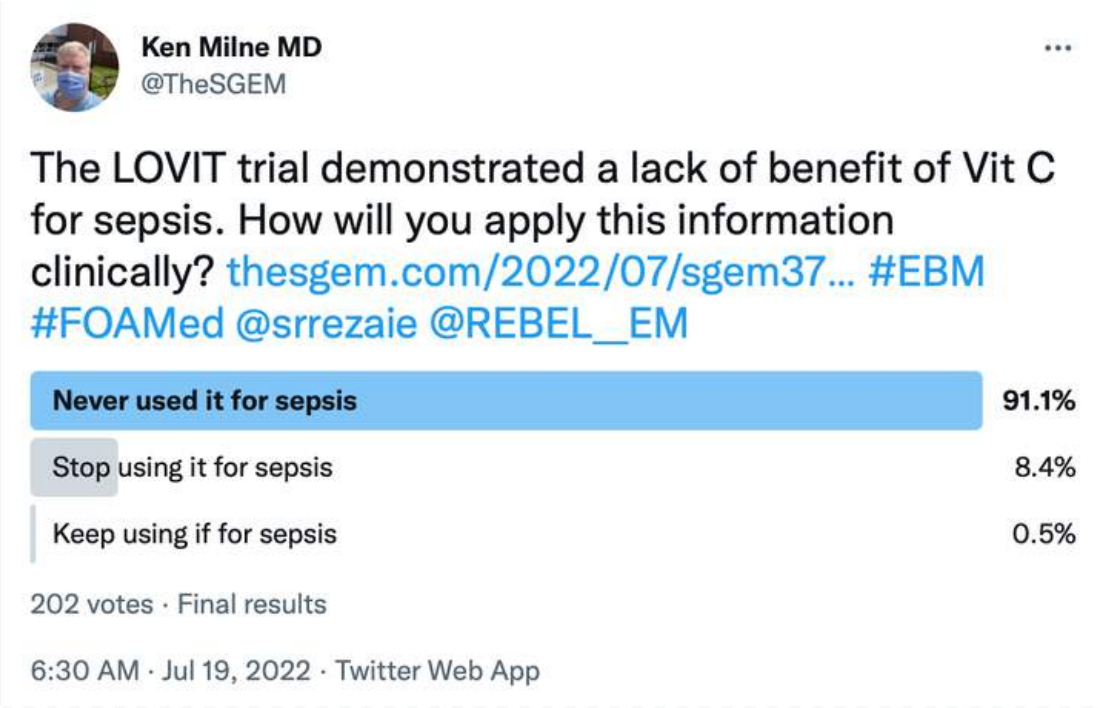
Clinical Application: After the publication of the original Marik protocol for Vitamin C therapy in sepsis there has been a slew of RCTs showing a lack of a patient-oriented benefit for Vitamin C therapy in sepsis. At this time, Vitamin C therapy should not be used outside of a randomized clinical trial. There would also need to be a compelling reason for an RCT to be approved by ethics committee to overcome the multiple studies failing to report a statistical improvement.

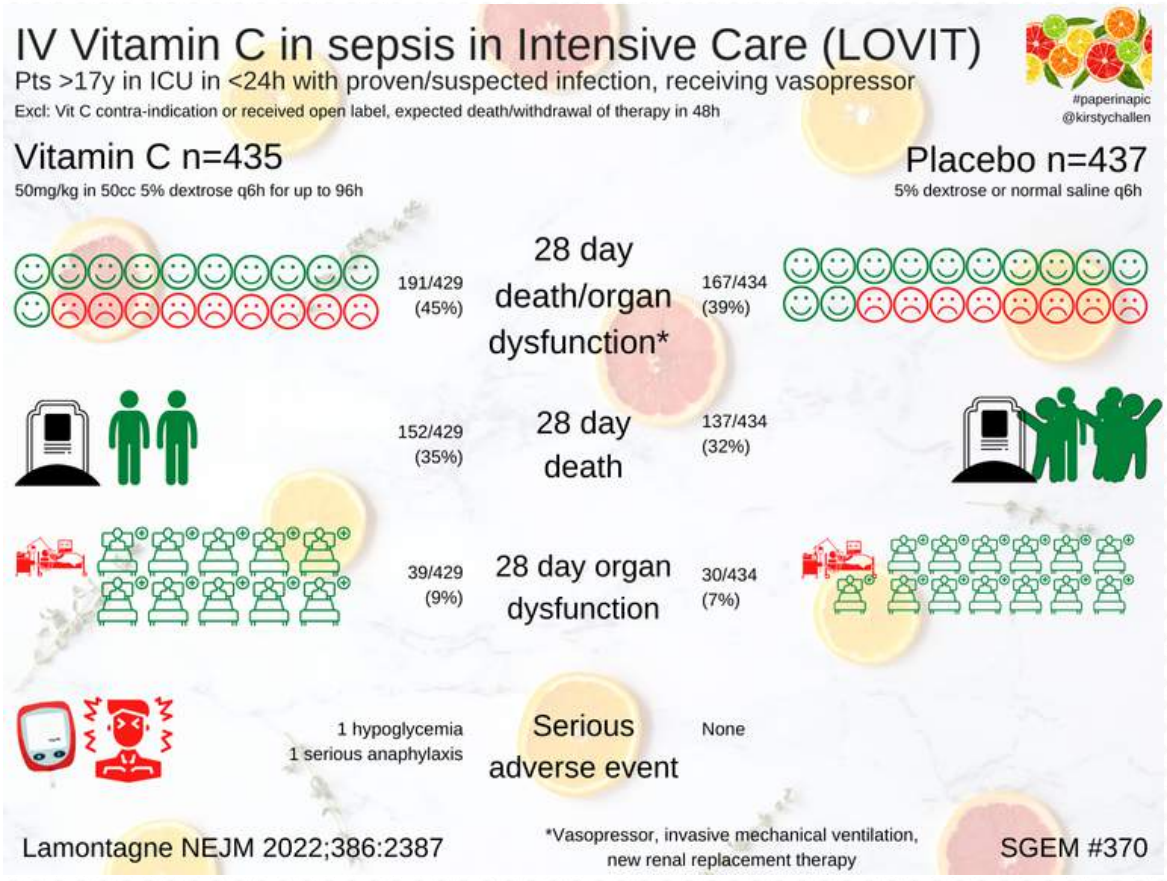
What Do I Tell My Patient? You may have heard about vitamin C therapy in patients with sepsis. At this time, it does not appear this is a medication that should be used and in the most recent trial showed evidence of harm.

Case Resolution: It is decided to not use Vitamin C therapy in the patient admitted to the ICU and to continue good supportive care with fluids, vasopressors, and antibiotics.

Other FOAMed:

- St. Emlyn's: Vitamin C and Sepsis (again)





372

USE THE FORCE FOR BUCKLE WRIST FRACTURES IN CHILDREN

Clinical Question:

What is the appropriate management of Torus fractures in children?

Bottom Line:

It is very reasonable to treat distal radius Torus fractures with the offer of a soft bandage and immediate discharge

Guest:

Jack is nine years old, and he presents to emergency department (ED) with an arm injury. Today he was running at school, and he fell over onto his outstretched arm. His right arm is neurovascularly intact, with no swelling or deformity. He has bony tenderness at the distal radius. The X-ray shows a buckle fracture of his right distal radius.

Case Overview:

Jack is nine years old, and he presents to emergency department (ED) with an arm injury. Today he was running at school, and he fell over onto his outstretched arm. His right arm is neurovascularly intact, with no swelling or deformity. He has bony tenderness at the distal radius. The X-ray shows a buckle fracture of his right distal radius.

Background:

We covered buckle fractures way back in Season#1 of the SGEM on SGEM#19. In that episode from ten years ago we made the distinction between a buckle fracture and greenstick fractures. Buckle fractures (also called torus fractures) are defined as a compression of the bony cortex on one side with the opposite cortex remains intact. In contrast, a greenstick fractures the opposite cortex is not intact.

Buckles of the distal radius are the most common fracture seen in children and very commonly present to the ED [1-2]. Despite being a common injury they are often managed differently. Some clinicians apply casts, some a splint, some have orthopedic follow up, some have no follow up [3].

This practice variation is not new. A survey done almost 20 years ago in Canada demonstrated the variability of managing buckle fractures by Pediatric orthopedic surgeons and pediatric emergency physicians [4]. An RCT published 12 years ago reported that a soft bandage wrapping treatment for four weeks was not statistically different for discomfort, function or fracture displacement

Background:

compared a below elbow back slab cast for one week followed by circumferential cast for three weeks despite some more pain in the first week with the soft bandage [5].

Yet here we are ten years later doing an SGEM episode on whether it is ok to put a soft bandage on these pediatric patients with a distal radius buckle fracture. It is a great example of how knowledge translation can take years or even decades for clinically relevant information to reach the patients' bedside due to leaks in the EM knowledge translation pipeline [6-7].

Reference: Perry et al. Immobilisation of torus fractures of the wrist in children (FORCE): a randomised controlled equivalence trial in the UK. The Lancet 2022

P

Population: Children between 4 and 15 years of age with a distal radius torus fracture that had been confirmed by x-ray.

- Exclusions: Other fractures, although a concomitant ulnar fracture did not lead to exclusion. Injury over 36 hours old, any cortical disruption seen on x-ray, and any reasons that meant follow-up would not be possible, such as a language barrier, lack of internet access or developmental delay.

I

Intervention: Rigid immobiisation

C

Comparison: Tensor (crepe) bandage

- **Primary Outcome:** Pain on day three measured using the Wong-Baker FACES Pain Rating Scale [8]. Participants also recorded their pain score on day one, seven and weeks three and six.
- **Secondary Outcomes:** Measured a variety of other outcomes at the same time points, unless otherwise specified:
  - Functional recovery using the PROMIS (Patient Report Outcomes Measurement System)Upper Extremity Score – a patient or parent-reported measure of physical function of the upper limbs

- Health-related quality of life outcomes, using a EuroQol EQ-5DYa standardised questionnaire, suitable for children, which asks about quality of life, including activities of daily living and pain.
- Analgesia use and type taken (measured on days 1, 3 and 7)
- Days of school absence
- Health care resource use i.e. a new splint (measured at weeks 3 and 6), return to hospital
- Treatment satisfaction measured using a 7-item Likert scale determined on day 1 and week 6
- Complications

- **Trial:** The FORCE study was a multi-centered, randomized, non-blinded, equivalence trial conducted at 23 Emergency Departments across the UK.

Authors' Conclusions

"This trial found equivalence in pain at 3 days in children with a torus fracture of the distal radius assigned to the offer of a bandage group or the rigid immobilisation group, with no between-group differences in pain or function during the 6 weeks of follow-up."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [ ] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.
- [ ] 12. Financial conflicts of interest

This trial was funded by the UK National Institute for Health and Care Research. It is stated in the manuscript that "The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report."

Results

Key Results:

They screened 1,513 patients between January 2019 and July 2020 for inclusion in this trial. The researchers randomized 965 children, 61% were boys, and a mean age of 10 years.

They screened 1,513 patients between January 2019 and July 2020 for inclusion in this trial. The researchers randomized 965 children, 61% were boys, and a mean age of 10 years.

More than half of those who declined to participate in the FORCE trial said they preferred rigid immobilisation, while only 1% indicated a preference for the soft bandage.

Of the 458 (94%) participants in the “offer of a bandage” group chose for it to be applied in the ED. Of the 451 (95%) participants in the rigid immobilisation group were given a removable splint. The remaining 5% in this group were treated with either a plaster cast (back slab or circumferential) or a soft cast.

We did mention crossover in the quality check list. A total of 57 children (11%) changed from bandage to rigid immobilisation while only 1 patient changed in the other direction.

- **Primary Outcome:** Pain on day three measured using the Wong-Baker FACES Pain Rating Scale.
  - There was no statistically significant difference in pain scores with the mITT 3.21 (bandage) vs 3.13 (rigid) with effect size -10 (95% CI; -0.37 to 0.17)
  - They dichotomized into aged 4-7 years and aged 8-15 years and the results were equivalent for the total population and the two subgroups with both the ITT analysis and the PP analysis

Case Outcomes

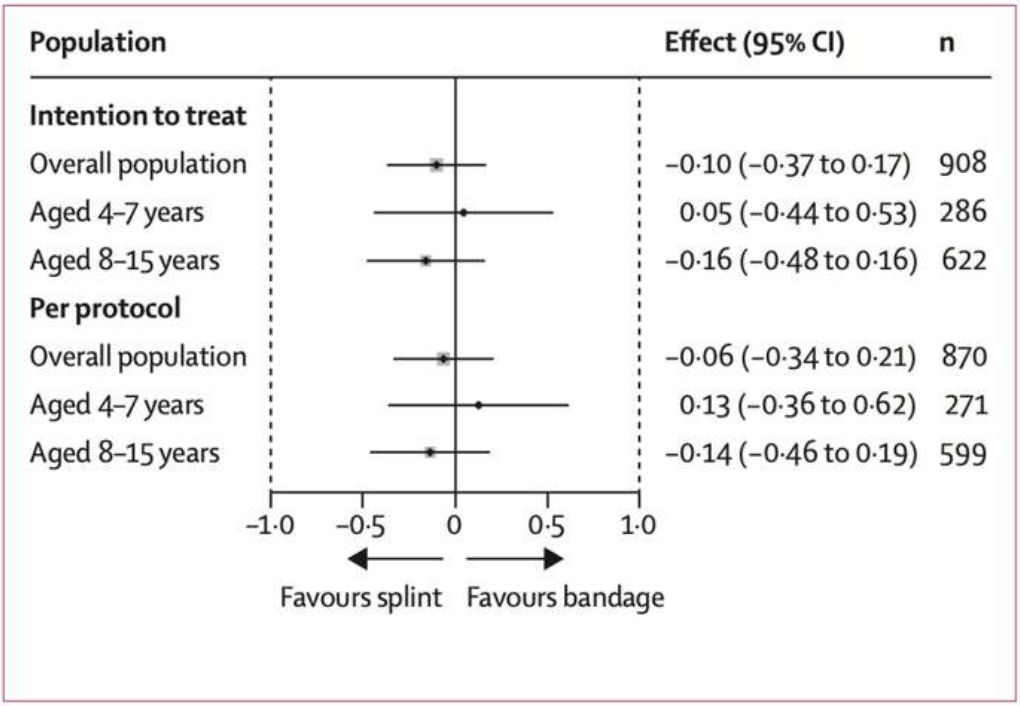


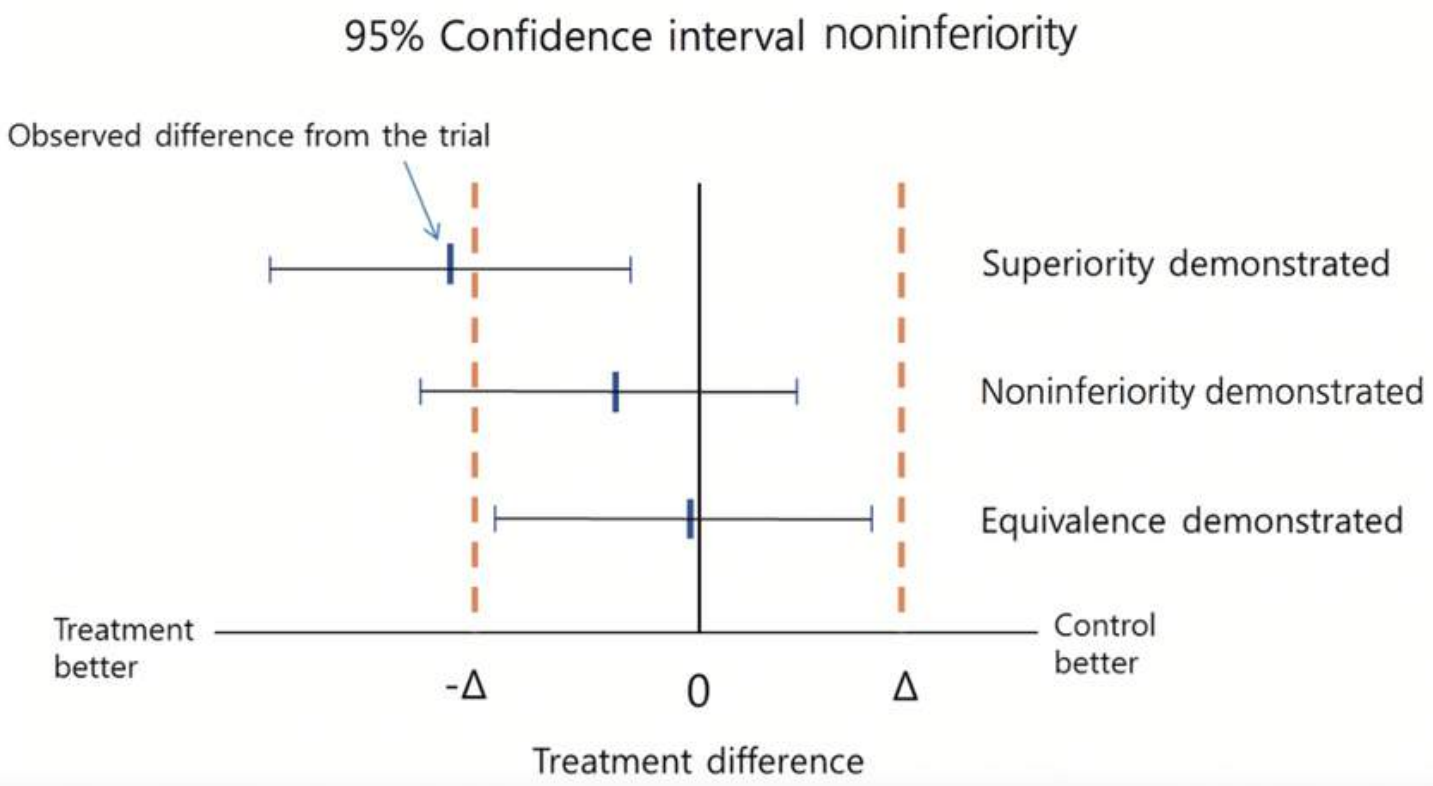
Figure 2: **Day 3 Wong–Baker Scale score treatment effects compared with equivalence margin**

- **Secondary Outcomes:** There was no statistical difference between the two groups in terms of secondary outcomes either (including PROMIS scores and EQ-5DY-3L utility scores). Parents in the rigid immobilisation group were more satisfied on Day 1 but there was no difference by 6 weeks. Because the number of complications reported was very low no formal statistical comparison were made. There were no cases of worsening deformities.
  - There was no difference in complication rate in either group. Both treatment options led to a similar number of missed school days – around one and a half.
  - There was a (small) difference in analgesia use though. 83% of the bandage group had painkillers, compared to 78% in the rigid immobilisation group on the first day, though there was no significant difference down the track.

Time to Talk Nerdy:

1. Something for Coming: Families did not like having no treatment provided. The trial was originally set up to compare rigid immobilisation with no treatment and discharge. A family focus group, carried out by the researchers, suggested that the offer of no treatment at all was unacceptable, and so the study was changed to compare rigid immobilisation with the offer of a soft bandage.

2. Equivalence Trials: We don't often see trials designed to check for equivalence. The most common design is a superiority trial. The more conservative way to analyze superiority trials is with an ITT analysis. In contrast, non-inferiority trials it is better to conduct a PP analysis. Our friend Dr. Justin Morgenstern from First10EM has tweeted his thoughts about non-inferiority trials citing an article that says non-inferiority trials are unethical [9]. The FORCE trial did both types of analyses (ITT and PP) and demonstrated equivalence.



Time to Talk Nerdy:

3. Clinician Variability: Not everyone diagnoses a torus fracture in the same way. We know the technical definition but what you would call a torus fracture might not be the same as me. Defining the line between a buckle of the cortex and a break is tricky. It's open to interpretation – some people have a broader net than others.

4. Don't Just Do Something Stand There: This is a very important philosophy in medicine that I learned from Dr. Jerry Hoffman. It was explained very well in an article called "Don't just do something, stand there! The value and art of deliberate clinical inertia" [10]. Clinicians have a desire to usually do something, and this is called intervention bias [11]. More care is not always better care. The use of a soft bandage to treat a distal radius buckle fracture in children is an excellent example. Not putting on a rigid immobilization can be part of high-quality care. The clinician can empathize with the parents, provide symptom management to the child, educate them about the natural history of the injury, manage expectations and perform shared decision-making.

5. No Imaging: Could we move to a time where we don't do x-rays or even use POCUS for these childhood injuries? If we know that these injuries don't need any treatment, do we really need to x-ray them at all, could we get to a point when we can use clinical assessment of the patient and the arm, potentially US to confirm that it's just a buckle, and then leave it at that? This could lead to shorter lengths of stay in the ED and less radiation.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions.

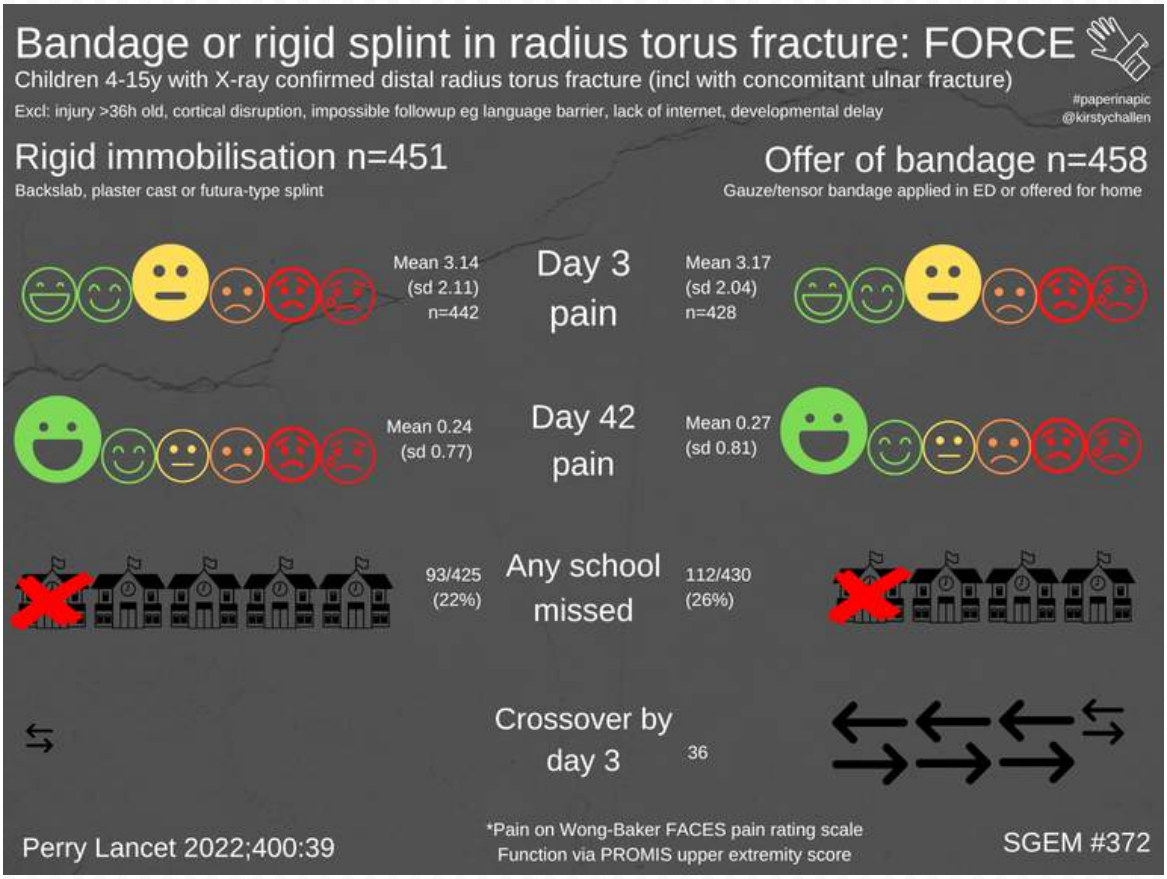
Clinical Application: It's always great to have more evidence to back up what we are already clinically doing. These torus fractures in children heal well, don't need ridged immobilization, and can be treated the same way we treat wrist sprains

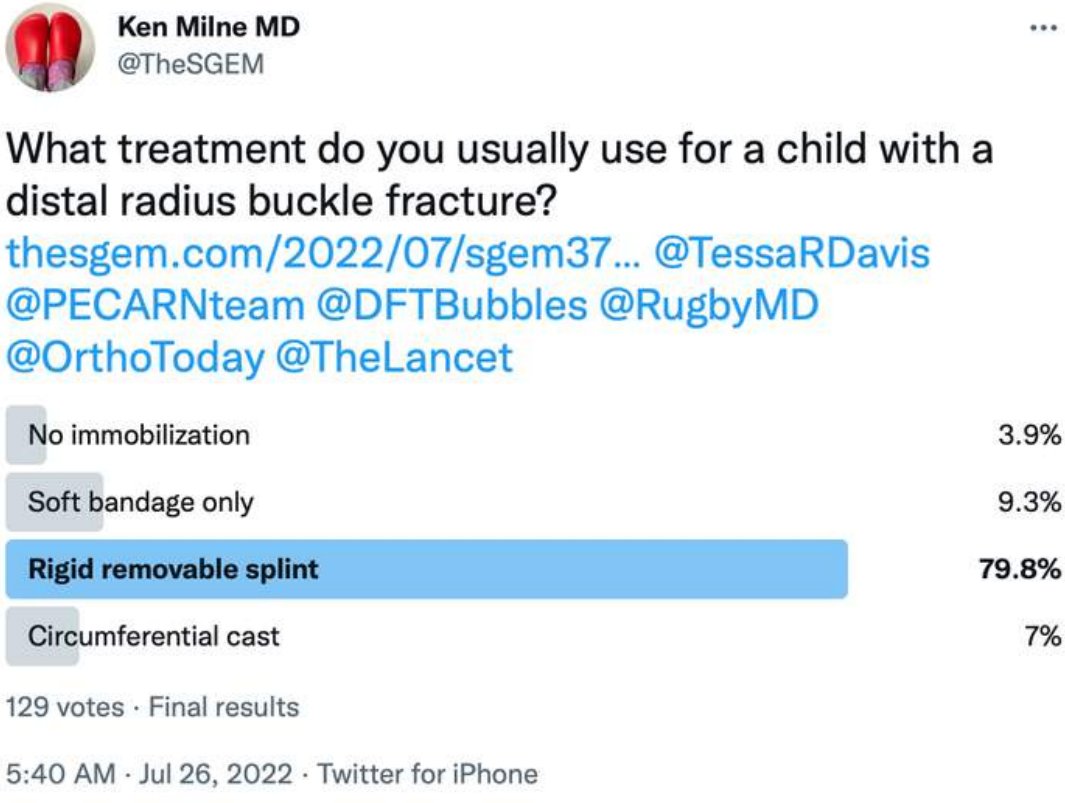
What Do I Tell the Parent? Jack has a small bump in his bone that is essentially the same as a sprain, and we manage it in the same way. You can give some analgesia over the next few days in needed and encourage Jack to use his arm as he feels comfortable. It will improve over the next couple of weeks.

Case Resolution: Jack gets offered a soft bandage which he is happy to use. He is discharged home with simple analgesia (ibuprofen or paracetamol) and no scheduled follow up is arranged.

Other FOAMed:

- Don’t Forget the Bubbles – The FORCE Trial





373

GOING ULTRASOUND FOR SMALL BOWEL OBSTRUCTIONS

Clinical Question:

Does using point of care ultrasound firstline in suspected small bowel obstruction reduce cost, length of stay and radiation exposure?

Bottom Line:

POCUS as first-line imaging in suspected SBO could avoid significant numbers of CT scans in US.

Guest:

Dr. Kirsty Challen is a Consultant in Emergency Medicine at Lancashire Teaching Hospitals. She is also the creator of all those wonderful Paper in a Pictures.

Case Overview:

A 63-year-old woman presents to your emergency department (ED) with two-day history of nausea, vomiting and constipation. She tells you that she had appendicitis complicated by perforation and peritonitis ten years ago and you suspect she has adhesional small bowel obstruction. You call your surgical colleague who, predictably, asks you to order a CT. The patient asks if there is an alternative as she had several CTs on her last admission and is worried about her radiation exposure and her co-pay.

Background:

Somewhere between two and four percent of patients presenting to US EDs with abdominal pain have a small bowel obstruction (SBO) – those who are managed operatively (who are only 20-30%) account for 60,000 hospitalizations and 565,000 inpatient care days per year.

We know that clinical examination has poor sensitivity and specificity for diagnosing SBO and that imaging is therefore necessary. CT is generally the first choice of imaging, the “abdominal series” of plain X-rays have been demonstrated to have poor predictive value, but a 2018 meta-analysis found 92.4% sensitivity and 96.6% specificity with ultrasound [1].

A 2020 national UK report into patients treated for bowel obstruction found delays in imaging and diagnosis and recommended CT with IV contrast as the first-line investigation [2].

Background:

Somewhat surprisingly, we've never covered SBO on the SGEM, although Ped EM Superhero, Dr Anthony Crocco shared his views on the (lack of) utility of abdominal X-rays in paediatric constipation back in 2016 (SGEM Xtra: RANThony#4).

Reference: Brower et al. Point-of-Care Ultrasound-First for the Evaluation of Small Bowel Obstruction: National Cost Savings, Length of Stay Reduction, and Preventable Radiation Exposure. AEM July 2022

P **Population:** Patients with ICD-10 coding “intestinal obstruction” from 2018 National Hospital Ambulatory Medical Care Survey.

I **Intervention:** POCUS-first approach

C **Comparison:** CT imaging as baseline

- **Primary Outcome:** Cost savings
- **Secondary Outcomes:** Reduction in ED length of stay, reduction in radiation exposure and preventable cancer
- **Type:** Monte Carlo Modelling

This is an SGEM HOP episode, so we are pleased to have two of the authors on the show. Dr. Charles Brower is a second-year resident training in Emergency Medicine at the University of Cincinnati. His primary research interest is the intersection between clinical operations and ultrasound to improve patient outcomes in an efficient and cost-effective way.

Also joining us is Dr. Andrew Goldsmith. He is the director of Emergency Ultrasound in the Department of Emergency Medicine at Brigham and Women’s Hospital at Harvard Medical School

Authors' Conclusions

"If adopted widely and used consistently, a POCUS-first algorithm for SBO could yield substantial national cost savings by averting advanced imaging, decreasing ED LOS, and reducing unnecessary radiation exposure in patients. Clinical decision tools are needed to better identify which patients would most benefit from CT imaging for SBO in the ED."

Quality Checklist for Cost Analysis Studies

Part 1: Are the recommendations valid?

- Did the investigators adopt a sufficiently broad viewpoint?
- Are the results reported separately for patients whose baseline risk differs?
- Were costs measured accurately?
- Did investigators consider the timing of costs & outcomes?

Part 2: How can I apply the results to patient care?

- Are the treatment benefits worth the harms and costs?
- Could my patients expect similar health outcomes?
- Can I expect similar costs at my setting?
- Are the criteria relevant to my practice setting?
- Have the criteria been field-tested for feasibility of use in diverse settings, including settings similar to mine?

Results

Key Results:

In the US, a POCUS-first approach for imaging of SBO would avert a mean of 143,000 (+/- 31,000) CT scans annually, saving $30.1million (+/- $8.9million). 507,000 bed hours (+/- 268,000) could be saved, and 98 (+/-28) excess cancer deaths prevented.

Realization Rate >>	20%	40%	60%	80%	100%
CT Scans Averted	29,000	57,000	86,000	114,000	143,000
Cost Savings (USD)	$6.0M	$12.0M	$18.1M	$24.1M	$30.1M
Time Savings (Bed Hours)	102,000	203,000	305,000	406,000	507,000
Reduction in Radiation (person-mSv)	0.3M	0.6M	0.9M	1.2M	1.5M
Cancer Cases Prevented	39	78	117	156	195
Cancer Deaths Prevented	20	39	59	79	98

Time to Talk Nerdy:

Listen to the SGEM podcast to hear Charles and Andrew answer our five nerdy questions.

1. Monte Carlo Simulation: Can you describe this for us in clinician-friendly language? And why is it the right method for your question?

2. Modelling Assumptions: Models are only as good as the information fed into them (garbage in, garbage out!). How reliable was the information you were able to get for your assumptions (eg numbers of patients needing confirmatory CT)?

3. Sensitivity Analyses: Can you explain the importance of sensitivity analyses? Why did you do the ones you did?

4. Subgroups: It's likely that the effects of a change in practice would vary across different patient groups (especially cancer incidence dependent on patient age) but you have presented population-wide results. Did you consider modelling different subgroups?

5. Supporting Evidence: You have commented that the simulation nature of your study is a limitation. Do you have any plans for further research to address this?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions for the US, but don't consider that they can be extrapolated to Canada, UK, Australia or elsewhere without further study.

Clinical Application: We may be able to avoid significant numbers of CTs for suspected SBO by using POCUS as first-line imaging.

What Do I Tell My Patient? We can perform bedside ultrasound which can demonstrate SBO – it is likely though that if operative intervention is needed the surgeon will still want you to have a CT scan performed.

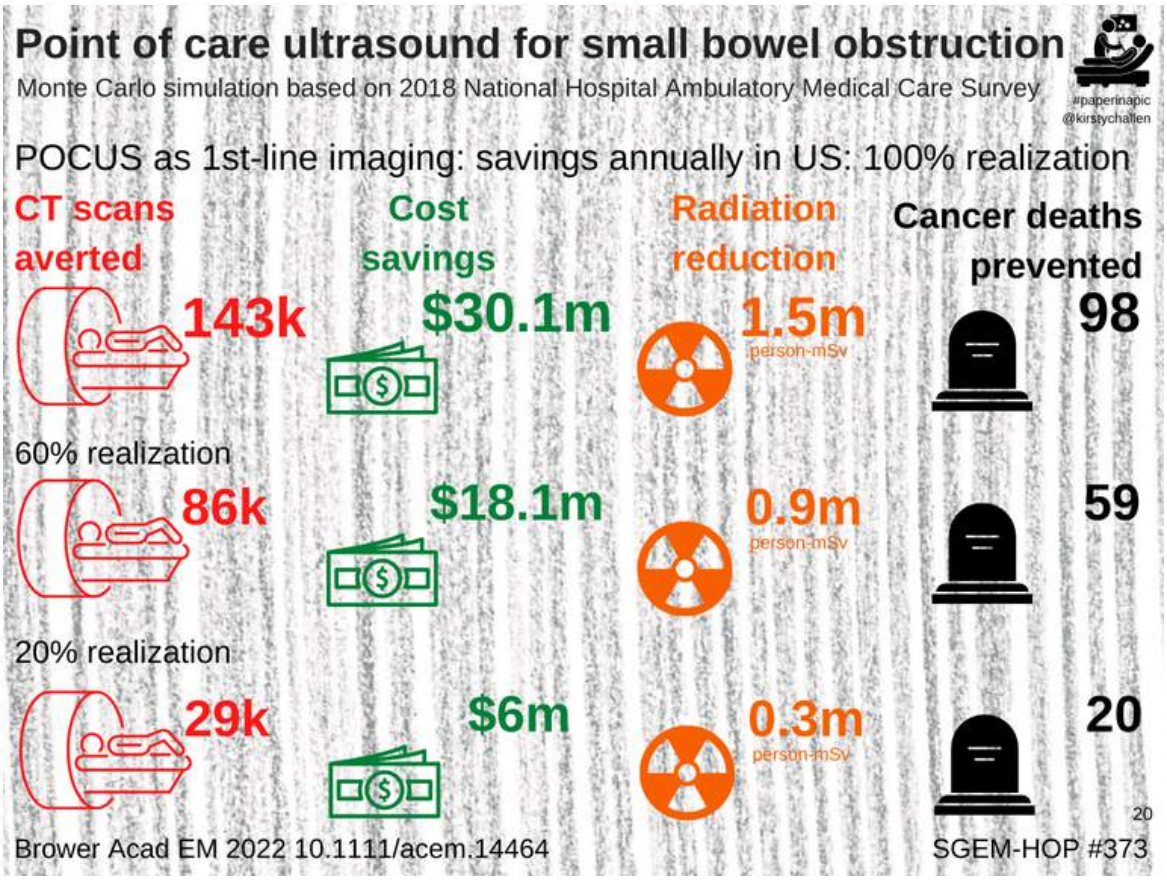
Case Resolution: You meet your surgical colleague at the bedside and perform POCUS, which shows SBO. After discussion with the patient, she is admitted for conservative management and a CT is avoided.

Ken Milne MD
@TheSGEM

What do you usually use to diagnose a small bowel obstruction? #EBM #SGEMHOP thesgem.com/2022/07/sgem37...

Physical Exam	2.7%
CT Scan	**70.5%**
POCUS	8.2%
Plain X-rays	18.5%

146 votes · Final results



374

BAD HABITS – MEDICATIONS FOR OPIOID USE DISORDER IN THE EMERGENCY DEPARTMENT

Clinical Question:

What are patient's perspectives regarding the initiation of medications for opioid use disorder in the ED?

Bottom Line:

Consider offering MOUD to patietns in the ED and tailor treatment to the individual needs and circumstances of each patient.

Guest:

Dr. Chris Bond is an emergency medicine physician and assistant Professor at the University of Calgary. He is also an avid FOAM supporter/producer through various online outlets including TheSGEM.

Case Overview:

A 24-year-old male presents to the emergency department (ED) after a fentanyl overdose. He is successfully resuscitated using naloxone and is stable after an observation period. You are interested in seizing this opportunity to offer some type of help to this patient to prevent another opioid overdose in his future.

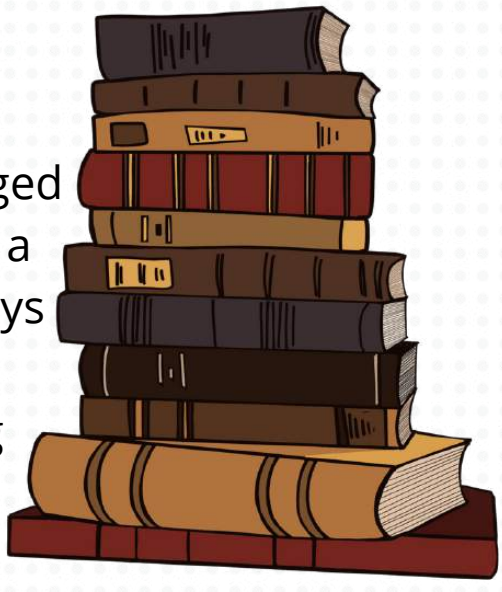
Background:

We have done a few shows on opioids over the past decade:

- Incidence of opioid use disorder (SGEM#264)
- Observing patients after giving naloxone (SGEM#241)
- Department guideline to prevent opioid use disorder (SGEM#55)

Drug overdose deaths continue to rise in the United States with opioids being the number one cause (1). There are several medications available to treat Opioid Use Disorder, including methadone and buprenorphine, which are the most effective means to decrease future illicit opioid use and death (2-5). The ED has been identified as a low barrier environment where medications for OUD (MOUD) can be initiated, even in resource-constrained settings (3,6,7).

Despite the relatively easy availability of buprenorphine, less than 5% of patients discharged from the ED after a non-fatal opioid overdose fill a prescription for buprenorphine in the next 90 days (8-11). Past studies have focused on clinician-reported barriers to administering or prescribing buprenorphine in the ED (11-19).



Background:

However, the perspectives and preferences of patients have not been so thoroughly explored. Shared decision making (SDM) puts patients at the center of clinical decisions and has been shown to increase knowledge, trust, and adherence in other clinical decisions (20-23).

An SDM framework that fosters conversations and addresses common misconceptions around MOUD initiation may improve the patient-provider interaction and ultimately increased ED-based MOUD administration.

Reference: Schoenfeld et al. “Just give them a choice”: Patients’ perspectives regarding starting medications for opioid use disorder in the ED. AEM August 2022

As this is a qualitative study, we will use a modified PICO question

P **Population:** Patients with opioid use disorder

I **Intervention:** Exploring patient perspectives and experiences with OUD and using medications for OUD

C **Context:** Improving the initiation and adherence to treatment with medications for OUD from the ED

This is an SGEMHOP episode and it is my pleasure to introduce Dr. Elizabeth Schoenfeld. She is an Emergency Physician and researcher, and the Vice Chair for research in the Department of Emergency Medicine at UMass – Baystate. Her research focuses on Shared Decision-Making (SDM) in the setting of Emergency Department care.

Dr. Schoenfeld and her co-authors used the Ottawa Decision Support Framework for their study. Listen to the podcast to hear her describe this tool in more detail.

Decisional Needs

What do people need to help them make the decision?

- Are they **ready** to talk about it?
- Do they have enough **information**? Do they endorse **misinformation**?
- Do they have unrealistic **expectations**?
- Do they know what they **value**?
- What are their **personal and clinical needs**?
- Do they have adequate support and resources **(self-efficacy, skills, motivation)**?

Example Questions*

Are you familiar with buprenorphine (suboxone) and/or methadone? What do you know?
  Probe understanding and myths
Tell me about your experiences
  Probe challenges, benefits, logistics
What do you think about these medications?
What do you think about starting these medications in the Emergency Department?

Decisional Support

What can health care professionals do to help people make the right decision for themselves?

- How can professionals establish **rapport** and facilitate **interactive communication**?
- What would **tailored support** look like?
- What **information** do professionals need to share?
- What **myths** should be addressed?
- How can professionals help clarify **values**?
- Do they know what they **value**?
- What are their **personal and clinical needs**?

Example Questions*

From your experience, what do doctors need to know in order to have this conversation?
If you were offered this medication in the ED, what else would you need to know?
What advice would you give to doctors who are new to this conversation?
What else could the ED do to help you decide to start one of these medications?

Derived from Ottawa Decision Support Framework[25]

Factors Relevant for Decision-Making

What factors should a conversation aid address in order to help people make a decision?

- Which **benefits** of the options are most important?
- Which **risks** of the options are most important?
- What **side effects** of the options should be discussed?
- What **consequences** of the options are relevant?
- What other **factors** are important to people for decision-making?

Example Questions*

In your experience, what are the pros and cons of buprenorphine? Of methadone?
  Which of these is most important to you at this time? What about at other times?
What else factors into a person's decision to try buprenorphine or methadone?
  Are there situations where one medication is preferred over the other? Or people for whom one is a better choice?

Contextual Factors Relevant to Recovery Conversation

What is the context of the conversation (personal, environmental, etc)?

- What is the **bigger picture** around this decision?
- How do the available options fit into the **bigger picture in this person's life**?
- What **factors from the bigger picture** will affect this person's ability to have this conversation and make a decision that works from them?
- What factors from the bigger picture might **change the efficacy or other characteristics** of the options?

Example Questions*

Tell me about a time when you tried to stop using opioids
  Why did you try to stop? What motivated you?
  What helped you? What got in your way?
  If you used opioids again, how did that happen?
What makes it harder to stay in recovery?
What helps you stay off opioids?

Derived from research team's experience creating conversation aids[26,27]

Authors' Conclusions

"Although participants were supportive of offering buprenorphine in the ED, many felt methadone should also be offered. They felt that treatment should be tailored to an individual's needs and circumstances, and clarified what factors might be important considerations for people with OUD."

CASP Checklist for Qualitative Research

- [x] 1. Was there a clear statement of the aims of the research?
- [x] 2. Is a qualitative methodology appropriate?
- [x] 3. Was the research design appropriate to address the aims of the research?
- [x] 4. Was the recruitment strategy appropriate to the aims of the research?
- [x] 5. Was the data collected in a way that addressed the research issue?
- [x] 6. Has the relationship between researcher and participants been adequately considered?
- [x] 7. Have ethical issues been taken into consideration?
- [x] 8. Was the data analysis sufficiently rigorous?
- [x] 9. Is there a clear statement of findings?
- [x] 10. How valuable is the research?

Results

Key Results:

There were 26 participants interviewed, seven of whom were recruited and interviewed in the ED and 19 who were recruited and interviewed via video conferencing.

There were 26 participants interviewed, seven of whom were recruited and interviewed in the ED and 19 who were recruited and interviewed via video conferencing.

The mean age of study participants was 36 and the majority had used an unprescribed opioid within the past two years. The majority had also tried both buprenorphine and methadone. Nearly all participants had ED visits related to opioid use and the goals for participant heterogeneity outlined in the methods were met.

There are three themes we pulled out of the results section. Elizabeth added her own comments on the podcast after each theme was discussed.

1. **Decisional Needs and Factors Relevant for Decision-Making**

Factors for decision making generally fell into either social, pharmacological, or emotional categories.

Focusing on pharmacological factors, participants noted the logistical ease of using buprenorphine (at home dosing vs. methadone's observed dosing at a pharmacy) and that it was effective in helping with withdrawal and avoiding street drugs.

Disadvantages of buprenorphine were the ability to sell it and buy illicit opioids, the need to be in severe withdrawal to initiate it and that it could trigger precipitated withdrawal. It was also noted that with methadone you could continue using opioids as needed whereas this wasn't an option with buprenorphine.

Results

Nearly all patients were unaware that buprenorphine could be initiated in the ED and thought it should be offered. Whether it was initiated on that ED visit or not, even offering it helped to “open the door” for future use and lessen stigma surrounding MOUD.
Many patients also thought that any conversation surrounding MOUD should include both buprenorphine and methadone.

2. Informal Decisional Support

Participants identified that it was important for clinicians to avoid appearing judgmental and hoped clinicians had additional training in discussing the pros and cons of MOUD. They also recognized that clinicians were not experts in MOUD and should be honest about their knowledge of MOUD.

Several noted a “peer recovery” coach in the ED with lived experience would be more beneficial than a physician.

“Readiness” was also described as an important factor and patients noted that they would often be at different stages of readiness to change on each visit to the ED. They further identified it was important to offer MOUD at each visit because of this.

Coordination with outpatient care was also identified as important, eg. OUD clinic and outpatient resource list, psychiatric care, naloxone kit training, peer recovery coach contacts and comfort medications such as clonidine or acetaminophen would all be useful.

3. Additional Relevant Themes Identified by Researchers

“Recovery” has a different meaning to different people. For example, it can mean complete abstinence from opioids and MOUD to one person, use of MOUD and no illicit opioids to another person, and even use of MOUD with

Results

reduced use of illicit opioids to a third.
Relapse was a part of every single story and getting to the point of non-use always took multiple attempts and different methods.

Participants felt psychiatric care should be integrated into OUD care as opioid use was frequently in response to their mental health problems such as depression or PTSD.

Time to Talk Nerdy:

Listen to the podcast to hear Elizabeth answer our five nerdy questions.

1. External Validity: Two thirds of your patients were recruited from urban MOUD clinics. How do you think this may have affected your results and do you think they have external validity to rural or resource low environments?

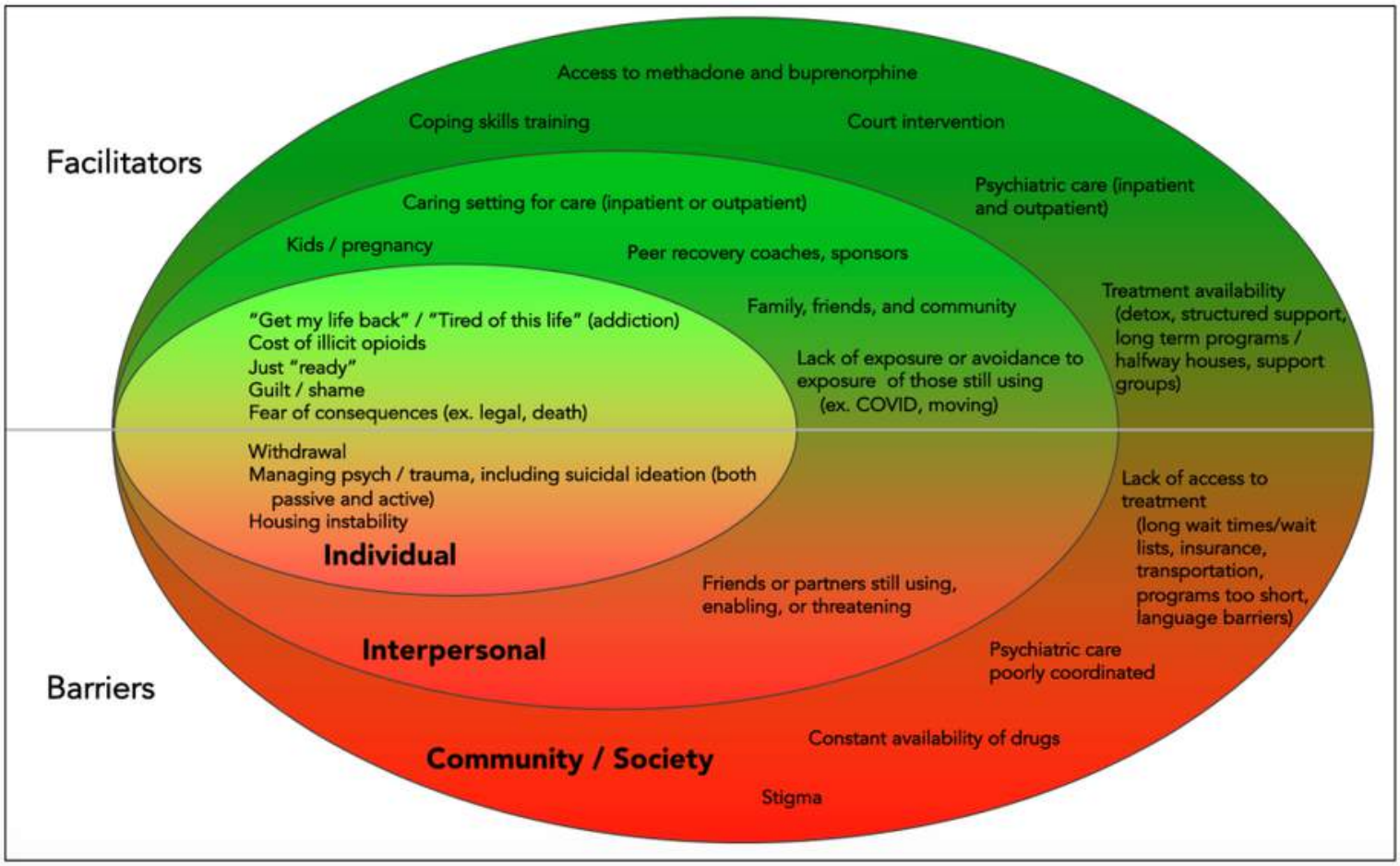
2. Shared Decision Making: You mention that you did not specifically ask patients about shared decision making but that it was brought up by many of them. Why wasn't this asked specifically?

3. Participant Heterogeneity: How did you determine the seven groups that you used as goals for establishing participant heterogeneity and what were the seven groups?

4. Non-English: One of the inclusion criteria was the ability to speak conversational English. How do you address this significant limitation for discussing cultural barriers to MOUD in non-English speaking populations?

5. Contextual Factors: You had a figure in your manuscript to help understand decisional needs in the context of the whole patient, salient themes of participants' recovery stories, organized via the socioecological model of addiction. Can you briefly explain this and we will put Figure 3 in the show notes?

Time to Talk Nerdy:



Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions.

Clinical Application: The patient agrees to take home four doses of buprenorphine-naloxone as well as instructions on when to take the first dose with respect to the development of significant withdrawal symptoms. He will try to follow up at a local clinic tomorrow.

What Do I Tell My Patient? I (Elizabeth) tell them they have to wait as long as they can – the worse they feel, the more it will help. They can take acetaminophen, clonidine, etc., to get them as far as they possibly can past their first use before they take it. We also give them instructions to let them escalate their dose – don't be stingy, 4mg is probably not enough – start with 8mg and let them go to 16mg or 32mg on the first day if needed.

Case Resolution: You discuss the availability of buprenorphine which can be prescribed from the ED and methadone from clinics within your city. You discuss the pros and cons of each treatment as best you understand them, and he is interested in trying buprenorphine at home. You also provide him with a list of outpatient clinics that can help with the multifactorial interventions needed to address his OUD.

Ken Milne MD
@TheSGEM

Does Dr. Saver's SRMA using the fragility index convince you the tPA stroke literature is "highly robust"? thesgem.com/2022/08/sgem-x... @UCLANeurology @Hamishmcmack @broomedocs @ravigarg415 @aleksmineyko @SAEMEBM

Yes: He convinced me	12.5%
No: He didn't convince me	**50%**
No: Already agree robust	8.3%
Unsure	29.2%

48 votes · Final results

6:09 AM · Aug 23, 2022 · Twitter for iPhone

Playlist

SGEM Season#10

The Skeptics' Guide to EM • 3 likes • 31 songs, about 2 hr 15 min

#	Title	Album	Date added	
1	People Are People Depeche Mode	People Are People	Jun 5, 2022	3:43
2	We Will Rock You Queen	News Of The World	Jun 5, 2022	2:01
3	Checking In, Checking Out The High Llamas	Gideon Gaye	Jun 5, 2022	5:45
4	Always On My Mind Willie Nelson	Always On My Mind	Jun 5, 2022	3:32
5	It Don't Matter to Me Bread	The Best of Bread	Jun 5, 2022	2:43
6	Take The Long Way Home - 2010 Remastered Supertramp	Breakfast In America (Deluxe Edition)	Jun 5, 2022	5:08
7	Bridge Over Troubled Water Simon & Garfunkel	Bridge Over Troubled Water	Jun 5, 2022	4:53
8	Alone Heart	Bad Animals	Jun 5, 2022	3:38
9	Free Fallin' Tom Petty	Full Moon Fever	Jun 5, 2022	4:16
10	Amendment Ani DiFranco	Which Side Are You On?	Jun 5, 2022	6:26
11	Copacabana (At the Copa) Barry Manilow	Dance Vault Mixes - Copacabana (At The ...	Jun 5, 2022	3:56
12	Walk The Dinosaur Was (Not Was)	Hello Dad...I'm In Jail	Jun 5, 2022	8:43
13	Bigger Isn't Better Leonard John Crofoot	Barnum (Original Broadway Cast Recording)	Jun 5, 2022	3:55
14	Mama Said Knock You Out E LL COOL J	Mama Said Knock You Out	Jun 5, 2022	4:49
15	Harder To Breathe E Maroon 5	Songs About Jane: 10th Anniversary Edition	Jun 5, 2022	2:53

SCAN HERE FOR PLAYLIST

16		I'd Do Anything For Love (But I Won't Do That) ... Meat Loaf	Bat Out Of Hell II: Back Into Hell	Jun 5, 2022	5:16
17		Meet Me Half Way - From "Over The Top" Soun... Kenny Loggins	Back To Avalon	Jun 5, 2022	3:39
18		We Care a Lot Faith No More	Introduce Yourself	Jun 5, 2022	4:03
19		Umbrella Rihanna, JAY-Z	Good Girl Gone Bad: Reloaded	Jun 5, 2022	4:35
20		Can't Take My Eyes off You Frankie Valli	Solo	Jun 5, 2022	3:23
21		Don't You (Forget About Me) Simple Minds	Once Upon A Time (Super Deluxe)	Jun 5, 2022	4:23
22		U Can't Touch This MC Hammer	Please Hammer Don't Hurt 'Em	Jun 5, 2022	4:17
23		Relax Frankie Goes To Hollywood	Welcome To The Pleasuredome	Jun 5, 2022	3:56
24		Grace, Too The Tragically Hip	Day For Night	Jun 5, 2022	5:34
25		Just A Normal Day Supertramp	Crisis? What Crisis?	3 days ago	4:02
26		Romeo Is Bleeding Tom Waits	Blue Valentine (Remastered)	3 days ago	4:52
27		Listen To Your Heart Roxette	Look Sharp! (Extended Version)	3 days ago	5:28
28		All My Loving - Remastered 2009 The Beatles	With The Beatles (Remastered)	3 days ago	2:07
29		Use the Force - Remastered Jamiroquai	Travelling Without Moving (Remastered)	3 days ago	4:00
30		Going Underground The Jam	Setting Sons (Super Deluxe)	3 days ago	2:54
31		Bad Habits Ed Sheeran	=	3 days ago	3:50

SCAN HERE FOR PLAYLIST