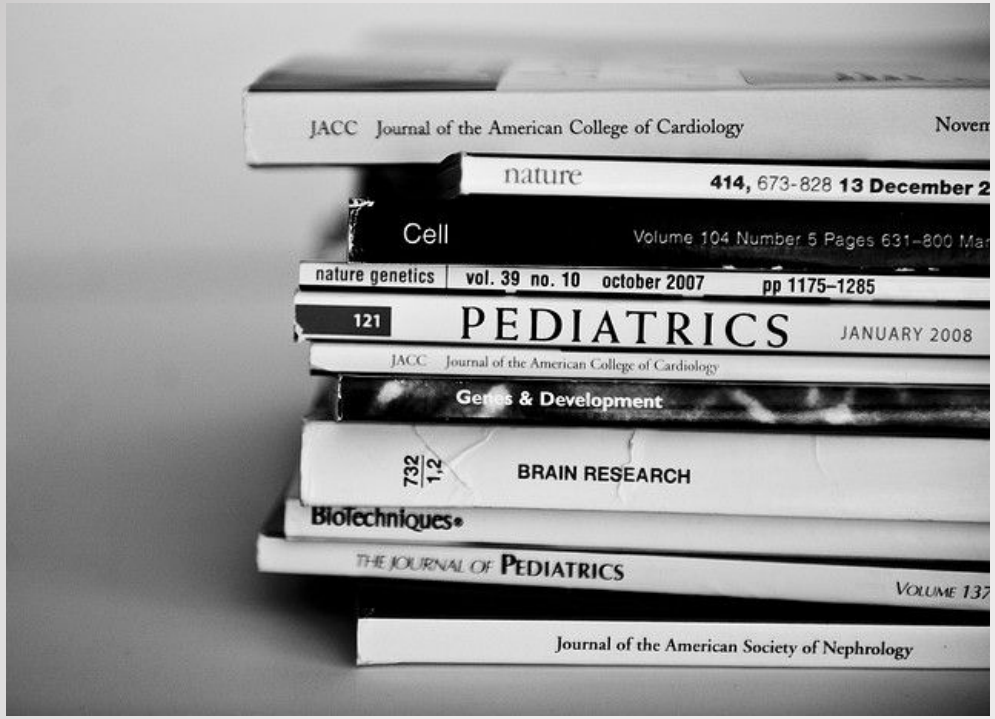
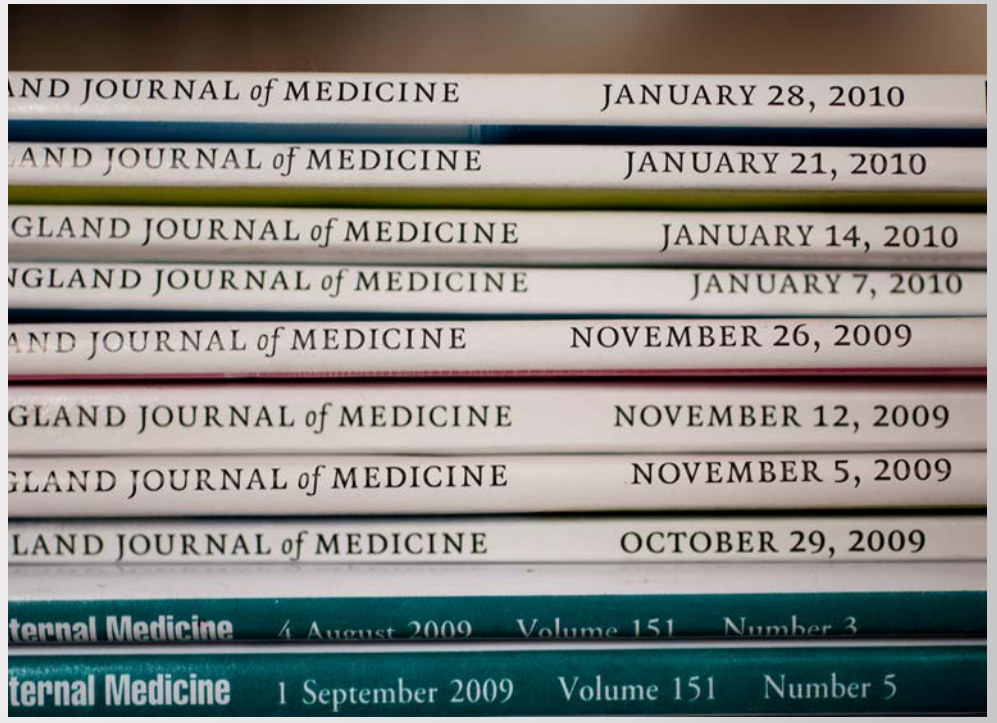


2015-Year in Review

Joshua LaBrin
Assistant Professor of Medicine
University of Utah

Agenda

- IV iron and anaphylaxis/tolerability
- Use of Antibiotics and Steroids in CAP
- Screening for Malignancy in Unprovoked VTE
- Risk of postoperative AKI
- Reducing Inpatient Delirium
- Residents and Hours

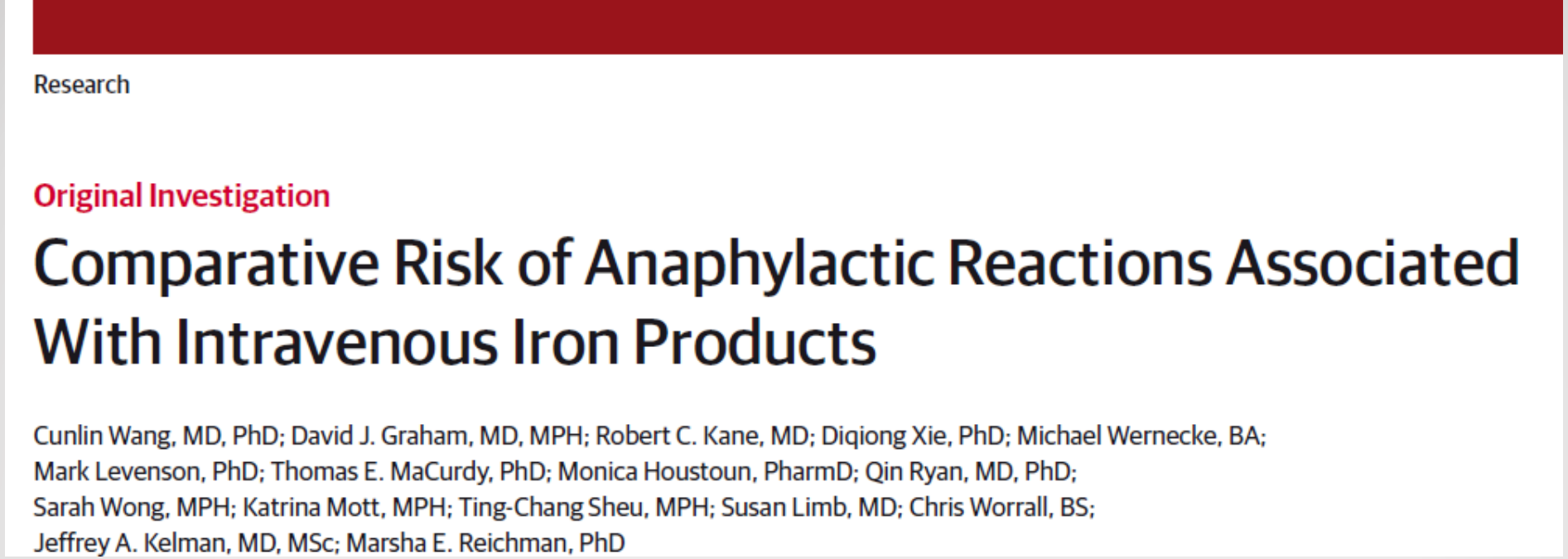


Clinical Trials in 2015

- Pubmed search “medicine”=4,090,684 articles
- Published between 1/1/2015-12/31/2015 → 357,337 articles
- English → 351,435 articles
- Humans → 107,917 articles
- Clinical Trial → 6,783 articles
- Today → 8!

Case

- 64 yo F with GERD, OA, HTN, CAD, admitted with tarry stools, Hgb 6.1
- History reveals high NSAID use
- Found to have multiple gastric ulcers, on PPI drip, Hgb 7.6 (s/p 2 units)
- Iron studies also sent, confirm significant Iron deficiency
- Intern wants to start oral iron supplementation, your resident suggests a dose of IV iron to “tank her up”
- Pharmacist not on rounds yet, and intern asks you “I thought IV iron had a risk of anaphylaxis. Is one type better than another?”



Research

Original Investigation

Comparative Risk of Anaphylactic Reactions Associated With Intravenous Iron Products

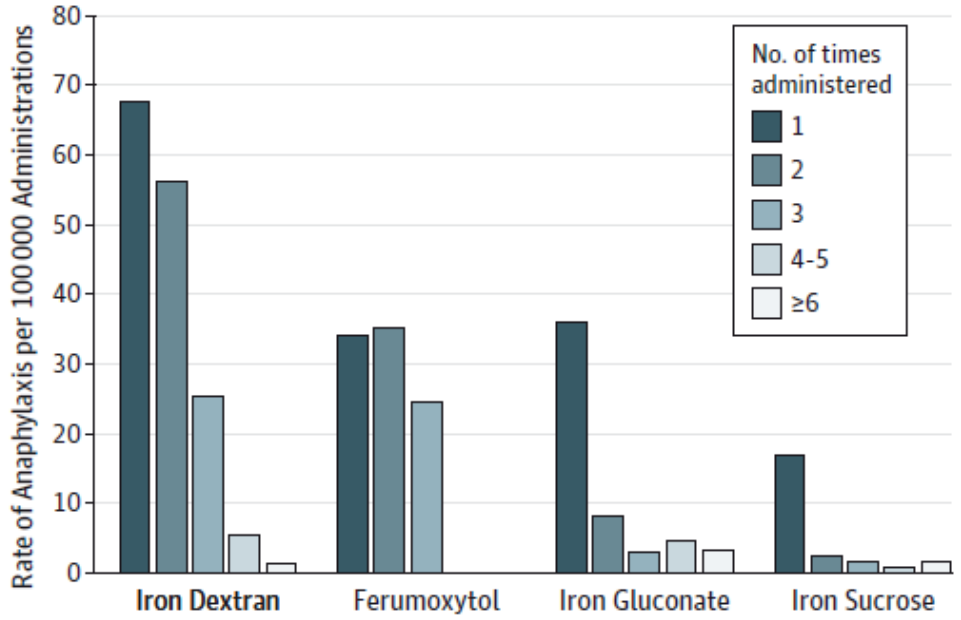
Cunlin Wang, MD, PhD; David J. Graham, MD, MPH; Robert C. Kane, MD; Diqiong Xie, PhD; Michael Wernecke, BA; Mark Levenson, PhD; Thomas E. MaCurdy, PhD; Monica Houstoun, PharmD; Qin Ryan, MD, PhD; Sarah Wong, MPH; Katrina Mott, MPH; Ting-Chang Sheu, MPH; Susan Limb, MD; Chris Worrall, BS; Jeffrey A. Kelman, MD, MSc; Marsha E. Reichman, PhD

- Retrospective new use cohort study of Medicare patients receiving IV iron
- Duration: 2003-2013
- Primary comparison: Dextran vs non-dextran
- Secondary comparison: Head to head, Iron Dextran vs gluconate/sucrose/ferumoxytol
- Outcome: Incidence of anaphylaxis

Results

- N=688, 183
- First exposure:
  - Dextran: 68/100,000 persons
  - Non-dextran: 24/100,000 persons
  - OR 2.6 (2.0-3.3)
- Compared to iron sucrose
  - Dextran: OR 3.6
  - Gluconate: OR 2.0
  - Ferumoxytol: OR 2.2
- Cumulative anaphylaxis risk (12-wk period)
  - Dextran: 82/100,000 persons
  - Sucrose: 21/100,000 persons

Figure 2. Rate of Anaphylaxis by IV Iron Products and Number of Administrations



No. of times administered	No. of users	No. of users	No. of users	No. of users
1	247 500	82 117	94 400	264 166
2	126 678	48 359	72 464	196 201
3	90 874	12 244	64 834	169 788
4-5	129 799	13 173	105 438	251 284
≥6	495 851	8778	312 971	550 444

IV iron and risk of adverse events

- Avni T, Bieber A Grossman A, et al. The safety of intravenous iron preparation: systematic review and meta-analysis. Mayo Clin Proc. 2015;90:12-23.
- Analysis included studies comparing IV iron to no iron, placebo, oral, IM
- Primary outcome: Serious Adverse Events (SAEs)
  - SAEs include infections, infusion, cardiovascular, neurologic, respiratory, gastrointestinal, thromboembolic, and constitutional severe reactions
- 103 RCTs involving 19,253 patients
- No difference in SAEs between IV iron and other forms overall
  - There was an increase in infusion reactions
- IV iron can be safely used

Overnight handover…

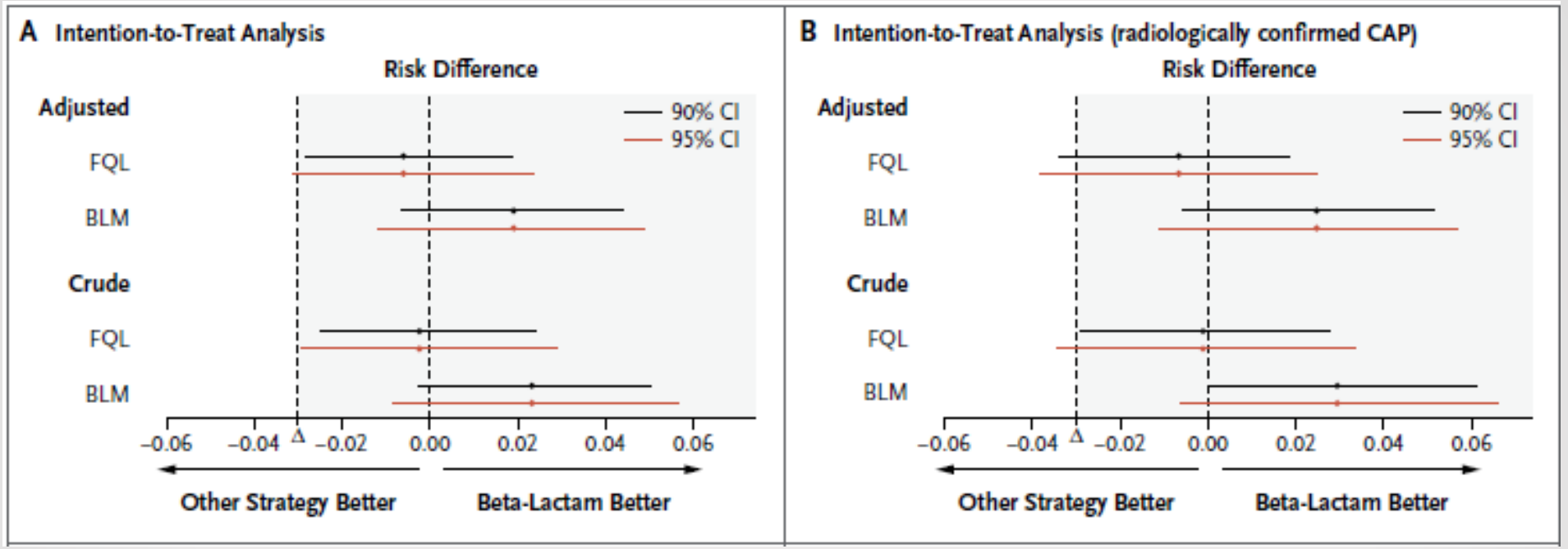
- Your team received a patient from the overnight team, admitted with LLL pneumonia
- ED gave 1 dose of Ceftriaxone and azithromycin
- Still febrile this morning, WBC has normalized
- No evidence of ongoing sepsis, still requiring 3L O2 via NC
- Urine antigens for legionella are negative
- Pharmacist mentions no new antibiotic orders have been written
- What do you tell your team?

ORIGINAL ARTICLE

Antibiotic Treatment Strategies for Community-Acquired Pneumonia in Adults

- Cluster randomized, crossover trial
  - 7 hospitals in the Netherlands (CAP-START study)
- Noninferiority study
- 2283 adult patients enrolled admitted with CAP to non-ICU setting
- Rotated Beta-lactam (BL) treatment with Beta-lactam/macrolide (BLM) or Fluoroquinolone (FQ) therapy every 4 months over a 2 year period
- Primary outcome was 90-day mortality

Results



- No difference in mortality
- No difference in LOS or complications
- Limitations: low # of atypical pathogens and BL resistance; "motivated deviation" higher in BL group
- In the absence of suspicion for atypicals, BL monotherapy may be a reasonable choice

Annals of Internal Medicine

REVIEW

Corticosteroid Therapy for Patients Hospitalized With Community-Acquired Pneumonia

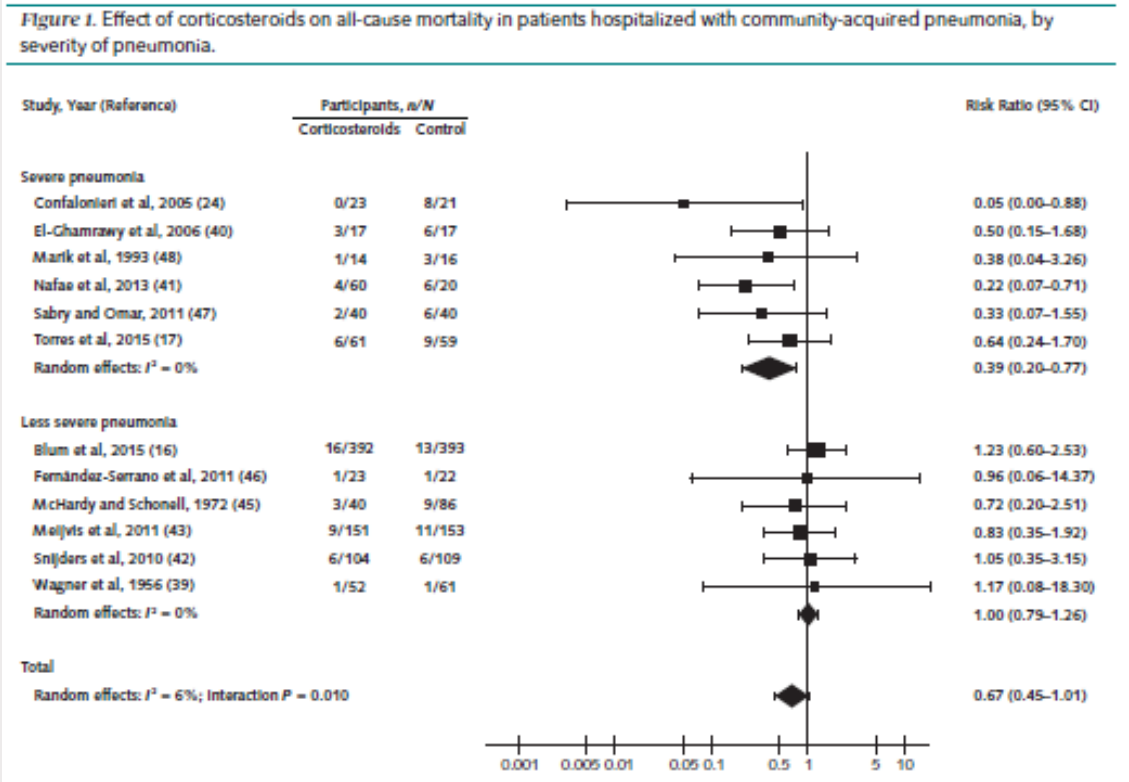
A Systematic Review and Meta-analysis

Reed A.C. Siemieniuk, MD; Maureen O. Meade, MD; Pablo Alonso-Coello, MD, PhD; Matthias Briel, MD, MSc; Nathan Evaniew, MD; Manya Prasad, MBBS; Paul E. Alexander, MSc, PhD; Yutong Fei, MD, PhD; Per O. Vandvik, MD, PhD; Mark Loeb, MD, MSc; and Gordon H. Guyatt, MD, MSc

- Meta-analysis of Randomized Clinical Trials
- Studies evaluating effect of adjunctive corticosteroid therapy on mortality, morbidity, and duration of hospitalization with community-acquired pneumonia (CAP)
- Hospitalized Adults with CAP
- Patients at high risk for adverse events were excluded

Results

- 13 randomized trials (including 2 from 2015)
- 2005 patients
- Systemic corticosteroid therapy (20-60 mg daily dose of prednisone/equivalent) associated with:
  - Reduction in mechanical ventilation (3.1% vs 5.7%) and development in ARDS (0.4% vs 3.0%)
  - Reductions in time to clinical stability (1.22 d) and duration of hospitalization (1 d)
- Mortality reduction noted mainly in subgroup of severe CAP (7.4% vs 22.0%)
- Increase in hyperglycemia requiring treatment noted; not GI bleed
- Dose/duration still unclear (2018?)



Next patient on rounds…

- 52 yo F with HTN, who was admitted with a new DVT
- No prior VTE history; no recent travel, surgery or other traumatic events; nonsedentary
- Your team has received this patient from the overnight team, already started on heparin, with plans made for CT scan to evaluate for other causes of her DVT
- Patient is feeling much better, and hoping to be discharged today
- She asks your team if this scan is really necessary…

ESTABLISHED IN 1812 AUGUST 20, 2015 VOL. 373 NO. 8

Screening for Occult Cancer in Unprovoked Venous Thromboembolism

Marc Carrier, M.D., Alejandro Lazo-Langner, M.D., Sudeep Shivakumar, M.D., Vicky Tagalakis, M.D., Ryan Zarychanski, M.D., Susan Solymoss, M.D., Nathalie Routhier, M.D., James Douketis, M.D., Kim Danovitch, C.C.R.P., Agnes Y. Lee, M.D., Gregoire Le Gal, M.D., Philip S. Wells, M.D., Daniel J. Corsi, Ph.D., Timothy Ramsay, Ph.D., Doug Coyle, Ph.D., Isabelle Chagnon, M.D., Zahra Kassam, M.D., Hardy Tao, M.D., and Marc A. Rodger, M.D., for the SOME Investigators*

- Multicenter, open-label randomized, controlled trial
- Patients with first unprovoked venous thromboembolism (VTE) randomized to:
  - Limited occult-cancer screening (basic blood testing, chest radiography, and screening for breast, cervical, and prostate cancer)
  - Limited occult-cancer screening in combination with CT abdomen/pelvis, with enhancement of the liver, distended bladder, virtual colonsocopy and gastroscopy, and parenchymal pancreatography
- Primary outcome=Confirmed cancer missed by screening strategy
  - Detected by the end of the 1-year follow-up period
- Secondary outcome=Recurrent VTE, all-cause mortality, cancer mortality

Results

- 854 patients randomized
- 33 with new cancer diagnosis
  - 14/431 (3.2%) in the limited group
  - 19/423 (4.5%) in the limited + CT group
- Primary outcome
  - 4/14 (29%) missed in limited group
  - 5/19 (26%) missed in limited + CT group
- No significant difference between groups for primary (P=1.0) or secondary outcomes
- Routine screening with CT did not provide a clinically significant benefit

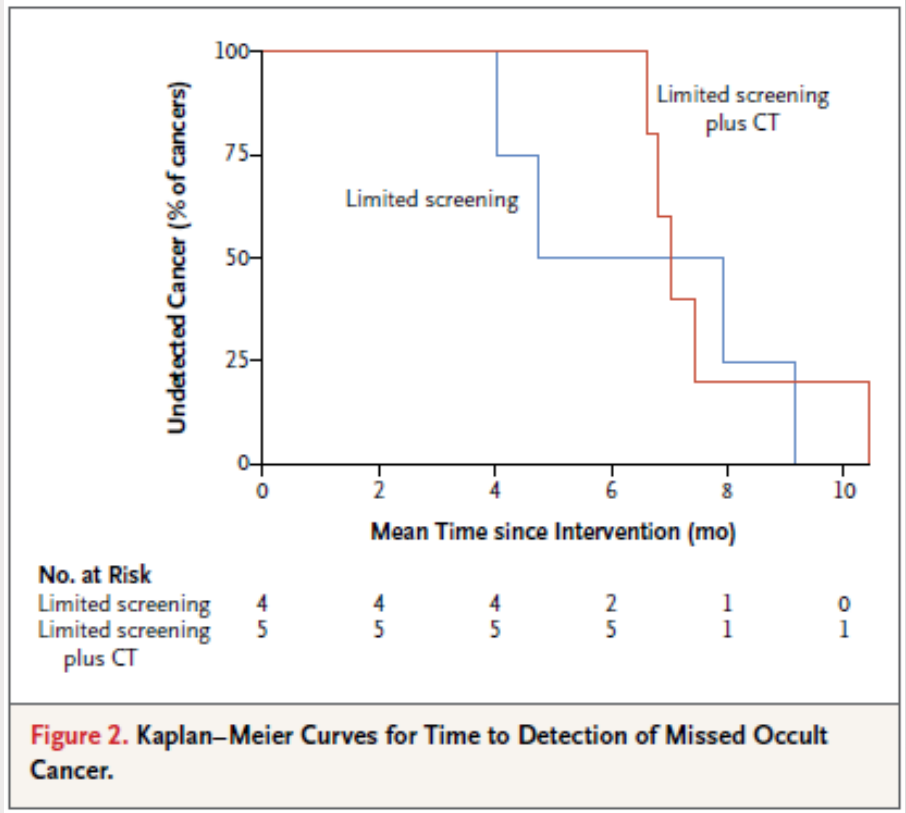
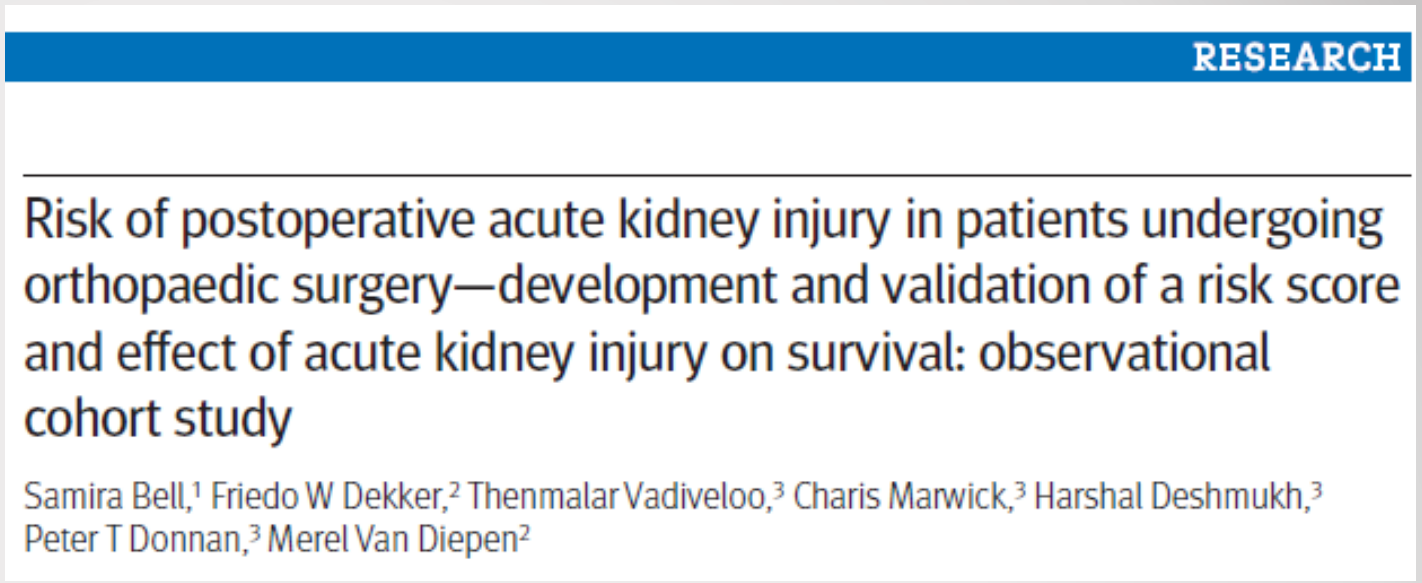


Figure 2. Kaplan–Meier Curves for Time to Detection of Missed Occult Cancer.

(Un)expected development

- You were consulted by ortho for medical clearance
- 74 yo M with HTN, T2DM, CKD, obesity, admitted with R hip fracture
- Went to OR 2 days ago
- Hgb 10.2, Cr 1.56 (at baseline)
- You get paged, notified that Cr up to 3.3
- You mumble to yourself, “I knew this would happen!”
- Intern asks you, “How did you know that would happen?”


RESEARCH

Risk of postoperative acute kidney injury in patients undergoing orthopaedic surgery—development and validation of a risk score and effect of acute kidney injury on survival: observational cohort study

Samira Bell,[1] Friedo W Dekker,[2] Thenmalar Vadiveloo,[3] Charis Marwick,[3] Harshal Deshmukh,[3] Peter T Donnan,[3] Merel Van Diepen[2]

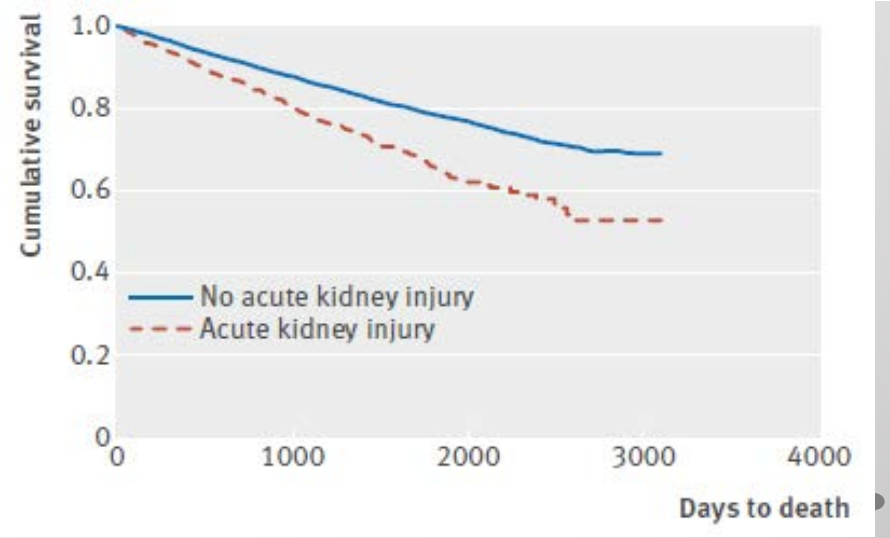
- Ortho surgeries from 2005-2011 from 2 Scottish hospitals
  - A 3rd hospital was included in the validation cohort
- Outcomes: Development of acute kidney injury (AKI) within the first postoperative week, and 90-day/1-year survival
- 10,600 adult patients: 6200 in development group, 4400 in validation group
- Mean baseline eGFR of 71 ml/min
- Logistic regression analysis used to identify risk factors

Results

- Postop AKI rates:
  - 11% (development group), 7% in validation
- 7 predictors identified:
  - Older age
  - Male
  - Diabetes
  - Lower eGFR
  - Use of ACEi or ARB
  - 3 or more prescribed drugs
  - High ASA grade
- Survival lower in patients with AKI vs no AKI (Short and Long-term)

Table 4 | Incidence of acute kidney injury across different risk categories in development and validation cohorts

	Development cohort		Validation cohort	
Predicted risk	No of patients	Incidence of acute kidney injury (No)	No of patients	Incidence of acute kidney injury (No)
<0.05	1377	0.03 (36)	972	0.03 (32)
0.05-0.10	1795	0.07 (123	1247	0.03 (36)
0.10-0.15	951	0.14 (129)	658	0.10 (64)
0.15-0.20	481	0.19 (90)	363	0.12 (42)
0.20-0.25	292	0.25 (72)	170	0.17 (29)
>0.25	398	0.31 (122)	225	0.16 (37)



Your team gets paged…

- Another of your patients has become more agitated, and the nurse is paging for an order for Haldol
- You review the case: 83 yo M with HTN, T2DM, Glaucoma, BPH, admitted with dehydration 2 nights ago.
- When you enter the room, the patient is confused, the room is dark, and he appears to be frightened
- The nurse also notes that the patient's family has not brought his hearing aids yet
- Your student shakes his head and asks, "There really isn't anything you can do to stop delirium other than medications, is there?"

Original Investigation | HEALTH CARE REFORM

Effectiveness of Multicomponent Nonpharmacological Delirium Interventions

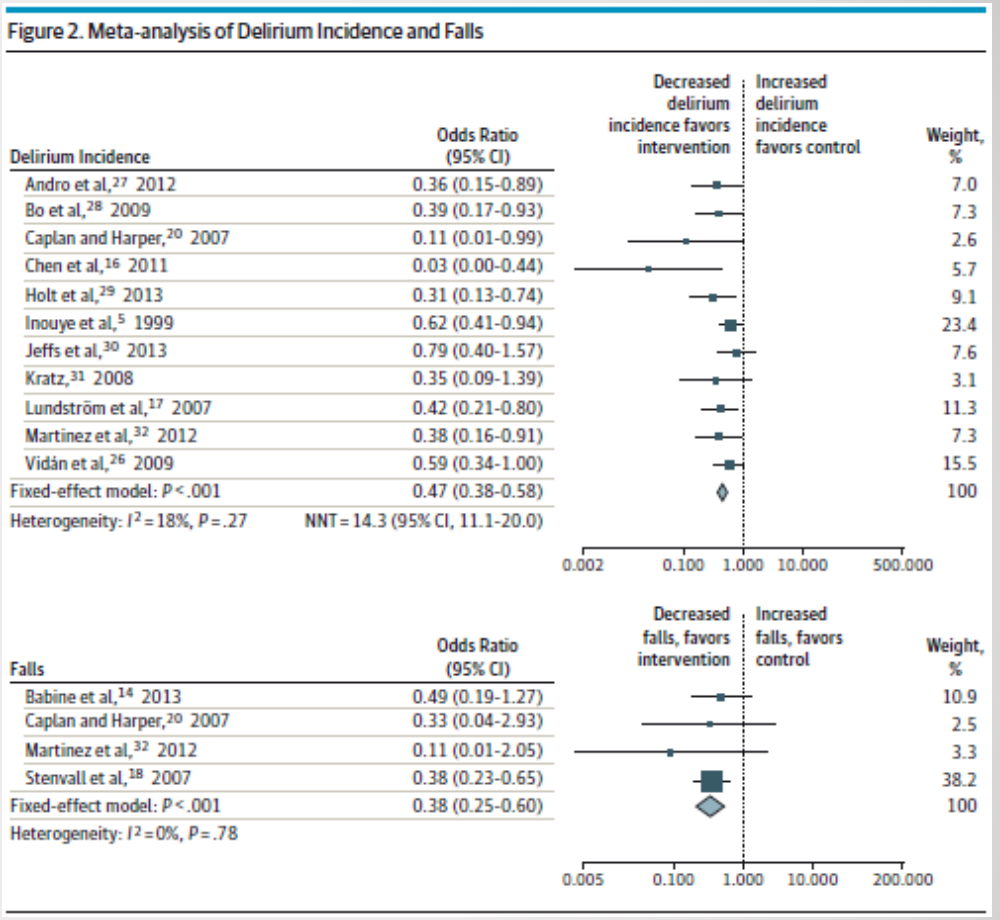
A Meta-analysis

Tammy T. Hshieh, MD; Jirong Yue, MD; Esther Oh, MD; Margaret Puelle; Sarah Dowal, MSW, MPH; Thomas Travison, PhD; Sharon K. Inouye, MD, MPH

- Review of studies comparing Nonpharmacologic multicomponent interventions (NPMIs) to controls
- Outcomes included Delirium incidence, falls, LOS, discharge to institution, change in functional status or cognitive status
- 14 studies including 4267 patients (mean age-80)
  - 9 studies used >4 interventions (variations of Helping Elder Life Program)
  - Included medical and surgical patients

Results

- NPMIs reduced risk for incident delirium and falls
  - OR 0.47 and 0.38
  - RRR compared to controls of 40% and 57%
- No difference in other outcomes measured
- Estimated savings of 16 billion in the US



Finishing Rounds

- You gathered your team to discuss current national initiatives surrounding patient safety with one of your senior colleagues
- Some discussion ensues afterwards about other initiatives that the residents are aware of
- One of the interns says “What about duty hours, they’ve made things better, right?”
- Your resident states “Well, that was one of the goals…”
- You chime in “…and there have been even more changes recently”
- Resident: “Dr. XXX, what did you think about duty hours when you were training?”
- Senior physician (on his way out), “Duty hours? HAHAHAHAHAHA…..”

A Narrative Review of High-Quality Literature on the Effects of Resident Duty Hours Reforms

Henry Lin, MD, Emery Lin, MD, Stephanie Auditore, JD, and Jon Fanning, MS

- Literature search from 1987-2013 about the effects of Duty Hours Reforms (DHRs)
- Used the Medical Education Research Study Quality Instrument (MERSQI) scoring system to determine "high-quality" studies
- 72 "high-quality" studies were included (10 RCTs)
- Most consistent effect was an increase in total cost to the healthcare/educational system
- Mixed results in resident quality of life, education, performance and patient complications
- No increase in patient mortality

Table 2

Summary of "High-Quality" Articles About Effects of Duty Hours Reforms on Patient Safety, Resident Education, Resident Well-Being, and Costs

Topic	Total studies	High-quality studies			
		Total[a]	Positive effect	No change	Negative effect
Patient safety					
Complications	79	25	9	13	5
Mortality	22	22	7	15	0
Resident education (skills and cognitive performance)	45	6	6	3	0
Interventions	35	11	8	3	0
Costs	10	7	0	0	7

[a]Some studies reported differing effects of duty hours reforms on subtopics within the same topic and were included in multiple columns.

Summary

- IV iron is safe compared to other forms
- Iron sucrose seems to be the better option
- 1 antibiotic in CAP may be all that is needed
- Steroids may be more useful in CAP than previously thought
- First unprovoked VTE does not require CT workup
- We may be able to better assess perioperative AKI risk
- Nonpharmacologic bundles can reduce inpatient delirium
- Jury's still out on DHRs and their effects

References

- Wang, C., Graham, D. J., Kane, R. C., Xie, D., Wernecke, M., Levenson, M., ... & Mott, K. (2015). Comparative risk of anaphylactic reactions associated with intravenous iron products. JAMA, 314(19), 2062-2068.
- Avni T, Bieber A, Grossman A, et al. The safety of intravenous iron
- preparations: systematic review and meta-analysis. Mayo Clin Proc. 2015;90:12-23.
- Postma DF, van Werkhoven CH, van Elden LJ, et al; CAP-START Study Group. Antibiotic treatment strategies for community-acquired pneumonia in adults. N Engl J Med. 2015;372:1312-23.
- Siemieniuk RA, Meade MO, Alonso-Coello P, et al. Corticosteroid therapy for patients hospitalized with community-acquired pneumonia: a systematic review and meta-analysis. Ann Intern Med. 2015;163(7):519-528.
- Bell, S., Dekker, F. W., Vadiveloo, T., Marwick, C., Deshmukh, H., Donnan, P. T., & Van Diepen, M. (2015). Risk of postoperative acute kidney injury in patients undergoing orthopaedic surgery—development and validation of a risk score and effect of acute kidney injury on survival: observational cohort study. BMJ, 351, h5639.
- Carrier M, Lazo-Langner A, Shivakumar S, et al; SOME Investigators. Screening for occult cancer in unprovoked venous thromboembolism. N Engl J Med. 2015;373:697-704
- Hshieh TT, Yue J, Oh E, et al. Effectiveness of multicomponent nonpharmacological delirium interventions. JAMA. 2015;175(4):512-520.
- Lin, H., Lin, E., Auditore, S., & Fanning, J. (2016). A Narrative Review of High-Quality Literature on the Effects of Resident Duty Hours Reforms. Academic Medicine, 91(1), 140-150.