# UTSW Internal Medicine Journal Watch (April 2014)

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1. **The ProCESS Trial: A Randomized Trial of Protocol-Based Care for Early Septic Shock**

   **Commentary:** This eagerly awaited multicenter RCT was the follow-up and validation study to the original Rivers' trial that launched the era of early goal-directed therapy (EGDT) that has defined sepsis management and guidelines for the past decade. With 1341 patients from 31 EDs, patients were randomized to one of 3 arms (EGDT per the Rivers' protocol; Protocol based therapy with less stringent goals and without requiring central venous catheterization in all patients; or Usual Care) with primary outcome of 60-day in-hospital mortality. The overall conclusion was no difference in the primary or secondary outcomes in any of the 3 groups. While it is premature to completely discard protocols in the management of severe sepsis as a means to standardize care, this study highlights that the critical aspects of early sepsis management are 1) early recognition of sepsis, 2) timely, appropriate initiation of antibiotics, and 3) aggressive resuscitation guided primarily by the clinical status of the patient. The details of how these specific aspects are achieved or attempts to meet other pre-specified hemodynamic parameters are probably less important.

   **Links:** NEJM website

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Infectious Diseases

1. **HealthCare-Associated Infection After Red Blood Cell Transfusion: Systematic Review and meta-analysis**

   **Commentary:** This systematic review and meta-analysis adds to the growing body of literature in support of more restrictive RBC transfusion strategies vs. more liberal strategies. Building on evidence such as the landmark TRICC trial, this review focuses on the risk of Healthcare associated infections (HAIs) associated with blood transfusion, finding a higher risk of serious infections in all groups studied with a more liberal transfusion approach. These findings are biologically plausible since RBC transfusion has immunomodulatory effects that increase infection risks. In light of accumulating evidence, a hemoglobin threshold of < 7.0-8.0 g/dL for transfusion should be favored in almost all situations, with the possible exception of active ischemic heart disease/AMI.

   **Links:** [JAMA website](#)  [Full Article via UTSW](#)

2. **Management of Skin Abscesses in the Era of MRSA**

   **Commentary:** This review article discusses the literature and suggests a practical management approach to skin abscesses, including techniques for incision and drainage, indications for antibiotics, and guidance for antibiotic selection. Particular highlights include:
   1) Central role of drainage for skin abscesses
   2) Antibiotic therapy only necessary in a subset of cases
   3) Review of IDSA skin and soft tissue guidelines for oral therapy targeting MRSA
   4) Options for decolonization procedures in cases of recurrent MRSA infections.

   **Links:** [NEJM website](#)  [Full Article via UTSW](#)

3. **Blood Culture Use in the Emergency Department in Patients Hospitalized for Community-Acquired Pneumonia**

   **Commentary:** This short research letter (by lead author Dr. Anil Makam, former UTSW IM resident and recent addition to GIM faculty) explores trends in blood culture use in a sample of EDs across the country for CAP and documents a steady increase in rates of blood cultures. This occurs despite guidelines that advise that blood cultures should only be performed in those who meet criteria for severe community acquired pneumonia (CAP) or are being admitted to the ICU. Much of this trend is likely driven by misapplication of JCAHO and CMS performance measures rather than evidence-based science. In patients without severe CAP or not admitted to ICU, blood cultures are unlikely to be helpful and may lead to false positive results leading to unnecessary additional hospital days and antibiotics.

   **Links:** [JAMA website](#)  [Full Article via UTSW](#)

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Endocrinology

1. **A 52-Week Placebo-Controlled Trial of Evolocumab in Hyperlipidemia**

   **Commentary:** This is an exciting phase 3 trial of 901 patients using a new class of lipid-lowering agents, PCSK9 inhibitors (PCSK9 ordinarily degrades hepatic LDL receptors). Evolocumab (a human monoclonal antibody against PCSK9), given as a monthly SC injection, was compared with placebo in patients on varying lipid-lowering regimens (diet alone, low-dose atorvastatin, high-dose atorvastatin, and high-dose atorvastatin + ezetimibe). The addition of evolocumab, compared with placebo, reduced LDL from baseline by an average of 57% over 52 weeks of treatment, with significant reductions in apolipoprotein B, non HDL cholesterol, and triglycerides as well.

   In summary, evolocumab lowers LDL significantly more than placebo in patients on diet therapy, high/low dose statins, or statin + ezetimibe and is well tolerated by patients. There is building excitement about the prospect of PCSK9 inhibitors in our “lower is better” hypercholesterolemia patients.

   **Links:**  [NEJM Website](https://www.nejm.org/)

General Internal Medicine

1. **Screening for Prostate Cancer With the Prostate-Specific Antigen Test: A Review of Current Evidence**

   **Commentary:** Nice review of the pertinent studies contributing to the confusion and conflicting opinions related to prostate cancer screening. In the end, it reinforces that an informed decision-making discussion is the most important component and that the decision to screen must be individualized based on age, personal risk factors (race, family history) and life expectancy.

   **Links:** [JAMA website](https://www.jama.com/)  [Full Article via UTSW](http://www.utsouthwestern.edu)

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**Hematology/Oncology**

1. **Rituximab versus a watch-and-wait approach in patients with advanced-stage, asymptomatic, non-bulky follicular lymphoma: an open-label randomized phase 3 trial**

   **Commentary:** Follicular lymphoma is the second most common type of Non-Hodgkin’s Lymphoma in the western world. This is a low-grade lymphoma that usually does not require treatment for many months. One clinical approach is to watch and wait in a relatively asymptomatic patient. In this lancet oncology authors are looking at this approach and comparing with rituximab treatment. Rituximab was selected given its favorable response rate (~80%) in this patient population and relatively favorable side effect profile. This study does not show any over all survival benefit with rituximab treatment compared to watchful waiting in these patients but quality of life was significantly better as patients felt in control and were less anxious.

   In conclusion- patients who are not comfortable with watch and wait approach can be treated with Rituximab single agent.

   **Links:** [Lancet website](#) [Full Article via UTSW](#)

**Geriatrics**

1. **Drugs for Urinary Tract Infection**

   **Commentary:** A very good evidence based review of a very common and seemingly easy problem but one that physicians (housestaff, faculty and community) very commonly get wrong! In particular, the lack of recognition of asymptomatic bacteriuria and its needless treatment. Therefore I think it is worthwhile to spend the time carefully reading this article, also seems to be good subject content for written exams.

   **Link:** [JAMA website](#) [Full Article via UTSW](#)

**Palliative Care**

1. **Olanzapine for the prevention of chemotherapy-induced nausea and vomiting in patients receiving highly or moderately emetogenic chemotherapy: a randomized, double-blind, placebo-controlled study**

   **Commentary:** Small yet interesting study that compares 22 patients receiving standard nausea prophylaxis (ondansetron, aprepitant and dexamethasone) to 22 randomized to receive olanzapine in addition to standard therapy as aforementioned. The group receiving olanzapine had significantly better control of nausea and better quality of life. This is not really surprising news, given how effective we know haloperidol to be in this context. The take-home point is that anti-dopaminergic drugs are GREAT for chemo-induced nausea and vomiting. I am not sure it matters which one you choose.

   **Link:** [Pubmed abstract](#) [Full Article via UTSW](#)

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Cardiology

1. Application of New Cholesterol Guidelines to a Population-Based Sample

Commentary: The present study examines the New Cholesterol Guidelines and its implications for statin use in the US. These estimates from NHANES (National Health and Nutrition Examination Survey) demonstrate that an additional net 12.8 million US adults will be eligible for statins under the new ACC-AHA Cholesterol guidelines. The main increase is in those >60 years who meet the criteria of having a 10-year risk of CVD >7.5%. However, the actual event rates, efficiency, and yield of treatment in this group (ie: by evaluating clinical endpoints) was not evaluated.

Link: NEJM website  Full article via UTSW

2. Transcatheter Aortic-Valve Replacement (TAVR) with a Self-Expanding Prosthesis

Commentary: We have been performing the latest transcatheter aortic valve replacement (TAVR) procedure here at UTSW for the past year. The Edwards valve (made by Edward Lifesciences) was the only valve till recently that was FDA approved in the US for use in patients with severe AS who would be considered inoperable from the surgical perspective (Partner A trial). This study evaluated a newer valve called the self-expanding CoreValve (made by Medtronic) in patients who would have high surgical risk (and not inoperable as evaluated in the Partner A trial) and compared it with surgical aortic valve replacement. The study demonstrated a reduction in mortality with the CoreValve compared to surgical valve replacement at one year.

The relevance of this trial is that it provides the potential for another valve system option for TAVR, but more importantly, suggests a mortality benefit relative to surgery in high risk patients, which was not seen in prior trials. While there are subtleties to the trial designs, the study enhances the potential role of TAVR for appropriate patients.

Link: NEJM website

3. Aspirin in Patients Undergoing Noncardiac Surgery

Commentary: This study evaluated the use of perioperative aspirin (ASA) in patients at higher cardiovascular risk, including 1/3 with a history of vascular disease, undergoing non-cardiac surgery. There was no benefit in terms of death or MI, but an increased risk of bleeding. In stable patients at higher risk or with clinical CAD, it is reasonable to not start and/or hold ASA for non-cardiac surgery. An important caveat is this trial did not evaluate patients with recent stent (only ~5% of the population had history of stenting) or recent ACS, where withholding ASA may have increased harms.

Link: NEJM website  Full Article via UTSW
4. A Controlled Trial of Renal Denervation for Resistant Hypertension

Commentary: Renal denervation is a procedure that involves using a minimally invasive, endovascular catheter placed through the groin and using radiofrequency pulses the renal sympathetic afferent/efferent nerve endings are denuded. It is already widely used in Europe based on prior trials suggesting significant benefit of renal denervation for resistant HTN. This trial randomized patients to a sham procedure (where access through the groin was obtained similar to the therapeutic arm but the final intervention of denervation was not done) as well as the actual renal denervation procedure. There was no significant difference in BP reduction with renal denervation (drop of 14 mm Hg) relative to sham and usual care (drop of 11 mm Hg).

The study casts a doubt on the value of renal denervation as a therapeutic strategy for HTN and importantly, reminds us of the importance of a placebo effect and the essential nature of well-done clinical trials.

Link: NEJM website  Full Article via UTSW

Nephrology

1. Dialysis versus Nondialysis in Patients with AKI: A Propensity-Matched Cohort Study

Commentary: AKI is one of the most common dx in acutely ill hospitalized patients. Although there are some clear indications to start emergent dialysis, it is not clear what is the optimal time to start dialysis and what patients benefit from starting dialysis early in their course. In this report from a large cohort of patients with AKI the investigators used a propensity-matched analysis to compare time to all-cause mortality among dialyzed patients and non-dialyzed patients with AKI. Dialysis was associated with better survival for those patients with AKI and higher serum creatinine concentrations but dialysis was associated with lower survival when initiated for patients with lower serum creatinine concentrations. This information supports randomized trials to determine the benefits/risks of early vs late initiation dialysis in AKI and to try to determine which patients do benefit and what patients may be harmed by dialysis in the setting of AKI.

Link: ASN Website  Full Article via UTSW
1. Advances in the management of Hepatitis C

**Commentary:** In what seems to be incredibly exciting times for Hepatitis management, a cure for Hepatitis C finally seems to be on the horizon. To put this achievement in perspective, Hep C has overtaken HIV in terms of cause of death in the United States and is implicated in 28% of all cases of cirrhosis and 26% of liver cancers globally. In this month’s *New England Journal of Medicine*, three phase 3 clinical trials demonstrate that 12-week therapy with Sofosbuvir/Ledipasvir (SOF/LDV) can provide high cure rates (95-99%) among patients with genotype 1 chronic HCV infection, while eliminating the need for interferon and ribavirin. SOF/LDV, administered as one pill once a day regimen, represent new direct-acting antiviral agents specifically targeting the replication machinery of HCV. So far, their use has shown excellent safety profile and low rate of resistance or virological breakthrough. The combination of SOF/LDV will likely be available for clinical use in 2015. The cost-benefit implications of this game-changing treatment are discussed in the April issue of *Hepatology*.

**Links:**
- NEJM - SOF/LDV in untreated HCV genotype 1
- NEJM - SOF/LDV in previously treated HCV genotype 1
- NEJM - SOF/LDV for 8-12 weeks for chronic HCV without cirrhosis

2. Systematic evaluation of coding variation identifies a candidate causal variant in TM6SF2 influencing total cholesterol and myocardial infarction risk

**Commentary:** A study from UT Southwestern and a report from University of Michigan published back-to-back in *Nature Genetics*, report that a genetic variant Glu167Lys in TM6SF2, a gene with previously unknown function, increases individual risk of developing non-alcoholic fatty liver disease (NAFLD) while decreasing the risk of myocardial infarction (MI). Experimental data indicate that TM6SF2 encodes a protein promoting VLDL secretion from hepatocytes. Decreased function of TM6SF2, observed in individuals with the Glu167Lys variant, is associated with increased lipid accumulation in hepatocytes and decreased levels of lipids in the circulation. Further studies will be needed to understand the role TM6SF2 plays in NAFLD and MI, and whether it can be targeted with new drug therapies.

**Link:**
- UTSW - Full article
- U of Michigan - Full article

3. A histologic scoring system for prognosis of patients with alcoholic hepatitis.

**Commentary:** Alcoholic hepatitis (AH) is associated with up to 50% mortality but no histologic scoring systems are available for prediction of prognosis. A study published in *Gastroenterology* addresses this knowledge gap by presenting a scoring system based on fibrosis, bilirubinostasis, polymorphonuclear (PMN) infiltration and presence of megamitochondria. Advanced fibrosis or bilirubin deposits in the liver were predictive of poor prognosis. Surprisingly, PMN infiltrate identified patients with better outcomes, suggesting that inflammation is not only causative in AH, but may also be required for liver regeneration. This scoring system may be used for risk stratification of patients with prognostic uncertainty, or for the design of future trials in AH.

**Link:**
- Gastroenterology Journal
- Full article via UTSW
1. Impact of Celebrity Sickness on Public Perceptions of Major Medical Issues

Comment: This study done by our very own residents, Ambarish Pandey and Kazeen Abdullah, was recently published in the American Journal of Cardiology and received press in the Cardiology world. Apparently, when someone famous suffers from a major medical illness, public interest in that medical condition spikes. The authors objectively demonstrate this by looking at Google trends and popular social media like Twitter for important medical keyword searches. For example, they show that after Vice President received a left ventricular assist device (LVAD), google searches for the term “LVAD” spiked. Similar surges in interest were seen in “Pulmonary embolism” and “BRCA gene” when Serena Williams and Angelina Jolie were affected.

Link: Am J of Cardiology Full article via UTSW

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