Sometimes all you can provide is presence, and sometimes that is enough...

“The Doctor” by Luke Fildes (1890)

The artist recalls a personal tragedy of his own, when in 1877 his first son, Philip, died at the age of one in their home. His adult son noted: “The character and bearing of Dr. Murray throughout the time of anxiety, made a deep impression on my parents. Dr. Murray became a symbol of professional devotion which would one day inspire the painting of The Doctor”.

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A 69-year-old man with HTN, HLD, DM2 presented with chest pain. The pain was described as 9/10 substernal chest pressure which radiated to his left arm and woke him up. It was associated with nausea and light-headedness. Troponins in the ED are negative. The following EKG is handed to you by the ED physician:

**What is the diagnosis?**
A: Unstable angina  
B: STEMI  
C: Pericarditis  
D: Non-cardiac chest pain  
E: Sinus bradycardia
**Answer:**
B: STEMI.

This EKG shows sinus bradycardia with normal axis and intervals. He has flipped T-waves in V1-V3 as well as aVR and aVL. The most concerning portion of this EKG, however are the large, symmetric T-waves in II, III, AVF. In this EKG, the T-waves are as high as the QRS complexes in the inferior leads. This should raise suspicion for hyperacute T-waves, the first EKG change in an evolving STEMI. In addition, he may have 0.5mm ST elevations in III, AVF, not meeting STEMI criteria.

The astute intern and resident on this case were concerned about the inferior T-waves and repeated the EKG.

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ST elevations are clearly seen in II, III, AVF as well as in V5, V6. Patient has also developed ST depressions in V1-V2 which are suggestive of posterior STEMI. Final diagnosis? Inferoposterior STEMI. The cath lab was activated and patient was found to have 3v CAD with culprit lesion distal 100% occluded RCA/PDA successfully treated with thrombectomy. Post-cath EKG is shown below:
The patient now has resolution of his inferoposterior ST elevations which have been replaced by T-wave inversions.

**Discussion**
STEMI incidence has decreased dramatically with improved medical therapy. While residents know to look for ST elevations, the evolving changes of an acute STEMI are not commonly encountered. It is important to remember that the hyperacute T-wave will develop before the ST segment gets pulled up with it. If a T-wave looks too large compared to the QRS segment in the right clinical scenario, it is never wrong to repeat the EKG to determine if the patient is undergoing an evolving STEMI. In the case above, the patient could easily have been diagnosed with unstable angina and treated medically which would have delayed catheterization by at least a day.

**References**

**SUMMARY**

The NORSTENT was an open label trial that compared the efficacy of contemporary drug-eluting stents (DES, 96% of the patients received 2nd generation DES - everolimus or zotarolimus eluting stents) and bare-metal stents (BMS) in adult patients undergoing percutaneous coronary intervention (PCI) for stable angina or ACS. Patients with prior stents, coronary bifurcation lesions, life-expectancy less than 5 years, contraindications or intolerable side effects to PCI or dual anti-platelet therapy, and enrollment in another RCT were excluded. A total of 9013 patients were randomized in a 1:1 ratio to receive either DES or BMS and everyone was prescribed aspirin 75 mg daily for an indefinite period and clopidogrel 75 mg daily for nine months after PCI. The primary outcome was death from any cause and nonfatal spontaneous MI. Secondary outcomes included subcategories of death; fatal and nonfatal spontaneous or peri-procedural MI and stroke; hospitalization for unstable angina; revascularization of the target lesion, target vessel, or non-target vessel with PCI or CABG; definite stent thrombosis; major bleeding episodes; and health-related quality of life. After a median follow-up of 59 months, the rate of the primary outcome was not different between the two groups: 16.6% in the DES group and 17.1% in the BMS group (hazard ratio, 0.98; 95% CI, 0.88 to 1.09, p=0.66). There were no significant between-group differences in the rates of the individual components of the primary outcome. Also, there were no significant differences between the DES and BMS groups for the following secondary outcomes: rates of death from cardiac, vascular, or non-cardiovascular causes; rates of stroke; rates of hospitalization for unstable angina; rate of spontaneous and peri-procedural MI; major bleeding episodes; disease specific health status and quality of life. The rates of definite stent thrombosis were low in both groups: 0.8% in the DES group and 1.2% in the BMS group, but was higher in the BMS group (P=0.0498). The rate of any revascularization was higher in the BMS group: 16.5% in the DES group and 19.8% in the BMS group (hazard ratio, 0.76; 95% CI, 0.69 to 0.85; P<0.001).

**COMMENTARY**

The NORSTENT trial demonstrated no significant difference between contemporary DES and BMS in the rates of death from any cause or nonfatal spontaneous myocardial infarction among patients undergoing PCI for stable angina or ACS, after 6 years of follow-up. However, the rate of repeat revascularization and stent thrombosis were lower in the DES group as compared to the BMS group. Similar results were reported in the BASKET-PROVE trial after 2 years of follow-up. The results of this trial provide support to the evidence that patients receiving contemporary DES have lower stent thrombosis and repeat revascularization rates after intermediate-term follow up. The results of this trial must be interpreted with caution considering the recently published 5-year follow-up data of the EXAMINATION trial that showed reduced rates of primary outcome (death from any cause, recurrent myocardial infarction, or revascularization) among patients with STEMI receiving contemporary DES (everolimus-eluting stents) as compared to BMS.

[USTW link](#)
Summary
Obstructive left main coronary artery disease is associated with high morbidity and mortality, and current international and US guidelines recommend a coronary artery bypass graft (CABG). However, recent evidence has suggested that percutaneous coronary intervention (PCI) may be an acceptable alternative to the highly invasive procedure. A recent subgroup analysis from the Surgery between PCI with Taxus and Cardiac Surgery (SYNTAX) suggested that PCI may be non-inferior to CABG in regards to the primary end-point (rate of composite of death from any cause, stroke, or myocardial infarction in 3 years). In addition, there has been an improvement of stents used since prior studies showing CABG superiority were performed.

The Evaluation of XIENCE vs Coronary Artery Bypass Surgery for Effectiveness of Left Main Revasculation (EXCEL) trial enrolled 1905 patients meeting SYNTAX anatomic low or intermediate complexity criteria, and they were randomized to CABG or PCI with an everolimus-eluting stent (957 vs 948). The primary end-point occurred in 15.4% in the PCI group and 14.7% in the CABG cohort (P=.02 for non-inferiority). The secondary end-point (rate of composite of death from any cause, stroke, or myocardial infarction within 30 days) occurred in 4.9% in the PCI group and 7.9% in the CABG cohort (P<.001 for non-inferiority, P=.008 for superiority). Additionally, the rate of composite of death, stroke, myocardial infarction, or ischemia-driven revascularization within 3 years occurred in 23.1% vs 19.1% in PCI vs CABG.

Commentary
In the five-year follow-up to the SYNTAX trial (NEJM 2009), CABG procedures portended better outcomes than PCI for most patients with at least moderate left main disease or three-vessel disease. However, subgroup analysis suggested that low to intermediate anatomically complex groups might have non-inferior results from PCI when compared to CABG.

The results from the current EXCEL trial support prior conclusions that low and intermediate complex left main disease cohorts showed non-inferior benefit with PCI compared to CABG. These results may be attributed to improved management guidelines of post-PCI patients, use of everolimus-eluting stents (associated with a low rate of stent thrombosis), and the fact that the EXCEL trial used ultrasonographic imaging guidance in 80% of their PCI patients.

UTSW Link
**Hepatitis C Virus RNA Persists in Liver Explants of Most Patients Awaiting Liver Transplantation Treated With an Interferon-Free Regimen**

*Dr. Josephine Thinwa reviewing Gambato M et al. Gastroenterology 2016;151:633–636*

**Summary**

In patients with Hepatitis C with cirrhosis or hepatocellular cancer and requiring liver transplant, it is imperative that the virus be fully cleared from the patients liver and serum prior to transplant. In this study, the goal was to evaluate the duration of treatment with the new IFN-free regimens that would lead to eradication of the virus. Liver explants from 39 patients undergoing liver transplantation who had been treated with IFN-free regimen were analyzed by PCR for levels of HCV-RNA. The median treatment time before liver transplantation was 25 weeks and 68% of patients had undetectable serum HCV-RNA by four weeks into treatment. Despite undetectable serum HCV-RNA, 67% percent of the liver explants had detectable HCV-RNA. A comparison of the patients with HCV negative liver explants to the HCV positive explants showed that the former group received longer treatment duration of 99 versus 61 days for the HCV positive liver explants. However, the majority of the patients with liver explants positive for HCV-RNA still maintained virologic response 3 months post-transplantation. Six patients had relapse of HCV infection of the new transplanted liver and 4 of the 6 relapsed patients previously had HCV-RNA positive liver explants.

**Commentary**

The new era of hepatitis C IFN-free regimens has ushered in the long time elusive cure of HCV. However, cure is not always easy to ascertain particularly in patients in need for liver transplantation for cirrhosis or hepatocellular cancer. These transplant patients are at particularly high risk of recurrent HCV infection in their transplanted liver further risking organ rejection. In this small study, the duration of treatment although quite variable, seems to correlate with clearance of the virus from liver explants. Essentially, the longer you treat the more likely it is that the explanted liver is negative of HCV. The small sample size limits extrapolation of the data, but the data is suggestive that more HCV relapses after transplantation occur when the liver explants are HCV positive. The exact duration of treatment prior to transplantation to consistently lead to HCV clearance from the liver is yet to be well defined.

**UTSW Link**
SUMMARY
Since 2007, guideline-directed therapy for inpatient management of community acquired pneumonia as dictated by the American Thoracic Society (ATS) and Infectious Disease Society of America (IDSA) has advocated for shorter durations of therapy and use of clinical severity indices for tailoring therapy. Conventional practice remains erratic, however, and high quality evidence to support these recommendations is sparse. Uranga et al., enroll 312 adults across four teaching hospitals in Spain in a RCT to compare the efficacy of guideline-based therapy for CAP with clinical practice in achieving symptom resolution at ten and 30 days post-admission. Notable exclusions were the chronically immunosuppressed, those with frequent or recent contact with healthcare and those with prior resistant organisms.

Patients in the intervention arm were treated with a minimum of five days of antibiotics, at which time they were assessed for CAP-associated signs of clinical instability, including fever (temperature > 37.8\(^\circ\)C), tachycardia, respiratory rate > 24/min, PaO\(_2\) less than 60 mm Hg on room air. Presence of at least one of these warranted extending therapy. Patients in the control arm, meanwhile, were treated with antibiotics at the discretion of the admitting physician. Mean duration of therapy in the intervention arm was 5 days, as compared with 10 days in the control arm. There was no significant difference between groups in in-hospital mortality, complications, length of stay or clinical success rate at ten or 30 days. The intervention arm did, however, report significantly fewer readmissions at 30 days.

COMMENTARY
This study provides much needed high quality evidence to support non-inferiority of shorter antibiotic courses for inpatient CAP. Although its scope is limited to uncomplicated patients, the demonstrated benefit of reduced readmissions and theoretical benefit of decreased penicillin-resistance are valuable in supporting current guidelines. Notably, choice of antibiotic is not addressed in this study as this was left to the discretion of the admitting physician in both arms. More than 80 percent of patients received quinolones with the remaining 20 percent receiving a beta lactam and macrolide. Doses too were not standardized, despite prior reports of dose dependent differences in efficacy among both quinolones and macrolides. This further limits the generalizability of results, particularly to regions with different prescribing practices and potentially different resistance patterns.
Cognitive Behavioral Therapy for Insomnia in Older Veterans Using Nonclinician Sleep Coaches: Randomized Controlled Trial


SUMMARY
159 community dwelling veterans aged 60 and older with at least 3 months' duration of insomnia were randomized to group cognitive behavioral therapy (CBT) for insomnia, individual CBT for insomnia, or a control with general sleep education conducted in a group setting. Nonclinician health educators led both the interventions and the control arms. The intervention was conducted in 5 one hour sessions over 6 weeks and included training in stimulus control, sleep restriction, cognitive therapy, and sleep hygiene. The health educators received weekly telephone consultation from a psychologist with expertise in behavioral sleep medicine. Outcomes included variables based on a sleep diary, wrist actigraphy performed the same week as the sleep diary, and the Pittsburgh Sleep Quality Index survey (scale of 0-21 with higher scores indicating worse sleep). The Insomnia Severity Index, PHQ-9, and Medical Outcomes Study 12 Item Short Form Health Survey (SF 12) were secondary outcome measures. Outcome variables were measured at baseline, 1 week posttreatment, and at 6- and 12-months follow-up. Mixed effects models were used to evaluate the difference in change in sleep outcomes between the intervention and control groups. Data from the group and individual CBT arms was analyzed together as the “intervention” group, and there were no significant differences in any outcome at any time point between the individual and group interventions. Compared to the control group, the intervention group had larger statistically significant decreases in sleep onset latency, total wake time at night, sleep efficiency, Pittsburgh Sleep Quality Index score, and Insomnia Severity Index that remained significant at 12 months follow up. There were no significant effects on the SF-12 or PHQ-9 score. There were no significant differences in treatment effect between patients taking insomnia medications or other sedatives and those who were not.

COMMENTARY
CBT has been demonstrated to be an effective and safe treatment for insomnia and is a particularly valuable option for older adults who face increased risk of falls, fractures, and mortality with the sedative-hypnotics typically used to treat insomnia pharmacologically. Unfortunately, the use of CBT is limited by lack of access to therapists. This study demonstrates the ability of nonclinician health educators to successfully implement a CBT intervention that results in subjective improvements in insomnia in older adults, with sustained effects at 12 months.

UTSW Link
Hematology Oncology

Breast-Cancer Tumor Size, Overdiagnosis, and Mammography Screening Effectiveness


SUMMARY

Dr. Welch and colleagues attempted to determine the effect of screening mammography on the case fatality rate. Using SEER data, two time periods were compared – 1975 through 1979 (before widespread mammography) and 2000-2002. They also calculated the tumor-size distribution and size-specific incidence of breast cancer in women 40 and older. Their results indicate an increased proportions of small tumors were detected and a reduction in detection of larger tumors over the same time period – with an increase in the overall incidence of breast cancer. However, there was no change on the rate of metastatic cancer diagnosis over the 30 years of data, indicating possible overdiagnosis bias. Taken together, the authors estimate screening has decreased the incidence of large tumors by 30 per 100,000 women. They estimate screening has improved mortality by 8 per 100,000 and the benefit appeared to diminish further as treatment options improved.

COMMENTARY

Welch and colleagues tackle a complex issue with this paper – how to measure progress in screening for cancer. While the SEER database is known for its robustness, even they acknowledge the statistical methods are subject to bias. For example, women with invasive tumors less than 1cm had 10 year relative survival rates > 100% as compared to the general population, indicating a survival advantage to being diagnosed with breast cancer in their analysis. Additionally, there is no analysis of minorities who disproportionately receive fewer mammograms. Furthermore, it would be interesting to perform a cost-benefit analysis of the to determine costs of mammography to detect a single clinically significant tumor. However, their study highlights several important concepts in cancer screening. First, we must recognize that the true incidence of a specific cancer cannot be measured as it is clearly affected by observational intensity – the harder one looks for a cancer, the more likely one is to find it. Second, it is similarly not possible to predict biologic behaviors of many small tumors. As is the case with prostate cancer, small breast tumors were detected at an increased rate and many were never destined to become metastatic. Despite increased detection in their data, the rate of metastatic disease remained stable. Lastly, unless treatment options are stagnant over long periods of time, it is very difficult to assess the effect of screening on mortality. As technologies improved in screening modalities, so too did the treatment modalities. The authors in this paper provide an estimate that two-thirds of the improved mortality in breast cancer over their study period could be explained by better treatment as opposed to screening. Overall, this is a very thought-provoking article that highlights an issue internists will no doubt see change over the coming decades. In a fashion similar to the PSA test for prostate cancer, it does appear that mammography leads to high rates of overdiagnosis. For now, mammography is the best tool we have to detecting breast cancer, but its appropriate use will likely need continued study.

UTSW Link
**High Value Care**

**Association Between Intensive Care Unit Utilization During Hospitalization and Costs, Use of Invasive Procedures, and Mortality**

*Dr. Christopher A. Wrobel reviewing Change DW, Shapiro MF JAMA Internal Med. 2016; 176(10): 1492-1499.*

**Summary**

The authors of this study sought to evaluate ICU utilization for four common conditions in hospitals across Washington state and Maryland. They identified diabetic ketoacidosis (DKA), pulmonary embolism (PE), upper gastrointestinal bleed (UGI), and congestive heart failure (CHF) as the diagnoses to evaluate because of previous data that has suggested wide interhospital variability in ICU utilization for these four diagnoses (notably without any improvement in mortality). This data, however, was limited to the individual diseases, making conclusions about broad systemic trends difficult. The primary outcomes were risk-adjusted hospital-level mortality, use of invasive procedures (ie thrombolytics for PE or pulmonary artery catheterization for CHF), and hospital costs. 94 hospitals with data between 2010 and 2012 were included in the final analysis. There were approximately 150,000 hospitalizations for the 4 diagnoses queried, accounting for about 5% of total hospitalizations at these hospitals. Not surprisingly, the authors found wide variability in the ICU utilization between these hospitals. Risk adjusted ICU admission rates ranged from 16.3%-81.2% for DKA, 5%-44.2% for PE, 11.5%-51.2% for UGI, and 3.9%-48.% for CHF. Smaller hospitals as well as teaching hospitals were more likely to utilize the ICU for these conditions. Notably, there was no significant relationship between ICU utilization and in hospital mortality (Figure). Increased ICU utilization was associated with higher probability of invasive procedures, increased hospital costs (especially in patients hospitalized for CHF), but no significant difference in length of stay.

**Commentary**

The number of ICU beds has increased by nearly 20% just in the last decade, and yet, the ICU occupancy rate was unchanged between 1985 and 2010. While the population has aged and become more chronically ill, the idea that the population as a whole has just become sicker, necessitating more and more ICU beds, would seem to be an oversimplification. There are a host of hospital level (ie number of ICU beds, nurses) and physician level (ie hospitalist experience, physician comfort with risk) that ultimately factor into whether a patient receives their care in the ICU or not. As this study shows, there is tremendous variability between hospitals in how frequently ICUs are utilized to care for patients with common, albeit serious disorders. Most important from a value perspective is of course whether this increased utilization (and the costs that come with it), leads to better patient outcomes. Based on the data presented in this article, it does not appear that that is the case. Certainly, that comes with caveats as many patients with these conditions will unquestionably derive benefit from receiving their care in the ICU. The Society of Critical Care Medicine recently published updated guidelines for ICU admission, discharge, and triage (the first update since 1999). While not advocating for a
specific set of criteria that a patient must meet to be admitted to the ICU, the guidelines do recommend utilizing some form of system of prioritization. These may include scoring systems or cutoffs which utilize vital signs, symptoms, and or metabolic derangements as triggers for ICU level care\(^{4-7}\). As these and future risk stratification tools continue to be refined, we should hopefully approach optimal ICU utilization, leading to decreased costs and improved patient outcomes.

**REFERENCES**

Empirical Micafungin Treatment and Survival Without Invasive Fungal Infection in Adults with ICU-Acquired Sepsis, Candida Colonization, and Multiple Organ Failure: The EMPIRICUS Randomized Clinical Trial.


SUMMARY

Current guidelines recommend the use of empiric antifungal therapy in critically ill patients with risk factors for invasive candidiasis and septic shock of unknown origin(1). The EMPIRICUS trial is a multicenter, randomized, double-blind, placebo-controlled trial (N=251) evaluating the role of micafungin for the treatment of ICU-acquired sepsis of unknown origin in the context of culture-proven Candida colonization. The primary end point was 28-day survival free of proven invasive fungal infection (IFI); this was not significantly different in patients treated with micafungin versus those treated with placebo (hazard ratio 1.35 [95% CI 0.87-2.08]). Secondary outcomes reported (including overall survival at days 28 and 90) were also not significantly different between the two groups. However, patients with Sequential Organ Failure Assessment (SOFA) scores >8 experienced a non-significant improvement in 28-day survival.

COMMENTARY

Results from the EMPIRICUS trial suggest no clinical benefit in the use of empiric micafungin in this setting, adding to a litany of contradictory and negative studies in this field. A recent meta-analysis (2) examined 19 studies of antifungals in critically ill patients and reported a reduction in the development of proven IFI in the untargeted antifungal treatment group, although there was no significant difference mortality between the antifungal and placebo groups. Only two included studies evaluated micafungin, showing no overall effect on risk of developing IFI in subgroup analyses. Additionally, the subgroup of non-surgical patients showed no significant reductions in rate of IFI with antifungals. The take-home message is that while data supports empiric antifungals in post-surgical patients with proven fungal colonization, the picture in medical ICU patients is less clear. Results from the EMPIRICUS trial suggest that surrogate markers such as beta-D-glucan or multi-site Candida colonization are not helpful in deciding to initiate antifungals. While certain high-risk groups (SOFA score >8, GI perforation or acute necrotizing pancreatitis) may benefit from empiric antifungals (although this requires further confirmation in randomized trials), this study raises questions about the broader guideline recommendation of empiric antifungals in the critically ill MICU patient.

References


UTSW Link
Quality of End-of-Life Care in Patients with Hematologic Malignancies: A Retrospective Cohort Study


Summary
The objective of this study was to compare the quality of end-of-life care between patients with hematologic malignancies and patients with solid tumors. This was a retrospective cohort study that reviewed the medical records of 816 patients seen at MD Anderson Cancer Center in Houston, TX. These patients died as a result of advanced cancer between September 1, 2009 and February 28th, 2010. Each case was reviewed using multiple end-of-life care quality indicators well established in literature and endorsed by the American Society of Clinical Oncology and National Quality Forum. These indicators included emergency room visit within the last 30 days of life, hospitalization within the last 30 days of life, ICU admission within the last 30 days of life, and ICU death. They also noted the date of last administration of chemotherapy or targeted agent and palliative care involvement, if any. Patient characteristics and quality of end-of-life care indicators were compared between patients with solid tumors and those with hematologic malignancies.

Among the 816 patients that were studied, 113 (14%) had hematologic malignancies and 703 (86%) with solid tumors. There were significant differences in the quality end-of-life care indicators between hematologic malignancies and solid tumors. At the end of life, patients with hematologic malignancies were more likely to have emergency room visits (54% vs 43%; P=0.03), hospital admissions (81% vs 47%; P<0.001), ICU admissions (39% vs 8%; P<0.001), and death in ICU (33% vs. 4%; P<0.001). These patients were also more likely to receive chemotherapy (43% vs. 14%; P<0.001) within 14 and 30 days of life. They were also less likely to have a palliative care consultation (47% vs. 33%; P=0.006) and outpatient palliative care (48% vs. 22%; P=0.003).

Commentary
Prior studies have shown that early involvement of palliative care leads to improves quality of life, less aggressive care at the end of life, and longer survival. Unfortunately, there is still a vast underuse of palliative care services, particularly in patients with hematologic malignancies. This group of patients experience significant symptoms such as fatigue, nausea, pain, and dyspnea due to progressive cancer and their treatments. The disease itself puts patients at high risk of infections and coagulopathies due to cytopenias resulting in numerous hospitalizations and intensive care unit stays.

The increased utility of acute care facilities in the last weeks of life is likely related the high rate of hematologic complications related to the disease, but also the greater frequency of systemic therapies in the last days of life that lead to adverse effects. The hematologic malignancies are unique to oncology. Predicting the end-of-life phase can be particularly difficult. Aggressive, systemic chemotherapy is often prescribed in advanced cases, as there is still a chance of a cure in these patients, despite a considerable risk of poor outcomes.
Often times when it becomes clear that the end of life is nearing, it can be too late for meaningful palliative care or hospice services. In the future, we as physicians should expand our conceptions of palliative care from just end-of-life services. Many have proposed upstream integration of non-hospice palliative care services. Palliative care can offer much more than symptom management and hospice services. If incorporated earlier in the course, they can help patients better understand their treatment options. Ideally, palliative care would work alongside the oncologist find the balance of aggressive treatment and comfort for each individual patient and at different stages of their disease.

UTSW Link
New Hepatitis C Drugs are Very Costly and Unavailable to Many State Prisoners


SUMMARY

In 2015, the authors performed a cross-sectional survey of the commissioners of the state departments of corrections to acquire information about the number of inmates in each state known to be infected with Hepatitis C, the number receiving treatment, and the cost of the drugs. Within the 41 states providing data about Hepatitis C infections and treatment, there were 106,266 prisoners infected with Hepatitis C on or about January 1, 2015, which is about 10% of the prison population at that time. Of these prisoners, 0.89% (949) were receiving any form of treatment for Hepatitis C. The percentage of infected prisoners receiving treatment varied by state from 0% in Oklahoma, Pennsylvania, South Carolina, and Wyoming to 5.9% in New York, with 27 states treating less than 1% of infected prisoners. 10 states reported using primary care providers to treat Hepatitis C, but the other reporting states used specialty physicians.

Total annual spending on Hepatitis C treatment in the 41 states reporting data was $39.8 million with the departments each spending a median of 6% of their annual drug spending on Hepatitis C drugs. 44 states reported that they were seeking to obtain the drugs at a price lower than the US list prices of $84,000 for a 12 week course of sofosbuvir and $94,500 for a 12 week course of ledipasvir/sofosbuvir. 19 states reported financial data with a median purchase price of $76,084.50 for a course of sofosbuvir and $63,509.00 for a course of ledipasvir/sofosbuvir. While the Federal Bureau of Prisons, Department of Defense, and Department of Veterans Affairs receive at least a 24% discount on these drugs and Medicaid receives at least a 23% discount, 10 states reporting financial data received less than a 10% discount on sofosbuvir and 5 received less than a 10% discount on ledipasvir/sofosbuvir.

COMMENTARY

This study is the first known to estimate the number of state prisoners receiving treatment for Hepatitis C since the release of the direct-acting antivirals. Given that treatment of Hepatitis C in the prison setting has been previously demonstrated to be cost effective, and that nearly 1/3 of all Americans with Hepatitis C spend at least part of the year in a correctional facility, the less than 1% treatment rate of infected prisoners is surprising. Also, this population is at high risk of spreading the infection to others. One reason for the low treatment rate may be the high costs of the drugs. This study finds that not all state prisons are receiving the discounts available to federal organizations, and this may present an area for future improvement. Additionally, it is possible that access to specialists is a limitation, so training primary care providers to treat Hepatitis C may be another opportunity to increase treatment rates.

UTSW Link
US state prisoners receiving any treatment for hepatitis C as a proportion of inmates with known hepatitis C infections, January 1, 2016.

State prison systems’ cost of purchasing a twelve-week course of sofosbuvir and a twelve-week course of the combination drug ledipasvir/sofosbuvir, September 30, 2015.
Association between Overnight Extubations and Outcomes in the Intensive Care Unit


SUMMARY

This large multi-center retrospective cohort shows that night time extubations in the intensive care unit (ICU) are associated with adverse clinical outcomes. IMPACT database provided data for 97,844 adults aged >18 years admitted to the ICU for the first incidence of mechanical ventilation (MV). Exclusion criteria included patients with tracheostomies and restrictions to care based on advanced directives.

In the cohort assessed, 20.1% of extubations were conducted overnight. Statistically significant decrease in the frequency of night time extubations (23.3% in 2000 to 18.8% in 2009; P=.001) was noted between year 2000 to 2009. Overnight extubations occurred more frequently in patients who underwent MV for <12 hours (57.1% vs 19.8%; P<.001). Sub-cohorts were then created based on duration of mechanical ventilation. Propensity matched pairs of patients were constructed for each sub-cohort who had undergone day time vs night time extubations.

Re-intubation rates were similar between groups containing patients that were extubated after <12 hours of MV. However, ICU and hospital mortality increased in patients extubated overnight (5.6% vs 4.6%; P=.03 and 8.3% vs 7.0%; P=.01 respectively). ICU length of stay (LOS) shortened for the overnight extubation group while the hospital LOS stayed similar.

The sub cohort with MV >12 hours in the overnight extubation group had higher re-intubation rates (14.6% vs 12.4%; P<.001), ICU mortality (11.2% vs 6.1%; P<.001) and hospital mortality (16.0% vs 11.1%; P<.001) without any significant difference in ICU or hospital LOS.

COMMENTARY

The goal was to find the optimal time of day for extubation. Due to a large sample size, diverse patient population and multi-centric location, this study provides strong evidence to support daytime extubations. However a possibly important determinant of appropriateness of extubation: the level and type of training of the provider responsible for the decision to extubate, was not reported in this study. Additionally, the decade old data set of this trial makes it difficult to extrapolate results into modern day practice. Timing of extubation is a commonly encountered question, particularly during residency training. Prospective studies and randomized controlled trials linking the observed findings to specific patient populations are warranted. Until then, based on the results of this trial, attempts should be made to perform all planned extubations during the daytime, particularly for patients who have received MV for greater than 12 hours.

UTSW link
Quality Improvement

The Quality of Outpatient Care Delivered to Adults in the United States, 2002 to 2013
Dr. Christopher A. Wrobel reviewing Levine DM, et al. JAMA Internal Med.

SUMMARY
With the growing shift in US health care from a pay for service scheme to bundled payments, much attention is being given to improving the quality of health care delivered. In this vein, the authors of this paper sought to assess trends of the quality of US outpatient care, using several metrics of recommended care, inappropriate care, as well as an assessment of patient experiences. Data was drawn from the Medicare Panel Expenditure Survey (MEPS) which is a subset of data from the annual National Health Interview Study. The MEPS is supplemented by a series of self-reported surveys from a host of health care providers, including physicians and pharmacists. The quality measures assessed were drawn numerous sources, including the National Health Care and Quality and Disparities Report, United States Preventive Services Task Force (USPSTF), and the Choosing Wisely campaign. After eliminating controversial recommendations (ie PSA testing) as well as recommendations that changed significantly over the period studied, the authors evaluated 39 quality measures.

In evaluating population trends from 2003 to 2013, the authors found an increase in the rate of chronic disease, with 18% of the adult US population in 2013 having 3 or more chronic diseases as compared to 8% in 2003. Delivery of recommended medical care increased from 36% to 42% (Table). Specific therapies in which the largest improvements were made included β-blockers for heart failure (41% → 65%) and statins for stroke (34% → 57%), but overall, the rate of delivery of many recommended therapies remained largely unchanged. Rates of recommended counselling, including weight, exercise, and smoking, all showed slight increases. Cancer screening rates were essentially flat (73% → 75%), although significant gains were made in rates of colorectal cancer screening (48% → 63%).

In regards to the rates of inappropriate care, approximately 50% of patients in the analysis still received inappropriate antimicrobial therapy. Similarly, the rate of inappropriate cancer screening in older adults persisted at around 50%. Avoidance of inappropriate imaging remained unchanged at 90%. 14% of adults in this analysis, however, still inappropriately received radiographs for back pain (which the authors note is equivalent to 70 chest X-rays). Lastly, measures of patient experience (global health rating, physician communication, and access to care) all improved significantly.

COMMENTARY
While definite improvements have been in the delivery of outpatient care in the United States, the quality of outpatient care in the United States has not changed significantly in 10 years. 25% of patients still did not receive recommended cancer screening. 65% of patients with poorly controlled COPD did not receive an evidence based controller medication. Even more disappointing is the persistent practice of inappropriate cancer screening in the
elderly population. While this study is certainly limited by its inability to evaluate exclusions for certain therapies and fully capture all outpatient care delivery in the United States, its findings remain valid. Improving the quality of outpatient care in the United States will certainly require a multimodal approach utilizing all members of the healthcare system. Levine et al have provided a stark reminder of how far we still need to go to achieve optimal health care delivery in the United States.

**UTSW Link**

**Table**

<table>
<thead>
<tr>
<th>Measure or Composite</th>
<th>2002 (n = 2644)</th>
<th>2007 (n = 20678)</th>
<th>2013 (n = 24968)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended Clinical Care</strong></td>
<td>No.</td>
<td>Mean (95% CI)</td>
<td>No.</td>
</tr>
<tr>
<td>Recommended cancer screening/composite</td>
<td>14826</td>
<td>73 (71-74)</td>
<td>12077</td>
</tr>
<tr>
<td>Cervical</td>
<td>1068</td>
<td>90 (89-91)</td>
<td>7013</td>
</tr>
<tr>
<td>Breast</td>
<td>4160</td>
<td>81 (80-82)</td>
<td>3522</td>
</tr>
<tr>
<td>Colorectal</td>
<td>7923</td>
<td>68 (66-69)</td>
<td>6837</td>
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<tr>
<td>Recommended diagnostic and preventive testing composite</td>
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<td>79 (78-80)</td>
<td>20461</td>
</tr>
<tr>
<td>Dental checkup</td>
<td>25794</td>
<td>62 (61-63)</td>
<td>20347</td>
</tr>
<tr>
<td>Blood pressure measurement</td>
<td>25270</td>
<td>91 (90-92)</td>
<td>19974</td>
</tr>
<tr>
<td>Cholesterol measurement</td>
<td>16506</td>
<td>90 (89-91)</td>
<td>13625</td>
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<tr>
<td>Flu vaccine</td>
<td>9295</td>
<td>82 (80-84)</td>
<td>8219</td>
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<tr>
<td>Recommended diabetes care composite</td>
<td>1773</td>
<td>76 (75-77)</td>
<td>1743</td>
</tr>
<tr>
<td>HbA1c measurement</td>
<td>11388</td>
<td>79 (78-80)</td>
<td>1243</td>
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<tr>
<td>Eye examination</td>
<td>18059</td>
<td>72 (70-76)</td>
<td>1879</td>
</tr>
<tr>
<td>Eye examination</td>
<td>1761</td>
<td>62 (59-64)</td>
<td>1732</td>
</tr>
<tr>
<td>Recommended counseling composite</td>
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<td>83 (82-84)</td>
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<tr>
<td>Weight loss counseling</td>
<td>15597</td>
<td>80 (79-81)</td>
<td>12721</td>
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<tr>
<td>Exercise counseling</td>
<td>15596</td>
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<td>12747</td>
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<tr>
<td>Smoking cessation counseling</td>
<td>5346</td>
<td>84 (83-85)</td>
<td>7777</td>
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<tr>
<td>Recommended medical treatment composite</td>
<td>6014</td>
<td>76 (74-78)</td>
<td>6113</td>
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<td>Anticoagulation for atrial fibrillation</td>
<td>586</td>
<td>72 (70-74)</td>
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<tr>
<td>ACE/ARB for heart failure</td>
<td>288</td>
<td>75 (73-76)</td>
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<tr>
<td>B-Blocker for heart failure</td>
<td>189</td>
<td>76 (74-78)</td>
<td>128</td>
</tr>
<tr>
<td>Statins and/or platelet-aggregation inhibitors for CAD/WR</td>
<td>1195</td>
<td>23 (20-26)</td>
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<tr>
<td>B-Blocker for CAD/WR</td>
<td>1195</td>
<td>51 (47-53)</td>
<td>1134</td>
</tr>
<tr>
<td>Statins for CAD/WR</td>
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<td>52 (48-54)</td>
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<tr>
<td>Statins for diabetes</td>
<td>2413</td>
<td>56 (49-60)</td>
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<td>ACT/URS for diabetes and hypertension</td>
<td>1121</td>
<td>60 (57-63)</td>
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<tr>
<td>Statin for CVD</td>
<td>302</td>
<td>59 (54-63)</td>
<td>315</td>
</tr>
<tr>
<td>Anticoagulation for CVA</td>
<td>302</td>
<td>59 (54-63)</td>
<td>315</td>
</tr>
<tr>
<td>Controller medication for poorly controlled asthma</td>
<td>258</td>
<td>72 (65-77)</td>
<td>177</td>
</tr>
<tr>
<td>Controller medication for poorly controlled COPD</td>
<td>185</td>
<td>82 (77-85)</td>
<td>154</td>
</tr>
<tr>
<td><strong>Inappropriate Clinical Care Avoidance</strong></td>
<td>No.</td>
<td>Mean (95% CI)</td>
<td>No.</td>
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<tr>
<td>Inappropriate cancer screening avoidance composite</td>
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<tr>
<td>Colorectal cancer screening in older adults</td>
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<td>Inappropriate antibiotic use avoidance composite</td>
<td>9311</td>
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<tr>
<td>Inappropriate treatment avoidance composite</td>
<td>9311</td>
<td>92 (89-93)</td>
<td>8200</td>
</tr>
<tr>
<td>Anxieties, addictions, and psychoses in older adults</td>
<td>3881</td>
<td>93 (92-94)</td>
<td>2210</td>
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<tr>
<td>Benedications for depression</td>
<td>2213</td>
<td>93 (90-93)</td>
<td>1874</td>
</tr>
<tr>
<td>Opposite of headache</td>
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<td>89 (89-90)</td>
<td>208</td>
</tr>
<tr>
<td>Opposite for back pain</td>
<td>1488</td>
<td>98 (97-99)</td>
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<tr>
<td>NSAID use for hypertension, heart failure, or kidney disease</td>
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<td>88 (80-86)</td>
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<tr>
<td>Inappropriate imaging avoidance composite</td>
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<td>88 (80-90)</td>
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<tr>
<td>MRI/CT for back pain</td>
<td>1488</td>
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<tr>
<td>Radiography for back pain</td>
<td>1488</td>
<td>94 (92-95)</td>
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<tr>
<td>MRI/CT for headache</td>
<td>417</td>
<td>92 (90-93)</td>
<td>208</td>
</tr>
</tbody>
</table>
Rheumatology

Non-TNF-Targeted Biologic vs a Second Anti-TNF Drug to Treat Rheumatoid Arthritis in Patients With Insufficient Response to a First Anti-TNF Drug

Dr. Lauren Smith reviewing Gothenburg J, et al. JAMA. 2016;316(11):1172-1180

SUMMARY

For many years tumor necrosis factor (TNF) inhibitors have been used to reduce disease activity in patients with Rheumatoid Arthritis (RA) who have persistent symptoms on methotrexate therapy alone. Not all patients see improvement in disease activity with the addition of an anti-TNF agent. Clinically, the question often remains as to whether the patient should try another anti-TNF agent versus a non-TNF targeted biologic. This article describes a pragmatic, multicenter, open, parallel-group, randomized clinical trial with a superiority design comparing the use of a non–TNF-targeted biologic vs a second anti-TNF agent after failing an anti-TNF agent. The study included 300 participants, mostly women (80%), with average age of 57 who had RA for at least 10 years and an average DAS28-ESR score of 5.1. These patients were randomized to receive either a non-TNF biologic (abatacept, rituximab, or tocilizumab) or a second TNF inhibitor agent (adalimumab, certolizumab, etanercept, or infliximab). Response to therapy was assessed using the European League Against Rheumatism (EULAR) scale, where a decrease in the DAS28-ESR of at least 1.2 more was considered good and a 0.6 reduction was considered a moderate response. The primary end point of this study was reduction in disease activity after 24 weeks of using the additional therapy provided. At 24 weeks, 70% of patients in the non-TNF group and 52% in the second anti-TNF group achieved a good or moderate EULAR response. The study was continued for a year (52 weeks) to assess therapeutic maintenance; the good/moderate EULAR response continued in the biologic group compared to second TNF inhibitor group 60% to 43%, respectively. There were 18 adverse events in the non TNF biologic group, and 13 in the second anti-TNF group with infection and cardiovascular events being most common.

COMMENTARY

Approximately 1/3 of patients with RA have persistent disease activity and inadequate response to TNF inhibitor therapy. This study shows some evidence that switching to a non-TNF biologic can be more beneficial in reducing RA symptoms than switching to a second anti-TNF medication. However, this study has a few limitations worth pointing out. Participants were not blinded to the drug choice they received (too many different placebos required). Only 60% of people in each group took methotrexate during the study period which is known to improve the efficacy of biologics. Additionally, the study was not powered to detect differences between individual drugs. Despite these limitations the results of this pragmatic study show that non-TNF biologics may be an alternative to improve disease activity in patients refractory to TNF inhibitor therapy.

UTSW Link