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RETINAL DETACHMENT PROVOKED BY FLUOROQUINOLONES: CAVEAT EMPTOR

Etminan et al, JAMA, 2012, report on the association between oral fluoroquinolone use and subsequent retinal detachment, an intriguing relationship built originally from 4 isolated case reports. In this nested case-control study in British Columbia, a cohort of 989,591 patients was analyzed with identification of 4384 cases of retinal detachment. Each case of retinal detachment was matched to 10 historical controls for age and month of entry, and analyses were adjusted for gender, history of myopia or cataract surgery, presence of diabetes, and number of prescription pills used within the previous year. Of those with retinal detachment, 145 were current users of fluoroquinolones, 12 were recent users (took fluoroquinolones in the preceding week before diagnosis of retinal detachment), and 288 were former users (took fluoroquinolones within the previous year). Current use of fluoroquinolone antibiotics was associated with a significantly higher risk of retinal detachment (occurring in 3.3% of such cases, but only 0.6% of controls, giving an adjusted rate ratio of 4.5). The calculated absolute increase in retinal detachment risk was 4 cases per 10,000 person-years. The number needed to harm was estimated at 2500. Retinal detachment was not linked to recent or past fluoroquinolone use, and was also not linked to beta-lactam antibiotic use or beta-agonist treatment.

CHOOSING BETWEEN AN AV FISTULA AND AV GRAFT: A COST-UTILITY ANALYSIS

The 2 viable options for long-term vascular access in hemodialysis are a native arterio-venous fistula or a synthetic arterio-venous graft. Recently, the Fistula First initiative has highlighted the long-term benefits and decreased morbidity associated with using arterio-venous fistulas, though a high prevalence of fistula failures threaten to undermine this initiative. Rosas and Feldman, *Annals Surg*, 2012, perform a cost-utility analysis of both procedures, using a Markov decision-making model, amongst incident dialysis patients. They placed an AV fistula as first access option in 1 group, with an AV graft where fistula maturation was not secured; in the other group, an AV graft was placed as the first access option. The fistula-first surgical strategy yielded 2.19 quality-adjusted life years in comparison to 2.06 quality-adjusted life years with the AV graft-first strategy. An incremental cost-effectiveness was $9389 per quality of life year in the fistula-first option compared to graft-first option, and was under $50,000 per quality of life year when probability of maturation was >36%. The study concluded that AV fistula-first strategy was a superior surgical approach only when fistula maturation of at least 69% was assured, a figure which surpasses current AV fistula prevalence standards in most of the United States.

DRUG-ELUTING STENTS: EVEROLIMUS FOR EVER

Bare metal stents deployed in coronary artery disease are thought to be less thrombogenic, whilst drug-eluting stents are thought to be less susceptible to restenosis. At long last, we might be nearing the end of hostilities amongst stent manufacturers (and their surrogates): Palmerini et al, *Lancet*, 2012, published a meta-analyses of so-called second-generation drug-eluting stents (including paclitaxel and sirolimus) compared to bare-metal stents, showing that everolimus-eluting stents (composed of a polymer-coated alloy of cobalt plus chromium) were least likely to be associated with stent thrombosis, a potentially fatal complication, in the short-term (30 days) and long-term (up to 2 years post-deployment). Indeed, this study which included 49 randomized trials for a total of 50,844 participants, demonstrated that stent thromboses was even less in everolimus-eluting stents than was associated with bare metal stents (79% lower thrombosis risk at 30 days, 77% lower at 1 year, 65% at 2 years). This publication offers a serious challenge to the prevailing wisdom that all drug-eluting stents were prone to in-situ stent thrombosis as a result of drug-impaired stent endothelialization. This finding now needs to be tested in large randomized head-to-head studies, preferably incorporating acute MI patients, where the use of bare metal stenting has become standard of care.

AGE AS PROGNOSTIC FACTOR IN HEPATOMA SURGERY

The effects of age on clinical, pathologic and prognostic indices in hepatocellular carcinoma are very poorly understood. Su et al, *Arch Surg*, 2012, set out to compare outcomes, using age as a discriminant factor in patients undergoing surgical resection for hepatocellular carcinoma. A total of 1074 patients were enrolled for partial hepatectomy, those aged <55 years were defined as "young", whilst those >55 years of age were defined as "old". Post-surgical outcomes were compared using multivariate analysis and propensity score matching. Overall, young patients had better liver functional reserve but more aggressive tumor factors than old patients. Though cumulative 10-year survival was 41.3% in the "young" treatment group and 28.8% in the "old" treatment group, age itself did not appear to be an independent risk factor for either post-resection survival or tumor recurrence.

the SECOND OPINION

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FROM THE EDITOR

Janus, the first and most ancient of Roman gods after whom the month of January is named, is also the guardian of entrances and exits, boundaries and bridges, past and future, his duality symbolized by an opposite-facing bust. A two-faced god of shrine and hearth, only he is able to fully remember the past and foresee the future. He was impassive- some would say impervious- to the sly machinations of ancient man, burning incense in a show of false piety at his shrine whilst plotting mischief against his fellow men. The arbiter of time, Janus stood silent sentry at the end- or beginning- of each calendar year, closing out the past and its foibles whilst ringing in the future and its promise.

It is therefore fitting that come next January- January 1, 2013- the yearly ritual of Congressional "*doctor-fix*", i.e. kicking Medicare reimbursement cuts down the field, will finally come to an end. Or not. Either way, there will be no mourning or tears. Since incapacitating gridlock was let loose on Congress, she has nimbly deferred facing up to the challenge of fiscal balance under the Medicare Part B outpatient reimbursement program. Cuts were rumored to go into effect last March, at a painful but still survivable 27.4% decapitation, but that did not happen; now, the index rate has risen to 30.9%, come January 1. With each serial deferment, the stakes - and eventual costs- have reliably surged north. One day, there'll be hell to pay.

Similar cost-cutting measures are actively being considered or already enacted by legislatures across the globe. The cost of medicine for an aging population is becoming onerous for civil society, and with each new medical advance, sticker shock only gets worse. Modern society faces the tragic paradox of penury as the prize for prolonging life.

The response from physicians to what is essentially an economic dictate has veered from outrage to disbelief. In several countries, physicians have done the previously unthinkable: downed their tools in frustration or anger, a doomed tactic which only alienates the very public they have sworn to serve, and whose support will be crucial as the fiscal debate is finally joined. Indeed, strikes by physicians have become commonplace, with doctors walking off their jobs in France, protesting lower fees and limited work hours, and less petulantly, in public hospitals of Croatia, New Zealand, Israel and Ghana. Even in Canada, an economic if not cultural soul-mate of these United States, doctors recently staged a comparatively mild protest in Saskatchewan over poor pay. There have been local rumbles- nothing cataclysmic yet- across far-flung counties of Pennsylvania, Florida, New Jersey and West Virginia, where doctors have been locked in grim combat against malpractice attorneys. It only promises to get a lot worse.

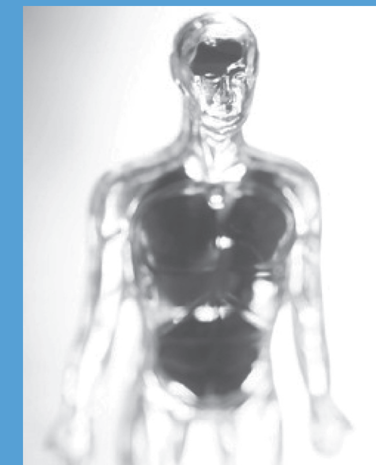
Perhaps, I should stake out my own ground at the very beginning: I do not believe that strikes- or any industrial action- is ever justifiable by physicians, either acting singly or as a trade union. Physicians are public servants in the truest sense, with an obligation to provide the greatest good at all times, in the interest of the larger society. That is why physicians are obliged to provide care, despite their own personal reservations or prejudice, to all those in need of medical assistance: murderers, rapists, drug dealers, and all manner of felons. That is why physicians are sworn to overcome their own personal revulsion or antipathy, and offer medical care to all, including those perceived as least deserving in our hierarchical society, without judgment or hindrance.

The underlying reasons for physician anomie are multi-headed. Doctors have witnessed an unprecedented surge in entitlements over the past 5 decades and are, understandably, loathe to have those abridged, either by consensus or arbitrarily through congressional *fiat*. Doctors have darkly hinted at several other non-physician interests feeding off the healthcare trough, as if that ought to excuse our own professional failings. There are powerful arguments that fiscal discipline ought to first focus on medical waste, excessive imaging and laboratory testing, inappropriate hospitalizations, and of course, personal investment in healthy lifestyles by the consumer. It is telling that most of a lifetime's medical expenditure- about 70 percent- is spent in the last 7 months of life. It is unfortunate that several post-industrial societies now keel at the edge of bankruptcy occasioned by entitlement programs, omnibus health coverage and bloated defense expenditure, accrued at the expense of more traditional pursuits of infrastructure, job creation and the endowment of future generations.

What are the options for physicians, especially here in the United States? Physicians should work collectively with other interest groups, such as the AARP, to midwife a workable compromise on Medicare reimbursements and introduce effective changes to healthcare administration. Political pressure is critical to meaningful tort reform, and in this, lawyers can be ready accomplices not armed opponents, or worse, pariahs. The fiction that all lawyers are foresworn enemies of the medical profession- engrained from anecdotal tales of courtroom brawls on "standard of care", dourly retold by battle-scarred veteran medics to each succeeding generation of physicians- must now be challenged and discarded. The drain on recruitment and good practice through high malpractice premiums, the practice of "defensive medicine", and of course, multiple (and unnecessary) specialist consultations, in the forlorn belief that there is safety in numbers, should all be re-examined. Residency training ought to be overhauled, to better address the realities of our time: the goal of diagnostic certitude is often an expensive red herring. Universal adoption of formulary drugs, eschewing trade names and high-cost therapeutic copycats, should help stem the unbearably high cost of prescriptions. It is time to begin recycling medical devices: why do we insist on burying so many cardiac defibrillators, in these austere times? And why are organs from deceased transplant recipients not re-harvested, if still useable? Our most dearly-held practices need to be codified and based on evidence, not tradition. In this respect, the specialist boards deserve kudos for the Choosing Wisely Campaign: no pre-operative chest radiographs in asymptomatic patients; no neuro-imaging tests for new-onset low back pain without "red flags" for malignant causation (or for syncope without focal neurologic findings on exam: the corollary being, of course, that you ought to fully examine your patients, anyway); no cardiac tests or EKG in low-risk asymptomatic patients on routine exams; no DEXA screens in patients younger than 65 y.o. in the absence of risk factors for early osteoporosis; no Paps smears in women under 21 y.o. or after hysterectomies. Maybe, I should add: no D-dimer assay until you've read the PIOPED data....

In all, we need to court and retain friends for a renewal of our chosen profession. *Nihil homini amico est opportuno amicus*. Even Janus himself, master of paradox and duality, would find it most fitting.

Beze Adogu, MD, PhD, FACP



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THE FUTURE IS HERE: ENDOVASCULAR BEATS OPEN REPAIR OF AORTIC ANEURYSMS

In the beginning, endovascular repair of abdominal aortic aneurysms (AAA) was the "default option", solely reserved for high-risk surgical candidates. Other comparative trials had indicated that endovascular repair led to lower post-surgical mortality and morbidity, with a shorter average duration of ICU care, less blood transfusion needs and shorter duration of mechanical duration. The problem with endovascular repair was a perception of higher cost and increased risk of late-onset post-surgical complications. Now, Jackson et al, *JAMA*, 2012, performed a retrospective analysis of Medicare recipients receiving AAA surgery. A total of 4529 patients were recruited, but only 703 actually underwent "open" repair. They found that all-cause mortality, AAA disease-specific mortality, duration of post-interventional hospital stay and incidence of repaired post-surgical incisional hernias were all better with endovascular surgery. Interestingly, hospital readmission rates, repeat AAA surgical repair and later lower limb amputation rates did not appear to differ between the two procedures. Clearly, this study shows that endovascular repair has "come of age", and is superior in outcomes to open AAA repair. The unanswered question is whether this is a true consequence of an innate superiority of endovascular techniques over open vascular repair, or a reflection of changing surgical experience (and expertise).

RE-ASSESSING HEPARIN PROPHYLAXIS: MOST ARE CALLED, BUT NOT ALL ARE CHOSEN

DVT prophylaxis of medical in-patients is a central tenet of hospitalist practice, in large part, from the proselytizing efforts of JHACO. Lederle et al, *Ann Intern Med*, 2011, set out to review trials on DVT prophylaxis from 1950 to 2011. Some surprising conclusions were reached: (1) the difference in mortality between medical in-patients receiving DVT prophylaxis and those who did not, was not significant though generally lower in those receiving heparin prophylaxis ($p = 0.056$); (2) heparin prophylaxis reduced the risk of pulmonary embolism (3 events per 1000 patients treated) but increased the risk of major bleeding (4 events per 1000 patients treated); (3) the clinical outcomes (DVT prevention or bleeding risk) were equivalent for unfractionated heparin vs low molecular weight heparin, as well as between graduated compression stockings vs no stockings. Conclusions: DVT prophylaxis is good on principle, but bleeding risk must be considered and factored in; graduated compression stockings is a waste of time (and effort); use whichever heparin you are most comfortable with.

CATHETER ABLATION OF ATRIAL FIBRILLATION IS PALLATIVE NOT CURATIVE

Treatment of symptomatic atrial fibrillation often focuses on ventricular rate control, and in drug-refractory cases, resort to catheter ablation by pulmonary vein isolation. Sorgente et al, *Am J Cardiol*, 2012, studied 103 patients with catheter ablation at Beth Israel Deaconess Medical Center, Boston, over an average post-procedure interval of 6 years. A total of 153 ablation procedures were performed on 103 patients (59% had only 1 ablation procedure, 34% had 2 procedures, 6% had 3 procedures, 1% had 4 procedures), and freedom from atrial arrhythmias was closely monitored over 6 years of post-ablation follow-up. In summary, 23% of single-procedure patients were arrhythmia-free at 6 years whilst 39% of multi-procedure patients were arrhythmia-free after the last ablation. It was not possible to predict those patients that would develop recurrent AF based on only 1 procedure, but patients with multiple ablations were more likely to experience recurrent AF if they had transient episodes of AF. Most relapses occurred within 1 year of catheter ablation.

GRIEVING AND MI RISKS IN SURVIVORS

Acute grief is a well-described cardiovascular risk factor: Mostofsky et al, *Circulation*, 2012, have now extended our numerative understanding of this phenomenon. In a cross-over analysis of the 1985 participants recruited for Determinants of MI Onset Study between 1989 and 1994, they found that 13.6% of heart attack victims had experienced the loss of a significant person in their lives 6 months or less before their cardiac event, and 1% had actually experienced such loss within the previous day. Indeed, they calculated that there was a 21.1-fold rise in MI rate within 24 hours of learning of such a "significant loss" compared to suffering an MI on any other day within the preceding 6 months, with a slow but steady decline in MI risk for each succeeding day thereafter. The risk of an acute MI within 1 week of the death of a significant person in one's life is 1 excess MI per 1394 grieving persons at low (5%) 10-year risk for cardiac events, but rises to 1 excess MI per 320 grieving persons amongst those with a high (20%) 10-year risk for a cardiac event.

DIABETES DURATION AS STROKE RISK: THE NORTHERN MANHATTAN STUDY

Diabetes mellitus is inherently vasculotoxic, and is a well-recognized risk factor for ischemic strokes. Less clear is whether the risk is secondary to duration of metabolic dysfunction, severity of disease or other associated clinical factors, such as age, fluctuating glycemic levels, treatment modality (insulin vs oral hypoglycemic agents), et cetera. Banerjee et al, *Stroke*, 2012, report that patients with >10 year history of diabetes mellitus had a 3x increased stroke risk compared to non-diabetics. They followed 3298 study participants recruited for the Northern Manhattan Trial, of which 22% had a history of type 2 diabetes mellitus at baseline, and none had a prior history of stroke at baseline. During follow-up, an extra 10% of study participants developed type 2 diabetes mellitus, over a median period of 9 years, and a total of 244 ischemic strokes were recorded. Presence of diabetes was associated with an increased stroke risk of 3% per year, reflecting a 70% higher stroke risk amongst diabetics of less than 5 years duration, 80% higher stroke risk amongst diabetics of 5-10 years duration, and 3x usual stroke risk amongst diabetics with over 10 years of clinical diagnosis.

HERE WE GO AGAIN: FOREIGN BIRTH AS A STROKE PROTECTION

By 2050, the Hispanic population will be the largest minority group in the USA. It is important to better understand the health challenges facing this heterogenous population, including any reversible predilection to specific diseases. It is in that spirit that Moon et al, Stroke, 2012, conducted a comparative study looking into stroke risk and socio-economic indices amongst native-born Hispanics (born in the US or immigrated to the US before age 7), foreign-born Hispanics and native-born non-Hispanic whites. Their study suggests that whilst foreign birth will preclude you from seeking the Presidency, it might also diminish your exposure to the devastation of acute strokes. Using age- and sex-adjusted models, native-born Hispanics were more likely (than non-Hispanic whites) to experience strokes, but the higher predilection towards strokes was attenuated after controlling for socio-economic factors. However, even after adjusting for socio-economic factors, foreign-born Hispanics were still significantly less likely (than non-Hispanic whites) to suffer a stroke. The study concluded that within this longitudinal model, foreign-born Hispanics had a lower stroke incidence than both native-born Hispanics and non-Hispanic whites, and had a risk factor profile which conferred relative protection against strokes. If one remembers similar assertions by Donnison et al in the early 1920s (and later on, by AG Shaper et al, in the late 1960s) about unacculturated nomadic tribes that were originally thought to be protected against arterial hypertension, it is more likely that immigrants over time will adopt the disease expressions of their "host" societies, with a steady disappearance of any protective advantage.

LIVING ON THE EDGE: ALCOHOL ABUSE IN SURGEONS

Oreskovich et al, *Arch Surg*, 2012, deserve congratulations for a job well done. They conducted a cross-sectional survey amongst members of that august assembly of surgeons, The American College of Surgeons, to determine the prevalence of alcoholism within the ranks. Interestingly, of the 25,073 surgeons sampled, only 28.7% completed the survey: you are free to draw your own conclusions from that measly response rate. Sadly, even amongst the participants, 15.4% attained an AUDIT-C profile consistent with alcoholism, with a point prevalence of 13.9% amongst male surgeons and 25.6% for female surgeons. The odds of being alcoholic or dependent were increased by (1) self-report of major medical error in previous 3 months (odds ratio 1.45); (2) symptoms of "burn out" (odds ratio 1.25); (3) symptoms of depression (odds ratio 1.48). Those less likely to suffer from alcohol dependence or abuse were male, had children, and worked for the VA medical centers. This study once more highlights the high prevalence of alcohol abuse amongst practicing physicians and calls for organizational approaches for early identification and appropriate intervention.

CIRCUMCISION FOR ALL?

Circumcision, the surgical removal of penile prepuce (foreskin), is primarily regarded as a religious ritual, first introduced some 3000-5000 years ago in West Africa and the Middle East. With the advent of AIDS, research has focused on the health benefits of removing less keratinized prepucial skin, which has a higher density of Langerhans cells (a target cell for HIV viral entry) as well as a higher predisposition to traumatic injury, providing ancillary portals for the entry of viral and non-viral sexually-transmissible pathogens. Circumcision is thought to protect against (urethral) chlamydial infections, ulcerogenic STDs (primarily syphilis and chancroid, but probably not HSV type 2), penile cancer as well as cervical cancer (in female sexual partners of circumcised males, presumably by limiting the transmission of HPV pathogen). The protective effect of male circumcision has been observed in several AIDS trials amongst homosexual males in US (Buchbinder et al, *J Acquir Immune Defic Syndr*, 2005) as well as within presumed heterosexual transmission from Africa and Asia, with a projected 44-71% reduction in HIV acquisition (Halperin & Bailey, *Lancet*, 1999). Indeed, most studies show a protective effect of circumcision on HIV transmission across all cultures, a few suggest a null effect, with Chao et al, *Int J Epidemiol*, 1994, being the only major publication suggesting increased HIV transmission in circumcised males. Amongst sero-discordant couples in Uganda, the risk of male-to-female transmission of HIV infection was dependent on both viral load and circumcision status: if the male partner has a viral load <50,000 copies/mL and was also circumcised, there was no HIV transmission to wife (Gray et al, *AIDS*, 2000). So far, the data supports a protective effect from circumcision only for penile-vaginal intercourse and probably not for insertive anal sex. Additionally, there may be confounding factors associated with circumcision, based on religion, cultural practices/hygeine and sexual mores. Also, any protection conferred by circumcision is partial at best, and as the CDC emphasizes, can only be used in conjunctive with proven preventative measures such as abstinence, mutual monogamy, reduced number of sex partners and correct/consistent condom use.

BENEFITS OF RED WINE: HYPE & HOPE

The health benefits of red wine has been controversial. Recently, Dr. Dipak Das, a Connecticut cardiovascular disease researcher, was outed for scientific fraud, based on falsified data on resveratrol, thought to be the active ingredient in red wine. Initial claims that resveratrol could slow down the aging process, through activation of so-called longevity enzymes (sirtuins), have been met with renewed skepticism. A new study from the Cedars-Sinai Medical Center in Los Angeles by Shufelt et al, *J Womens Health*, 2012, suggests that red wine may reduce the incidence of premenopausal breast cancer by acting as a "nutritional" aromatase inhibitor (a group of enzymes which prevent the conversion of androgens to estrogen, and occur naturally in grapes and red wine), in sharp contrast to the well-defined epidemiological link between excess alcohol consumption and increased risk of breast cancer. In a cross-over study, 36 healthy premenopausal women were assigned to 8 ounces (237 mL) of red wine at dinner daily for 1 month, then white wine for the next month, or the reverse sequence. Those on red wine demonstrated higher levels of free testosterone and luteinizing hormone, lower sex hormone binding globulin, and a lower trending (but not significantly lower) level of estradiol. Those findings support an aromatase inhibitor effect by red wine.

IS IT TIME TO SHUT OFF "EPI" DURING CODES?

Residency training for most of us was highlighted by generous doses of epinephrine, administered as a reliable therapeutic adjunct during management of in-hospital cardiac arrest. To forgo epinephrine is (still) unthinkable, but that might be about to change. A prospective, randomized, placebo-controlled trial of epinephrine use in out-of-hospital cardiac arrests in Japan between 2005 and 2008, showed that epinephrine administration was associated with a higher rate of return of spontaneous circulation but had no effect on survival to hospital discharge. In this pilot study by Hagihara et al, *JAMA*, 2012, receiving epinephrine outside the hospital setting increased the odds of return of spontaneous circulation (odds ratio 2.36) but at 1 month, those patients who had received epinephrine were significantly less likely to survive (odds ratio, 0.46) and less likely to have good functional outcomes, as shown by good or moderate cerebral performance at 1 month (odds ratio 0.31) as well as nil/limited neurologic disability (odds ratio 0.32). It was hypothesized that epinephrine improved central (aortic/coronary) perfusion pressure at the expense of other organs, including the brain. An accompanying editorial calls for head-to-head comparison trials.

VISITING THE ED CAN BE RISKY FOR THE FRAIL & VUNERABLE

Quach et al, *CMAJ*, 2012, report that visiting the emergency department is especially risky for the frail and vulnerable elderly population. This cohort study recruited 1269 elderly residents from 22 long-term care facilities, of which 424 had visited the emergency room during the period of study. For each ED visitor, 2 residents who did not visit the ED were randomly selected, and matched for age, gender and facility. Both groups were evenly matched, with minor differences in health status as adjudged by Charlson Comorbidity Index as well as visitors. A total of 5% of residents who visited the ED acquired new respiratory and gastrointestinal infections (incidence of 8.3/1000 patient-days) but only 2% of residents who did not visit the ED had new infections (3.4/1000 patient-days), giving an adjusted odds ratio of 3.9 for infection risk following an ED visit in this population.

UNDERSTANDING RACIAL DISPARITIES IN BETA-BLOCKADE FOR HEART FAILURE: ARE WE THERE YET?

Beta-blockers are integral to heart failure management, and are also often employed for systemic hypertension control, though in both cases, doubt persists as to their relative effectiveness in the African-American population. In the case of systemic hypertension, it is thought that a low-renin phenotype might explain the relative lack of effectiveness noted in several comparative studies. Lanfear et al, *Circulation Heart Failure*, 2012, performed a retrospective analysis of 1094 heart failure patients with ejection fraction under 50% (476 white, 618 African-American). The relationship between treatment with beta-blockers and all-cause hospitalizations/death was tested using proportional hazards regression, adjusted for other clinical variables and therapeutic interventions. Therapeutic beta-blockade was associated with better outcomes in heart failure patients, specified by a lower risk of death and hospitalizations in both groups, but more so amongst whites than African-Americans. Use of beta-blockers was 40-50% less effective in preventing death or hospitalization amongst African-Americans with heart failure. The big question is why?