


2:25 – 3 pm

Update from The Medical Literature 2015

SPEAKER
Frank J. Domino, MD



Presenter Disclosure Information

The following relationships exist related to this presentation:

- Frank J. Domino, MD: No financial relationships to disclose.

Off-Label/Investigational Discussion

- In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Update From The Medical Literature 2015

Frank J. Domino, M.D.
Professor
Dept. of Family Medicine & Community Health
Un. Of Massachusetts Medical School
Worcester, MA
Frank.domino@umassmemorial.org
Twitter: dominof
<http://www.hcplive.com/publications/family-practice-recertification>

Rapid Strep is Enough

- Systematic review and meta analysis on the efficacy of rapid antigen diagnostic testing for group A strep for pharyngitis in children and adults.
- Articles covering 48 studies and almost 24, 000 patients.
- GAS culture was used as reference.
- Sensitivity of RADT = 0.86; specificity = 0.96.
- In studies of just children, sensitivity = 0.87 and specificity = 0.96.
- Conclusions: RADTS in the diagnosis of GAS pharyngitis has high accuracy in both adult and pediatric populations.
- RADTs highly sensitivity to allow for NOT using throat culture when RADTS is negative.
- Use Centor scoring to guide testing.

Pediatrics. 2014; 134(4):771-781.

Modified Centor Scoring

• Hx of Fever	+1
• Tonsillar Exudates	+1
• Tender Ant. Cervical Nodes	+1
• Absence of Cough	+1
• Age < 15 Years	+1
• Age > 45 Years	-1

• Interpretation

- < 2 Points; no testing or treatment
- 2-3 Points; Rapid Strep; Treat if Positive
- > 3 Points; No testing, just Treat

Testicular Cancer & Muscle Building Supplements (MBS)

- Case control study on MBS on 356 new diagnoses of TGCC, and 513 of controls from CT and MA
- Most common MBS were creatine, protein, and androstenedione (or its booster)
- Risk of Testicular Germ Cell Cancers w/MBS was (OR = 1.65, 95% CI: 1.11-2.46).
- Highest Risk: those who:
 - used MSB before age 25 years,
 - used multiple types of MBS, and
 - used them for > 36 months

British Journal of Cancer. 2015; 112:1247-1250

HPV Vaccine in Adolescent Females Does Not Increase STI Risk

- Retrospective database review of insured females aged 12-18.
- Review of pharmacy & medical claims from 41 large us employers 2005-2010, vs. aged matched controls who did not receive vaccines.
- Studied STI incidence in vaccinated vs. unvaccinated females.
- Outcomes:
 - The overall incidence of STI increased with age, but there was NO statistical difference in STI infection in the HPV population vs. the unvaccinated population.
 - No Increase risk in those with females with prior contraceptive use.
- Conclusion: HPV vaccination in adolescent females is not associated with increased risk of STI.

JAMA Intern Med. 2015; 175(4):617-623.

Oral Morphine vs. Ibuprofen to Manage Post-fracture Pain in Children

- RCT of 134 children w/ uncomplicated fractures in Canadian emergency departments.
- Age 5-17 who sustained extremity fractures and were seen within 24 hours.
- Mean age was 10 with females comprising the majority.
- Pts received either ibuprofen 10mg/kg or oral morphine 5mg/kg q6 hours x first 24 hours
- Acetaminophen at 15mg/kg could be taken by both groups for breakthrough pain.
- Pain was assessed by *Faces Pain Scale – Revised*.
- Results: Morphine and ibuprofen were equally effective in controlling fracture related pain.
- No significant differences were found between acetaminophen use for breakthrough pain.
- Morphine → greater number of adverse events
 - Most common were nausea (35% MSO4 vs 21% Ibuprofen) and drowsiness.
- Conclusion: Ibuprofen is equivalent to morphine for fracture pain in children and teens.

CMAJ. 2014; 186(18):1358-1363.

USPSTF Updates Guidelines on Using Medications to Prevent Breast Cancer

- The USPSTF found "adequate evidence" Tamoxifen and Raloxifene lowers risk E2 receptor + breast cancer in **high-risk**, postmenopausal women [B]
 - High Risk: Family history of breast cancer or a personal history of breast biopsy
 - Stratify using: <http://www.cancer.gov/bcrisktool/> If: estimated 5-year risk of $\geq 3\%$.
 - Providers should "engage in shared, informed decision-making" with these women about risk-reducing medications vs risks of adverse events
- | | <u>VTE</u> (risk 0.5% over 5 years) | <u>Uterine Cancer</u> |
|---------------|-------------------------------------|-----------------------------|
| • Tamoxifen | 5-year risk of DVT/PE 1.2% | 6.2% vs 2.4% (↑ risk) |
| • Raloxifene: | 24 month risk of DVT/PE 2% | 3.3% vs 6.6% (REDUCED risk) |
- Medications should NOT be used for low (<3%) women

Ann Intern Med. 2013;159(10):698-708

Risks: Cancer. 2009 Oct 1;115(19):4442-9; Thromb Haemost. 2008 Feb;99(2):338-42; J Clin Oncol. 2008 Sep 1; 26(25): 4151-4159

Limited Accuracy of Breast Biopsy Diagnosis

- Observational study of pathologists who interpreted breast biopsy in US
- Review 60 breast biopsies where a diagnosis was known.
- Participants blinded to interpretation & Compared to Path Consensus Panel
- Results: Compared to consensus Panel diagnosis, overall concordance in diagnostic interpretations of participating pathologists = 73% (95% CI: 73.4-77.0).
- Disagreement higher: biopsies from high breast density, and among pathologists with low case volumes or who worked at non-academic settings.
- Highest concordance was for invasive carcinoma
- Lowest concordance was for DCIS and atypia.

JAMA. 2015; 313(11):1122-1132.

No More FLP

- Evaluation of National Health and Nutrition Survey and National Death Index on 16,000 middle age adults X 14 years.
- Compared fasting vs. non-fasting cohorts with ~ characteristics.
- For all cause mortality, fasting vs. non-fasting LDL produced similar prognostic values
- Researchers did not evaluate effect of fasting on triglyceride measurements (lowering triglycerides w/RX not been of benefit.
- Conclusion: Non-fasting Lipid Panel determination is effective for cardiovascular risk determination.

Circulation. 2014; 130:546.

Pass the Butter

- Systematic review of meta analysis of randomized controlled trials (RCTs) regarding the relationship between dietary fat consumption, serum cholesterol, and subsequent CAD.
- Trials were considered if published prior to establishment of dietary guidelines in 1977 by the US, and in 1983 by the UK.
- Outcomes: Six RCTs were included. All with inconsistent findings and information
- Five did not examine total fat consumption < 30% of daily caloric or total saturated fat consumption as < 10% of daily caloric intake (the current recommendation).
- Four trials examined use of vegetable oils, three substitution of saturated fats with vegetable oils, one examined a 20% fat consumption diet and one examined a 10% saturated fat diet.
- Conclusions: There was no statistical difference for either all cause mortality or CHD mortality in any of the groups evaluated. Serum cholesterol fell in all groups, but had a statistically larger fall in those with interventions aimed at lowering saturated fat intake.
- Data from RCTs available prior to 1983 do not support the subsequent and current dietary restrictions recommending fat consumption as < 30% of daily caloric intake or total saturated fat consumption as < 10% of daily caloric intake.

Open Heart. 2015; 2(1):e000196.

Men, Coffee Drinking, & Erections

- Observational data National Health and Nutrition Examination Survey (NHANES).
- ED was identified by a single question in a computer interview along with 24 hour dietary recall data focusing on estimated caffeine intake.
- **Outcomes:** Men with intakes in the 3rd quintile (85-170 mg/day; 2-3 cups) and 4th quintile (171-303 mg/day; 3-4 cups) were less likely to report erectile dysfunction compared to men in the lowest (1st quintile – 0.0-7 mg/day),
 - 2-3 Cups OR = 0.58; 95% CI: 0.37-0.89
 - 3-4 Cups: OR = 0.61; 95% CI: 0.38-0.97
- In overweight and obese men and in hypertensive men there was a significant inverse association between higher caffeine intake and erectile dysfunction compared to the lowest quintile; this was only true for men without diabetes.

PLOS ONE. 2015; 10(4):e0123547

Venlafaxine vs. Low Dose E2 for Hot Flashes

- RCT of 340 peri- and post-menopausal women
- Venlafaxine (75mg) vs. estradiol (0.5mg) vs. placebo.
- At 8 weeks:

	Vaso-motor Sx	Hot Flashes
Venlafaxine:	↓ by 48%	↓ by 1.8
Estradiol :	↓ by 53%	↓ 2.3
Placebo:	↓ by 29%	
- Previous dose E2 for MP symptoms was 1.0mg.

JAMA Inter Med. 2014: epub.

Device-guided *slow-paced respiration* for menopausal hot flushes: a randomized controlled trial

- Peri or postmenopausal women with ≥ 4 hot flushes/d (Ave: 8.5 (± 3.5))
- RCT of slow-paced respiration using a portable guided-breathing device x 12 weeks
- Practiced slowing their resting breathing (< 10 breaths per minute) for at least 15 minutes everyday or use an similar device played relaxing music
- **Results:**
 - After 12 weeks, paced respiration \rightarrow ↓ 1.8 HF/D (95% [CI] 0.9-2.6) (-21%) vs Music Group \rightarrow ↓ 3.0 HF/D (95% CI 2.1-3.8) (-35%) (P=.048).
 - Paced respiration \rightarrow 19% decrease in frequency of moderate-to-severe hot flushes vs 44% decrease with music listening (P=.02).
- **CONCLUSION:**
 - Device-guided slow-paced respiration \rightarrow modest improvements in the frequency and severity of their hot flushes, but was less effective than music-listening intervention

Obstet Gynecol. 2015 May;125(5):1130-8

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Medical Talk Shows and the Headache They Cause

- Investigators: 40 episodes of "The Doctor Oz Show" and "The Doctors" from early 2013.
- From each they identified recommendations for the listening audience.
- Recommendations reviewed to determine accuracy and appropriateness of each.
- **Outcome:** Found "at least weak or better" evidence for 54% of recommendations.
- "The Doctor Oz Show," medical literature supported 46% of the recommendations contradicted 15%, and showed no evidence for 39%.
 - There were approximately 12 recommendations per episode.
 - 39% of the recommendations were for dietary advice, but only 17% of those recommendations were of the magnitude of benefit described.
- "The Doctors," the medical literature was found supporting 63% of the recommendations, contradicting 14%, and no evidence for 24%.
 - On average 11 recommendations were made per episode.
 - The most common recommendation was "consult a healthcare provider" (18%). Magnitude of benefit was described for 11% of the recommendations.
- **Conclusions:** The vast majority of recommendations made on medical talk shows have weak or no evidence to support their claims.

BMJ. 2014; 349:g7346.

Varenicline and NRT Together Are Better Than Either Alone

- RCT of 450 long-term smokers to 12 weeks of varenicline (1mg BID) plus NRT patches (15mg X 16 hours/day) vs. varenicline plus placebo patches X 4 weeks
- **Outcomes:** At 24 weeks abstinence rates for 49% vs 33% (NNT = 7).
- Adverse events were similar in both groups. JAMA. 2014; 312:155.
- RCT of 350 smokers used nicotine patch for 1 week then randomized to 12 weeks of varenicline alone vs. varenicline plus bupropion.
- Abstinence determined by self-report and confirmed by expired CO.
- Drop-out rate was about 30% in each group.
- **Outcomes**
 - Abstinence: 40% for combination vs. 26% in varenicline alone.
 - Combination treatment was more effective in men who were smoking more than 20 cigarettes a day, but not for women or light smokers.

Am J Psychiatry. 2014: epub.

Med Errors at Discharge

- Analysis of 470 patients at hospital discharge for ACS or heart failure; average discharge medication list included 12 meds.
- In 51% of the patients, researchers found at least 1 discordant medication.
- 27% of patients were not taking at least 1 prescribed medication.
- 36% were taking at least 1 non-prescribed medication.
- 60% of patients misunderstood indication or dosing for at least 1 cardiac medication.
- Conclusion: number needed to harm = 2 for medication confusion at hospital discharge.

Mayo Clinic Proc. 2014; 89:1042.

Ultrasound Not CT for Renal Colic

- RCT at 15 ED's ~ 2,700 patients with suspected nephrolithiasis.
- CT vs. Ultrasound radiologist vs. ultrasound by ED physician.
- 6 month radiation exposure was lower in 2 US groups vs. CT.
- Rate of serious adverse events, ED re-admissions, and average pain scores were similar in all three groups
- 41% of ED ultrasound group and 27% of radiology ultrasound group underwent subsequent CT imaging.
- Overall ED costs remain lower for patients who received ultrasound first.

• **Conclusion:** Use US to evaluate suspected nephrolithiasis

NEJM. 2014; 371:1100.

Low Carb Diet Decreases Weight and Improves Framingham Risk Scores

- RCT of 148 obese adults: Low Carb vs Low Fat Diet
- Low carbohydrate diet CHO < 40g/day vs.
- Low Fat diet required < 30% of daily energy intake came from fats.
- No calorie intake goals were given. Followed for over 1 year.
- Energy intake in both diets dramatically fell from approximately 2000 calories/day to under 1500 calories/day
- In low carbohydrate diet protein intake ↑ by ~ 8g/day; also ↑ Fat intake
- while staying stable in the low fat diet.
- Fat intake ↓ in low fat diet significantly, with stable Protein intake
- At 12 months weight reduction was significantly greater in the low carb diet compared to the low fat diet -3.5kg (p=0.002) and Fat Mass -1.5% (p=0.011), as well as reductions in triglyceride levels and increases in HDL levels.
- **Conclusion:** low carbohydrate diet (< 40g/day) was more effective for both weight loss and cardiovascular risk factor reduction than low fat diets.

Annals of Internal Medicine 2014; 161(5):309-318

Eat Fiber: One Simple Message for Weight Loss

- Randomized controlled trial of 240 adults with metabolic syndrome.
- A single recommendation (increase fiber consumption to 30g /day), or the American Heart Association dietary guidelines X 12 months.
- Primary outcome was weight loss.
- **Outcome:** Weight loss was slightly greater in AHA (0.6 kg) after 12 months, but not statistically different.
- Total caloric intake in high fiber group was decreased by 200 calories vs. 464 in the American Heart Association diet.
- **Conclusion:** Weight loss and heart healthy outcomes can be achieved by following one simple message, to eat > 30g of fiber a day.

Ann Intern Med. 2015; 162(4):248-57.

Regular Nut Consumption Improves Mortality

- Cohort studies (Nurses Health Study 76,000 women & Health Professionals study 42,000 men).
- Nut consumption by FFQ
- Nut consumption was associated with significantly lower total all-cause mortality after adjusting for confounding variables.
- Nut consumption also correlated with indicators of health including increased physical activity, higher consumption of fruits and vegetables, limiting of tobacco use.
- **Conclusion:**
- This trial confirms previous data that nut consumption → decreased Mortality risk.

Nut Intake	Hazards Ratio for Death
< Once a week	0.93
Once weekly	0.89
2-4 times / week	0.87
5-6 times / week	0.85
> 7 times / week	0.80

NEJM: 2013; 369:2001.

Sleeve Gastrectomy

- Sleeve gastrectomy: bariatric surgery
- RCT comparing sleeve gastrectomy with roux-en-y gastric bypass in 217 patients.
- Mean BMI was 43.
- 30-day complication rate was 8% in the sleeve group vs. 17% in the traditional group (p=0.07). 1 Bypass patient died post-operatively.
- At 1 year mean weight loss was similar (Sleeve: 37kg vs. Bypass 40kg).
- **Conclusion:** Sleeve gastrectomy is as effective as other gastric bypass procedures with potentially lower complication rates.

Annals of Surgery 2013; 258:690.

Antibiotics given more than wanted

- MMRW survey of consumers in general U.S. population & 1500 healthcare providers
- >50% of healthcare providers believe patients expect antibiotics during a visit for a viral illness
- ~ 25% of consumers actually expect them
- Hispanics more likely to expect Abx (41% vs. 26%)
- 20% of consumers obtained Abx from source other than HC provider (grocery stores, friends and family, or leftovers from a previous illness).

MMWR / July 24, 2015 / Vol. 64 / No. 28

Vitamin B3 and Skin Cancer

- RCT oral nicotinamide 500mg bid (NIC) or placebo (PBO) for 12 months in two in Sydney, Australia
- 386 immune competent with ≥ 2 NMSC in past
- Mean age 66 years, and 63% were men.
- NMSC rate sig lower for NIC (1.77) vs PBO (2.42).
- Overall relative rate reduction (RRR) was 0.23 (95% CI: 0.04 to 0.38, $p = 0.02$)
- Treatment comparable for both BCCs, SCCs & AK
- No adverse event rates between the two arms

J Clin Oncol 33, 2015 (suppl; abstr 9000)

Digoxin Days are Over

- SR & MA of 19 studies of digoxin in >235,000 patients with AF & 91,000 with CHF
- 21% increase in the relative risk for death in people taking digoxin.
- AF: increased risk was 29%; CHF: 14%
- The authors "*calls for RCT of dose-adjusted digoxin therapy.... Until completed, digoxin should be used with great caution, particularly when administered for rate control in AF.*"

Eur Heart J. 2015 Jul 21;36(28):1831-8

Sauna Time

- Prospective cohort study in Finland of 2,315 middle-aged men (aged 42-60 years) x 20 Yrs
- After adjusting for cardiovascular risk factors
- Compared to a sauna once per week, the hazards ratio of sudden cardiac death
- 2-3 times per week HR = 0.78
- 4-7 times per week HR = 0.37 ($p = 0.005$).
- Best Outcome: sauna lasting > 19 minutes

JAMA Inter Med. 2015; 175(4):542-8

Where's That Golf Magazine?

- New Zealand Cohort study tracked waiting room magazines over 31 days.
- Magazines categorized as "non-gossipy" (i.e. Time, The Economist, etc.) vs. "gossipy" (not identified for fear of litigation).
- "Gossipy" was defined as having 5 or more photographs of celebrities on the front cover (most were found to have up to 10).
- Forty-seven of the 82 magazines were aged less than 2 months.
- At 31 days none of the "non-gossipy" magazines had disappeared.
- 96% of the "gossipy" magazines had disappeared
- Hazard ratio of "gossipy" magazine death was 14.51 (95% CI: 6.69-33.32).

- Conclusions:
- Someone Steals the Gossipy Magazines
- Assumption that offices have old magazines is a form of selection bias
- Patients who would not steal a pack of gum find no moral quandary taking the substantially higher cost agent from your room.

BMJ. 2014; 349:g7262

Smoking Cessation Improves Pain Scores

- Prospective cohort analysis of 5,000 patients with chronic axial or radicular pain compared smoking history and assessment of pain. Confounding factors included secondary gain, gender, age, and BMI.

Results:

- Compared to those who never smoked, patients who are currently smoking had significantly greater pain in all scale ratings.
- Compared to patients who continued to smoke, those who quit smoking during the course of care reported significantly greater improvements in pain in VAS ratings
- Those continued smoking reported no clinical improvement in pain.

Conclusion:

- For patients with chronic pain secondary to back disorders, smoking cessation led to significant reductions in pain scores.

J Bones Joints Surg Am. 2012; 94(23):2161-6.

Drugs of Choice for Neuropathic Pain in Adults

- Systematic review and meta analysis including 229 studies.
- Many of the studies published by drug manufacturers → specific attention for publication bias (unpublished trials that do not show a benefit).

• Most efficacious:

- Serotonin norepinephrine reuptake inhibitors (duloxetine) NNT=6.4 (95% CI = 5.2-8.4).
- Pregabalin NNT=7.7 (95% CI = 6.54-9.4).
- Gabapentin NNT=7.2 (5.9-9.2).
- For topicals, capsaicin patch NNT=10.6 (7.4-19).
- NNT for TCA, tramadol, and other agents had higher NNT.
- **NNT for "strong opioids" LEAST effective & had the highest NNT**
- Little benefit was found from topical lidocaine.
- Adverse Events: Topical agents were better tolerated
- Cost: Least for TCA and tramadol.

Lancet Neurology. 2015; 14(2):162-73.

Summary

- No More Throat Culture or Fasting Lipid Panel
- MBS→ Testicular Ca
- Teenagehood (Not HPV Vaccine) ↑ STI Risk
- Ibuprofen = MSO4 for Fx
- Calculate Breast Cancer Risk & Discuss Rx
- Coffee and Saturated Fats are OK
- Consider non-E2 for Hot Flushes (Rx, Music)
- Smoking Cessation: NRT & Varenicline effective
- US = CT for Suspected Renal Colic

Summary

- Low Carb Diets, Fiber and Nuts
- Cut Back More on Antibiotics
- Vitamin B3 for Skin Cancer Prevention
- Take a Sauna
- Carefully (& appropriately) Treat Chronic Pain)
- Buy Less Gossipy Magazines