Clinical Lessons Learned in 2015

Frank J. Domino, MD, Professor and Director of Medical Student Education, Department of Family Medicine and Community Health, University of Massachusetts Medical School, Worcester

Introduction: many new studies in medical literature; physicians often unsure how to interpret findings and apply to practice; evidence-based medicine (EBM) can sometimes confuse public, patients, media, and clinicians

Risk for celiac disease (CD): in United States, consumption of gluten-free diet more common in individuals without CD than in those who do have CD; Aronsson et al (2015) prospectively studied newborns at high risk for CD (because of, eg, family history); showed introducing gluten at <6 mo of age did not increase risk of developing CD

Lactobacillus in children: Gutierrez-Castrellon P et al (2014) studied effects of Lactobacillus given once daily in children ages 6 to 36 mo; resulted in decreased rate and duration of diarrhea, reduced rates of upper respiratory infections, preschool days missed, and days of work missed by parents (reduced by 50%); and decreased use of unnecessary antibiotics

Peanut allergy: in 2008, lack of evidence prompted American Academy of Pediatrics (AAP) to withdraw recommendation for children at risk for peanut allergy (because of, eg, family history) to avoid peanuts; Du Toit et al (2015) randomized 640 infants ages 4 to 11 mo at high risk (ie, with history of severe atopic dermatitis or allergy to eggs) to 2 g of peanut protein 3 times weekly vs avoiding peanuts until age 5 yr; also stratified infants based on reaction to skin testing with peanut antigen; in infants who received supplementation with peanut protein and had no skin reaction, incidence of peanut allergy at 5 yr 2%, vs 14% in infants who avoided peanuts; peanut supplementation in infants who had positive skin test associated with 20% reduction in allergy

Obesity in children: AAP recommendations — increased activity and decreased consumption of concentrated carbohydrates; breastfeed for as long as possible; replace cookies with fruit; no television in bedroom; avoid fruit juices; 60 min of moderate to vigorous activity daily

Rapid antigen detection test (RADT) for streptococcal pharyngitis: Lean et al (2014) reviewed 48 studies of 24,000 patients; concluded RADT extremely sensitive and specific; throat culture in children and adults not necessary; use Centor score to identify candidates for RADT; Centor score — 1 point each for tonsillar edema, erythema, exudate, fever, age 3 to 14 yr, anterior cervical chain adenopathy, and absence of cough (streptococcal pharyngitis highly unlikely in presence of cough); score results — 4 to 5 points, treat empirically with penicillin to prevent complications; 2 to 3 points, perform RADT; treat if RADT positive; if RADT negative plus Centor score ≤3 points, throat culture unnecessary

Analgesia for acute fracture: Poonai et al (2014) compared ibuprofen and morphine for management of pain in children with acute fractures; medications equally effective 2 days after injury; morphine caused more nausea, vomiting, and drowsiness; ibuprofen 10 mg/kg plus acetaminophen every 6 hr effective for pain relief

Human papillomavirus vaccine (HPV): retrospective analysis (Jena et al, 2015) of girls ages 12 to 18 yr showed overall risk for sexually transmitted infection (STI) increased with age and did not correlate with vaccination status; HPV vaccine in adolescent girls not associated with increased promiscuity or risk for STI

Muscle-building supplements (MBS): most common ingredients: creatine, protein, and weak androgens; case-control study (Li et al, 2015) showed MBS associated with 65% increase in rate of testicular cancer (odds ratio 1.65); risk highest in men <25 yr of age and with use of multiple formulas or use for >3 yr

Otitis media with effusion: randomized controlled trial (RCT; Williamson et al, 2015) of patients ages 4 to 11 yr compared autoinflation of eustachian tube (3 times daily for 1-3 mo) with usual care; outcomes — at 3 mo, improvement seen in 50% of intervention group vs 38% of control group; improved quality of life scores; no significant adverse events; good compliance among patients

Sublingual immunotherapy for allergic rhinitis and asthma: systematic review (Lin et al, 2013) of 63 trials in adults and children showed immunotherapy effective at decreasing exacerbations of asthma and moderately effective at decreasing symptoms of allergic rhinitis; not yet approved by US Food and Drug Administration

Prevention of breast cancer: United States Preventive Services Task Force updated recommendations; adequate evidence supports efficacy of tamoxifen and raloxifene for decreasing risk for estrogen receptor-positive breast cancer in high-risk (ie, 5-yr risk for breast cancer ≥3%) postmenopausal women; shared decision making important; discuss adverse events with patient (eg, increased risk for venous thromboembolism and uterine cancer); raloxifene decreases risk for uterine cancer; risk calculator available at cancer.gov/bcrisktool

Ductal carcinoma in situ (DCIS): currently treated via lumpectomy, radiotherapy (RT), and antiestrogen therapy; observational study (Narod et al, 2015) of >100,000 women with DCIS showed 20-yr breast cancer-specific mortality 3.3% lower than in women without DCIS

Educational Objectives

The goals of this program are to improve primary care for pediatric and adult patients through a review of recent evidence-based literature, and improve recognition and treatment of common health issues in men. After hearing and assimilating this program, the clinician will be better able to:

1. Cite the benefits of giving Lactobacillus to children.
2. Delineate the role of rapid antigen detection testing and throat culture in the evaluation of Streptococcus pharyngitis.
3. Assess the role of antiestrogen agents in the prevention of breast cancer in high-risk individuals.
4. Choose an appropriate treatment option for a patient with prostate cancer.
5. Weigh the risks and benefits of testosterone replacement therapy.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and planning committee reported nothing to disclose.
compared with mortality of 3.2% in general population; mortality risk greater in patients <35 yr of age and blacks; treatment via lumpectomy and RT reduced risk for recurrence of invasive breast cancer at 10 yr but did not reduce breast cancer-specific mortality or all-cause mortality; concluded that current standard treatment provides only minor benefit for intermediate outcomes

**Fasting lipid panel (FLP):** large study (Doral et al, 2014) compared fasting vs nonfasting; panel obtained in nonfasting state yields higher low-density lipoprotein and triglyceride values; since treatment does not improve cardiac outcomes, testing in nonfasting state no longer required

**Fat intake:** Harcombe et al (2015) showed that previously recommended limitation of fat <30% of caloric intake based on poorly executed studies and not associated with reduction in cardiac or all-cause mortality

**Erectile dysfunction (ED):** 2 to 3 cups/day of coffee decreases incidence; 3 to 4 cups/day not as effective; RCT of patients after acute low-risk myocardial infarction showed walking program reduced ED by 71% compared with status at hospital discharge (ED increased in control group)

**Treatment of hot flashes:** Joffe et al (2014) — RCT compared venlafaxine, estradiol, and placebo; venlafaxine greatly decreased rates of hot flashes; estradiol slightly more effective; placebo least effective; venlafaxine may be given to patients with intact uterus, with no withdrawal bleeding; device-guided slow-paced respiration — RCT compared controlled breathing using device vs listening to quiet music using similar device (control); both groups experienced reduction in hot flashes, but superior results seen in control group

**Postdischarge visits:** Mixon et al (2014) study showed discordant medication in 51% of patients 2 days after discharge; ensure patients bring all medication bottles to postdischarge visit for thorough review

**Smoking:** varenicline — nicotine agonist; concurrent nicotine replacement therapy (NRT) theoretically unnecessary; Koegelenberg et al (2014) — RCT of varenicline with or without NRT; abstinence rate higher with NRT (rates of adverse events similar); Rose and Behm (2014) — RCT of varenicline and NRT plus either bupropion or placebo; adding bupropion significantly improved abstinence rate in men smoking ≥1 pack per day

**Weight loss:** meta-analysis — showed successful weight loss increased by factor of ≈4 when provider enquires about it; offer help including referral to dietitian; recommend decreased carbohydrate intake; Bazzano et al (2014) — RCT of low-carbohydrate (<40 g/day) vs low-fat (<30% of daily calories) diet in 148 adults with obesity; both groups lost weight after 1 yr; low-carbohydrate group lost additional 3.5 kg, and had lower triglyceride levels and higher high-density lipoprotein levels; Ma et al (2015) — RCT of high-fiber diet (single component) vs American Heart Association (multicomponent) diet; weight lost in both groups, with no statistically significant difference between groups; simple recommendation to increase fiber (30 g/day) easier to implement and as effective as complicated regimens; speaker’s recommendations — explain low-carbohydrate food pyramid; encourage regular consumption of small serving of nuts (associated with decreased all-cause mortality)

**Diabetes:** in meta-analysis of 19 observational studies in patients with atrial fibrillation or heart failure (HF), digoxin associated with increased risk for death; data may be confounded because digoxin often added late for patients with worsening HF; RCT of 40 trials (1 million patients with HF) showed no mortality benefit with digoxin

**Sauna:** cohort study of men (Laukkonen et al, 2015) showed sauna use >19 min 4 to 7 times/week dramatically reduced risk for sudden death

**Suggested Reading**


**Health Concerns in Men**

Eliseo J. Perez-Stable, MD, Professor of Medicine and Chief, Division of General Internal Medicine, University of California, San Francisco, School of Medicine

**Epidemiology** (2013 data): compared with women, rates of death due to heart disease, cancer (mainly lung cancer), and accidental injury higher in men (women have higher rates of stroke); suicide — rate of completion 3 times higher in men (because of use of more effective means); be alert to men showing signs of depression and enquire about suicide; liver disease — incidence higher in men (because of alcohol use and higher incidence of STI [hepatitis B and C]); smoking — male preponderance seen in every racial and ethnic category

**Prostate cancer** (PC): incidence and aggressiveness greater among black men; lifetime risk 15%; present in 30% of men at autopsy (but often benign, causing death in only 3% of men); considered chronic disease requiring management by family practitioner, even if also treated by specialist; risk factors — first-degree relatives with PC, age, and ethnicity (Asians and American Indians have lowest rates)

Diagnosis: involves multiple (12-16) random biopsies; evaluate for extracapsular spread (via, eg, magnetic resonance imaging, positron emission tomography)

Treatment: active surveillance — for low-grade cancers; requires serial biopsies (eg, every 6 mo) to survey progression of histologic grade; serial prostate-specific antigen (PSA) testing; biopsy if PSA increasing; prostatectomy — compared with RT, associated with superior disease-free survival at 10- to 15-yr follow-up; causes more short-term effects on erectile function; incontinence usually limited to first year after surgery (but sometimes chronic); RT — causes same side effects, but less acute and at lower rates in first year; causes fatigue and systemic symptoms (with some overlap
from combined total androgen blockade); no extracapsular spread — offer prostatectomy or RT for cure; extracapsular spread — RT to control, plus androgen blockade; monitor annually (eg, every 6 mo for first 2 yr)

Prostatectomy vs observation: RCT of men of 700 men with localized cancer; 10- to 12-yr total mortality, 47%; total mortality reduced by 12% in prostatectomy group; PC-specific mortality after prostatectomy 5.8%, vs 8.4% for observation; need to consider short-term risk (morbidity and mortality) of major surgery; data suggest short-term morbidity from prostatectomy worthwhile, although mortality rate from PC not statistically significant; prostatectomy vs watchful waiting — in RCT (Bill-Axelson et al, 2014), total mortality at 23 yr after prostatectomy 57%, vs 71% with watchful waiting; PC-specific mortality after prostatectomy 19%, vs 28% with watchful waiting

Genomic testing: not used for screening; used to determine tumor subtype, which helps direct treatment; helpful when deciding on advisability of surveillance alone

Erectile dysfunction: original RCT of sildenafil (Viagra) in patients with ED (Goldstein et al, 1998) reported improved function in 56% of participants and successful coitus in 60% (compared with 22% in placebo arm); adverse effects — hypotension when combined with nitrates (combination contraindicated); potentiates hypotension with other drugs (eg, α-1 blockers); headaches; nasal congestion; other causes — alcohol, marijuana, cinmetidine, digoxin, and especially, diuretics (incidence of ED 20%); incidence with β-blockers 10% (same as with placebo); tricyclic antidepressants and selective serotonin reuptake inhibitors can cause significant cognitive side effects and decreased sexual desire; newer agents — avanafil, rapid-acting agent which can be used daily or as needed; tadalafil (Cialis) most commonly used as daily therapy; sildenafil now available in generic formulation and therefore favored by payers

Peyronie disease: uncommon; treatment — pentoxifylline; local procedures (results not optional; side effects include ED and painful intercourse)

Andropause: value of checking serum testosterone controversial; modest age-related decrease in testosterone; clinical consequences unclear; normal age-related changes in function similar to hypogonadism; clinical measurement of testosterone does not reliably diagnose problem for individual men; test requires repetition; normal physiologic changes of aging — decline in testosterone ≈100 ng/dL (between ages 20 and 80); diurnal variation in testosterone flattens with age

Effects of low testosterone: decreased sexual activity; poor morning erection; low libido; ED; decreased bone mass; fractures (testosterone may contribute to osteoporosis, but stronger correlation seen with estradiol levels); sarcopenia with complaints of weakness; increased risk for depression; diminution of cognitive function; metabolic effects — central obesity, increased levels of insulin and C-reactive protein, and increased rate of diabetes; treatment — in patients with symptoms and low levels of testosterone, administration of testosterone not shown to impart benefit; endocrinologists recommend repeat testing of testosterone (ideally in morning in younger men); if level consistently low (on ≥2 tests), target treatment to serum level 300 to 400 ng/dL; results — 5 small RCTs show improved bone density in spine (not femoral neck) and muscle mass, but no benefits for strength, quality of life, or mood; potential adverse effects — acceleration of PC, worsening of benign prostatic hypertrophy and sleep apnea, and increased hemoglobin levels; recommendations — treat only men with documented very low levels and symptoms (ie, weakness and fatigue); predefine clinical outcomes for success; monitor prostate with digital rectal examination and PSA every 3 mo; reevaluate symptoms after 3 mo

**Suggested Reading**


**Acknowledgments**

Dr. Domino spoke at the University of California, San Francisco, School of Medicine, in Maui, HI. For information about forthcoming CME activities presented by the University of California, San Francisco, School of Medicine, please visit: cme.ucsf.edu/Index.aspx or check our website, Audio-Digest.org, under upcoming meetings. The Audio Digest Foundation thanks the speakers and sponsors for their cooperation in the production of this program.

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| Review Educational Objectives on page 1 | 5 minutes |
| Take pretest | 10 minutes |
| Listen to audio program | 60 minutes |
| Review written summary and suggested readings | 35 minutes |
| Take posttest | 10 minutes |
1. According to studies in the recent pediatric medical literature, which of the following is true?
   (A) Introduction of gluten at <6 mo of age in high-risk infants increases risk for development of celiac disease
   (B) Administration of *Lactobacillus* to children has no effect on the incidence of upper respiratory tract infection
   (C) Administration of peanut protein in children at high risk for peanut allergy reduces the risk for developing peanut allergy
   (D) For patients at moderate risk for streptococcal pharyngitis, rapid antigen testing should be followed by throat culture

2. A 6-yr-old boy presents with tonsillar edema but with no fever, cough, or anterior cervical chain adenopathy. Based on his Centor score, you request a Rapid Antigen Detection Test (RADT), which is negative. The most appropriate approach for this patient is which of the following?
   (A) Prescribe penicillin and request a throat culture
   (B) Request a throat culture only
   (C) Advise watchful waiting
   (D) Prescribe penicillin, with no throat culture

3. According to the case-control study by Li et al (2015), the odds ratio for development of testicular cancer associated with the use of muscle-building supplements is which of the following?
   (A) 0.75
   (B) 1.0
   (C) 1.30
   (D) 1.65

4. Which of the following is a true statement about new recommendations from the United States Preventive Task Force on the prevention of breast cancer?
   (A) Tamoxifen is recommended for high-risk premenopausal women
   (B) Raloxifene is recommended for high-risk postmenopausal women
   (C) Raloxifene is associated with reduced risk for venous thromboembolism
   (D) Raloxifene is associated with an increased risk for uterine cancer

5. Choose the correct statement about ductal carcinoma in situ.
   (A) Risk for mortality is higher in women >40 yr of age
   (B) Risk for mortality is lower in black women
   (C) Lumpectomy and radiotherapy reduce the risk for local recurrence of invasive cancer
   (D) Lumpectomy and radiotherapy reduce breast cancer-specific mortality

6. Based on randomized controlled trials in patients with menopausal hot flashes, which of the following is true?
   (A) Venlafaxine is very effective
   (B) Estradiol is ineffective
   (C) Device-guided slow-paced respiration is ineffective
   (D) Listening to relaxing music is ineffective

7. Which of the following has(have) been shown to improve weight-loss outcomes?
   (A) Enquiring of patients about weight loss
   (B) Low-fat diets
   (C) Low-carbohydrate diets
   (D) All the above

8. In comparisons of prostatectomy and radiotherapy in patients with early prostate cancer, prostatectomy was associated with _______ disease-free survival at 10- to 15-yr follow-up and _______ short-term effects on erectile function.
   (A) Inferior; fewer
   (B) Inferior; more
   (C) Superior; fewer
   (D) Superior; more

9. Which of the following types of drugs has a significant association with erectile dysfunction?
   (A) β-blockers
   (B) α-1 blockers
   (C) Diuretics
   (D) Tricyclic antidepressants

10. Testosterone replacement therapy is prescribed for a symptomatic male patient who has demonstrated low testosterone levels on >2 tests. Therapy is most likely to improve which of the following?
    1. Bone density in the spine
    2. Bone density in the femoral neck
    3. Muscle mass
    4. Strength
    5. Mood
    6. Sleep apnea
    (A) 1,2,4,5
    (B) 1,3
    (C) 2,3,4
    (D) 1,5,6

Answers to Audio Digest Family Medicine Volume 64, Issue 04: 1-C, 2-C, 3-A, 4-B, 5-A, 6-B, 7-D, 8-A, 9-C, 10-B