Top 10 Changes to My Practice: 2014

Frank J. Domino, M.D.
Professor
Dept. of Family Medicine & Community Health
University Of Massachusetts Medical School
Worcester, MA
Frank.domino@umassmemorial.org

Learning Objectives
1. Review evolving concepts that may affect one's practice
2. Recognize the effects of statin drugs on non-cardiovascular health outcomes
3. Apply evidence-based strategies for treating common acute infections in primary care
4. Identify diet and lifestyle interventions that are effective in managing chronic disease

"Medical" Marijuana
- Best Evidence
- AIDS Wasting
- MS: Spasticity/Pain
- Hep C: During Tx

Not Medical Marijuana
- Most commonly used drug in pregnancy
- Increases risk for low birth weight and pre-term labor
- Adolescent use increases risk of schizophrenia

Impulsivity, Attention, Memory, and Decision-making Among Adolescent Marijuana Users

- Compare attention, memory, decision-making, and impulsivity between adolescent MJ users vs non users.

RESULTS:
- MJ use impaired short-term recall memory and ↑ impulsivity after controlling across all measures.

Age of Onset of Marijuana Use and Executive Function

- Chronic MJ users (divided into early & late onset) vs non-MJ smokers on battery of neurocognitive tests.

Conclusions:
- MJ smokers: poorly on measures of executive function.
- Early onset smoked more MJ/week than late onset & had worse neurocognitive scores.
- Early exposure altered brain development → enduring neuropsychological changes.

Pediatric Screening Update

Hyperlipidemia: 9-11 years and 17-21 years (A/I)
- H/H: 15 & 30 months (B/I)
- HIV: Offer universal screening 16-18 years when prevalence > 0.1% (A/A)
- Cervical cancer: start at 21 years (D/A)
- Alcohol & Drugs: all adolescents
- CRAFFT (Car, Relax, Alone, Forget, Friends, Trouble) (A/B)

Depression: 11-21 years
- PHQ-2: Over the past 2 weeks, have you been bothered by: little interest or pleasure, feeling down or depressed (-/B)

Methods to Address Parental “Need” for an Rx

- Say the words “antibiotic associated diarrhea,” watery stool and possible trip to the ER for IV fluids.
- Consider Pelargonium Sidoides syrup (0.5 teaspoon TID).
- Acetaminophen (15 mg/kg every 6 hours) combined with ibuprofen (10 mg/kg every 6 hours).
- Limit use of cough suppressants and/or decongestants (especially under age 6 years).

Texting and Driving

- Observational study
- Data collection device placed in cars
- Near crashes defined as opportunities where drivers were at least partly responsible

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Risk factors for adverse outcomes in teen drivers:
- Reaching for cell phone
- Texting
- Daling cell phone
- Reaching for something else in car
- Looking for something on roadside
- Eating

How Long Does a Cold Last?

For 90% of the children:
- Croup resolved in 2 days
- Sore throat resolved in 2 to 7 days
- Ear aches resolved in 7 to 8 days
- Common URI symptoms resolved within 15 days
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- Bronchitis within 21 days
- Acute cough within 25 days
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Determine symptom duration of acute common respiratory tract infections in healthy children aged birth to age 18 years.

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Conclusions:
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Limited data on adolescent MJ users vs non users.

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Treating Common Pediatric Infections

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<th>Infection</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otitis Media</td>
<td>6 to 23 months of age when strict criteria are met¹</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>Antibiotics if Centor scores or rapid strep testing demonstrate benefit²</td>
</tr>
<tr>
<td>Upper Respiratory</td>
<td>For rhinorrhea induced cough or a cold, oral decongestants</td>
</tr>
<tr>
<td>Inspection</td>
<td>Anti-viral medications for influenza are of no benefit</td>
</tr>
<tr>
<td>Cough</td>
<td>Cough without rates, wheezing or respiratory distress, honey (with or without lemon) is more effective than agents like diphenhydramine per Cochrane systematic review³</td>
</tr>
</tbody>
</table>


- GOOD NEWS: Motor vehicle traffic mortality rate ↓ 25%
- Suicide surpassed motor vehicle traffic crashes as the leading cause of injury mortality
- Mortality rates rose substantially for:
  - Suicide (↑ 15%)
  - Unintentional poisoning (↑ 128)
  - Falls (↑ 71%)
- Accidental Poisoning: 100 people PER DAY

Prescription Drug Poisoning

2010:
100 people die from drug overdoses every day in the United States.
91% of all unintentional poisoning deaths were caused by prescription opioids, more than cocaine and heroin combined.
Nonmedical use of prescription painkillers costs health insurers up to $72.5 billion annually in direct health care costs... and an estimated $600 billion in total societal costs.

Courtesy of Phil Buldoc, M.D.

Lifestyle Intervention Effect on Diabetes

Lifestyle intervention associated with significantly lower risk for progression of diabetes for up to 10 years after the intervention (relative risk = 0.35)
Lifestyle interventions not associated with changes in blood pressure or cholesterol; insufficient evidence on cardiovascular outcomes and all-cause mortality.

Brief Postprandial Exercise on Patients w/ Pre-Diabetes = Large Work Out

- 15 minutes of exercise after meals three times a day VS 45 minutes once a day in those with impaired fasting glucose.
- Outcomes: The three short exercise regimen or the late morning 45 minute regimen lowered 24 hour average glucose significantly

“Breaking” Prolonged Sitting

Randomized controlled trial of 70 healthy adults sitting at a desk for 9 Hours

<table>
<thead>
<tr>
<th>Physical Activity:</th>
<th>Regular Activity:</th>
</tr>
</thead>
<tbody>
<tr>
<td>walk 30 Min, then sit</td>
<td>walk 100 seconds every 30 min</td>
</tr>
</tbody>
</table>

Regular Activity lowered
- Insulin
- Glucose
- Triglycerides

Courtesy of Phil Buldoc, M.D.
1 in 3 elders fall every year
Falls are leading cause of non-fatal & fatal injuries
Falls → $30 billion in HC costs per year

Exercise Intervention Lowers the Risk of Falls in Senior Citizens
- Meta-analysis of 17 randomized controlled trials
- 4,300 community dwelling elders; mean age 77 years
- Exercise programs included interventions to address gait, balance, and strength training.
- Compared to placebo intervention, exercise resulted in significantly lower numbers of falls
- Intervention was effective regardless of baseline fall risk.

Risk of Hip Fracture in Nursing Home Patients Who Use Hypnotics
- Medicare Part D stopped covering benzodiazepines (BZDs) due to hip fracture concerns, thus decreasing use dramatically in nursing homes.
- Self-Controlled, Case Cross-Over Studies Done on Nursing Home Patients

Non-Traumatic Rotator Cuff Tears
- Study Design: RCT of 3 different methods of treating symptomatic non-traumatic tears of supraspinatus tendon
- Population: 180 shoulders in 173 patients > 55 years
- Interventions:
  1. Physiotherapy
  2. Acromioplasty and physiotherapy
  3. Rotator cuff repair, acromioplasty and physiotherapy
- Follow-up: 3, 6, and 12 months post intervention (93% follow-up)
- Outcomes:
  - No differences in…
  - Mean change in Constant score 17.0, 17.5, and 19.8, respectively (P = 0.34)
- Conclusions: At 1-year, operative treatment is no better than conservative treatment, which should be considered as the primary method of treatment.

Physical Therapy (PT) vs Surgery for Meniscal Tear
- Randomized Controlled Multicenter Trial
  - 351 adults > 45 years old with meniscal tear & mild-to-moderate osteoarthritis on imaging
  - Surgery vs PT followed by PT alone
  - At 12 months...
    - No differences in WOMAC scores, implying no difference in symptoms or quality of life
    - Frequency of adverse events did not differ significantly between groups

Acute Bronchitis Gets Better with Time
- Study Design: Randomized controlled trial in Spain
- Methods: Compared amoxicillin-clavulanate or ibuprofen with placebo
- Population: 416 adults with uncomplicated acute bronchitis
- Results: Neither amoxicillin-clavulanate nor ibuprofen associated with a greater likely hood of cough resolution than placebo (after adjusting for multiple variables)
- Adverse Effects: GI discomfort significantly more common in amoxicillin group (12%) than ibuprofen group (5%) and placebo group (3%)
- Conclusions: Antibiotics and ibuprofen are of no benefit in those diagnosed with acute bronchitis
How Effective Are Anti-viral Agents for Influenza?

Common agents to treat the flu:
- Oseltamivir
- Zanamivir

RCTs of these drugs demonstrating efficacy are limited and mostly funded by the pharmaceutical industry.

New meta analysis of 90 observational studies:
- Hospitalized influenza patients during H1N1 pandemic
- Mortality slightly but not significantly lower among patients who received anti-virals
- 60% lower risk for composite severe outcome, common pneumonia, and mortality if antivirals started ≤ 48 hours of developing symptoms compared with later.

Azithromycin and Levofloxacin Use and Risk for Cardiac Arrhythmia and Death

Cohort study of US veterans who received an outpatient antibiotic; comparison of risk for cardiac arrhythmia and death across different antibiotics.

Compared to amoxicillin:
- Azithromycin had significantly increased risk of death and cardiac arrhythmia, but not on days 6 through 10.
- Levofloxacin had significantly greater risk of death and serious cardiac arrhythmia that continued from day 1 through 5 and 6 through 10.

Clarithromycin Increases Risk of CV Events and Death

Methods: Prospective analysis of 3,000 UK patients hospitalized for acute COPD exacerbation or community acquired pneumonia (CAP).

Results after 1-Year Follow-up:
- 20% of COPD patients and 10% of CAP patients hospitalized for CV events
- Compared to non-use, clarithromycin use associated with:
  - Significantly higher risk for CV events (HR: 1.5), acute coronary syndrome (HR: 1.7), and acute cardiovascular mortality (HR: 1.5), but not all cause mortality in COPD patients
  - Increased risk for CV events (HR: 1.7), but not acute coronary syndrome, cardiovascular mortality, or all cause mortality in CAP patients
  - CV risk increased only with use > 7 days; but persisted for months after ending clarithromycin
- Beta-lactams not associated with increased CV risk.
- Number needed to harm: COPD group = 8, CAP group = 11.

Proton Pump Inhibitors (PPIs) Prescribed Inappropriately in Teaching Hospitals

Retrospective review of hospitalized patients discharged from an internal medicine service in Colorado (6.5 million patients)

- 73% of patients who received PPI’s had no indication for it.
- PPI’s increase risk of C. difficile-associated diarrhea, pneumonia, drug interactions, and fractures.

PPIs and H2RAs: Increased Risk of B12 Deficiency

Observational study of 200,000 patients in the Kaiser Permanente population

- Patients who received a prescription for > 2 years of PPIs had increased risk of developing a B12 deficiency (odds ratio = 1.65).
- Dosing PPI 1.5 or more pills per day increased odds ratio to 1.95.
- Gastric acid inhibition (especially PPIs) increases risk of developing B12 deficiency.

Diuretics and Statins Increase Diabetes Risk

Study Design: Re-analysis of data from NAVIGATOR trial (Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research) to evaluate outcome risks, in particular new onset diabetes.

Methods: Comparison of patients treated with:
- Beta blockers
- Diuretics
- Statins
- Calcium channel blockers

Outcomes: At 5 years, risk of new onset diabetes was
- Increased for diuretics and statins (hazard ratio 1.23, and 1.32, respectively).
- Not increased for beta blockers and calcium channel blockers

Conclusions:
- Among people with impaired glucose tolerance and multiple cardiovascular risk factors, diuretics and statins increased the risk of new onset diabetes.
Does Statin Use Increase Risk for Obesity?

Cross-sectional study of 27,000 adults aged ≥20 years from National Health and Nutrition Examination Survey

- Caloric intake significantly less for statin users than non-users (2000 vs. 2179 kcal/day, P=0.007) in the first year
- Starting in 2005, statin user caloric intake almost 10% higher than intake in first year, whereas no significant change among non-users.
- Among statin users:
  - Fat consumption increased significantly (≈ 14.4%).
  - BMI increased 1.3% vs. 0.4%.

Calorie and fat intake increased among statin users starting approximately in 2005 compared to non-users. This led to an increase in BMI.


2013 Lipid Guidelines

<table>
<thead>
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<th>Population</th>
<th>Recommended Therapy</th>
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<tr>
<td>Patients with atherosclerotic cardiovascular disease (ASCVD)</td>
<td>+ 75 years: high intensity statins [A]</td>
</tr>
<tr>
<td>Patients with Diabetes Mellitus (DM)</td>
<td>40-75 years and 10-yr risk &gt; 7.5%: high intensity statins [F]</td>
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<tr>
<td>Adult Patients with LDL &gt; 190 or TG &gt; 500: 2°cause</td>
<td>High intensity statins [B]</td>
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<tr>
<td>Adult (&gt;21) with Risk &gt; 7.5% (no ASCVD, no DM)</td>
<td>Moderate or high intensity statins [A]</td>
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A = Strong evidence to support recommendation, or high certainty based on evidence that net benefit is substantial
B = Moderate evidence to support recommendation, or high certainty that net benefit is moderate
C = Expert opinion, which means there is insufficient evidence, or evidence is unclear or conflicting, but this is what the Work Group recommends

2013 Blood Pressure Guidelines

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<td>CKD patients &gt; 18 years</td>
<td>Ramipril 10 mg/day vs Placebo</td>
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Compared with placebo group at 6 months,
- 75 seconds longer pain-free walking time for ramipril
- 225 seconds longer maximum walking time for ramipril
- Greater patient-reported improvements in walking distance, walking speed, stair climbing, and physical health-related quality of life with ramipril

Ramipril for Peripheral Artery Disease (PAD)

Randomized controlled trial in patients with PAD using walking times on a treadmill and other measures

Adverse events:
- Statins to cause 120 excess myopathy cases, 200 rhabdomyolysis cases, and 12,300 statin-induced diabetes cases
- No adverse outcomes for apple consumption (1 improved BMI)

Cost of statin treatment (just Rx): $295 million vs $423 million for apples


Statins & Prostate Cancer

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<th>Outcomes</th>
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| 66,000+ Israeli Men age 45-85 years taking 1 or more statins or no statins | Analysis of prostate cancer risk by drug class (hydrophobic, or hydrophilic) Adjusted for age, immigrant status, economic status, diabetes, BMI, and cardiovascular disease | Statins for ≤12 months lowered prostate cancer risk (HR 0.72, CI 0.63-0.81) Statins for >5 years lowered HR to 0.26 (CI 0.22-0.31) Association strongest for:
- Simvastatin (HR 0.51, CI: 0.47–0.56)
- Atorvastatin (HR 0.48, CI 0.33-0.68)
- Rosuvastatin (HR 0.22, CI 0.08-0.75). Decreased prostate cancer incidence with:
- Increasing total dose
- Hydrophobic statins
- Longer treatment |


JNC8 2013 Blood Pressure Guidelines

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Apple a Day for Primary Prevention of CHD Death

- Modeling study of theoretical influence of “a statin a day” versus “an apple a day”
- 17 million in UK not taking statin for primary disease prevention
- Meta-analysis to predict relationship of nutritional factors & disease mortality
- 70% compliance

Projected reduction in annual vascular deaths:
- Statin: 9,400
- Apple: 8,500 (95% CI, 6,200-10,800).

Cost of statin treatment (just Rx): $295 million vs $423 million for apples


Eggs Are OK

Meta-analysis of 17 prospective cohort studies in which egg consumption was measured with food frequency questionnaires

Outcomes:
• No association between egg consumption and risk for CHD or stroke
• Sub-group analysis of diabetic patients
  • Slight increased risk on heart disease (relative risk 1.5) with egg consumption
  • Decreased risk for hemorrhagic stroke (relative risk 0.8).

Chicken eggs have 200 mg cholesterol
American Heart Association recommends cholesterol intake < 300 mg/day

Rong Y, et al. BMJ. 2013;346:e8539

Dietary Fiber and Cardiovascular Disease

Meta-analysis of 22 observational studies looking at association between dietary fiber types and risk for CHD in CVD events

Findings were similar for all types of fiber

Each 7-gram increase in total dietary fiber (= 1 cup of green vegetables or 2 apples) associated with significantly lower risk for CHD and CVD events (risk ratio = 0.9).

Equivalent to:
• 25 grams per day for women
• 38 grams per day for men

Threapleton DE, et al. BMJ. 2013;347:f6879

Dietary Fiber Intake and Cardiometabolic Risks among US Adults, NHANES 1999-2010

Cross-sectional analysis of NHANES data 1999-2010
23,168 men and nonpregnant women aged 20+ years
Evaluated associations between dietary fiber intake and cardiometabolic risks (metabolic syndrome, cardiovascular inflammation, and obesity)

Risk ratios (95% CI) for highest vs lowest quintiles of dietary fiber intake:
Metabolic syndrome: 0.78 (0.69-0.88)
Inflammation: 0.66 (0.61-0.72)
Obesity: 0.77 (0.71-0.84)

Link between higher dietary fiber and lower cardiometabolic risks suggests need for new strategies and policies to increase dietary fiber intake.


Low Glucose and Aggression in Marriage (HANGRY)

Glucose levels measured in 107 married couples

Measurement of aggressive impulses:
each evening participants stuck between 0 and 51 pins in a voodoo doll that represented their spouse.

To incite aggression: couples competed against their spouse in a 25 trial task which allowed the winner to blare a loud noise at their losing spouse.

Outcomes:
• Lower blood glucose = greater number of pins in doll
• Lower blood glucose = higher intensity and longer duration of noise
• Relationship satisfaction negatively correlated with number of daily pins stuck

People with lower glucose levels had higher aggressive impulses.

Bushman BJ, et al. PNAS. 2014;111(1); 3254-3257.

Chewing Gum after C-Section

Meta-Analysis of RCTs on Use of Chewing Gum after C-section on ileus

Gum chewing (compared with no gum chewing) led to reductions of:
• 6.42 hours to first flatus
• 3.62 hours to first bowel sound
• 6.58 hours to first stool
• 5.94 hours to LOS

No evidence for any side effects caused by gum chewing

Gum chewing is associated with early recovery of bowel motility and shorter LOS for women after C-section.


Calcium Consumption Does Not Improve Bone Density

Cross-sectional study of U.S. residents age > 50 measuring calcium intake using dietary recall and bone mineral density (BMD) testing

• Mean calcium intake: 400 mg to > 2000 mg a day
• BMI-adjusted analysis showed little relation between calcium intake and BMD of hip or lumbar spine
• Increased calcium intake increases risk of cardiovascular disease

Calcium Supplementation Increases Risk of CV Death

Prospective cohort study of 390,000 adults (mean age 61 years)
- ≈ 50% of men and 70% of women used calcium containing supplements
- Median daily calcium intake: ≈ 700 mg (men and women)
- After 12 years (adjusted for multiple cardiac risk factors), calcium supplementation associated with significant increase in CV death in men, but not women
- In men >1000 mg/day compared with no supplementation associated with 20% higher risk for CV death, almost entirely due to heart disease
- Calcium intake not associated with stroke


High Calcium Intake Associated with Earlier Mortality in Women

Prospective cohort study of 61,000 women in Sweden born between 1914 and 1948
- Median follow-up: 19 years
- Calcium intake, supplements, etc. obtained from food frequency questionnaires at baseline (1987-1990) and 1997
- Compared with calcium intakes <1000 mg/day, intake >1400mg associated with significantly higher rates of deaths from all causes (HR: 1.4), cardiovascular disease (HR: 1.5), and ischemic heart disease (HR: 2.1), but not from stroke
- Vitamin D did not modify the associations.


Multivitamin and Mineral Supplements Are of No Benefit

Systematic review for USPSTF looking at studies of vitamin and mineral supplements for primary prevention of cardiovascular disease, cancer, or all-cause mortality
- None of the vitamin and mineral supplements had suggested benefit
- For vitamin E, good evidence of no benefit
- For beta-carotene, strong association between excess, lung cancer, and death

USPSTF = US Preventive Services Taskforce

Vitamin E Provides Little Benefit for Mild to Moderate Alzheimer’s Disease

Randomized controlled trial of 213 US veterans with mild to moderate Alzheimer’s Disease
- 2000 IU per day of Vitamin E vs Memantine vs Both vs Placebo
- All patients taking an acetylcholinesterase inhibitor at time of enrollment
- After 2.3 years on average,
  - Decline in ADL score was slightly less fast in the vitamin E group compared with placebo group (14 points vs. 17 points)
  - No benefit with combined therapy or memantine alone


Closing Lacerations in >12 Hours

Observational study of >2,500 patients with non-bite lacerations in 3 California emergency rooms
- Lacerations closed ≤12 hours vs Lacerations closed >12 hours
  - 30-day infection rate of 2.6% did not differ by time to closure or cause of laceration
  - More patients with head and neck lacerations presented <12 hours
  - More patients with extremity and torso lacerations presented >12 hours
  - Risk factors for wound infection: diabetes, lower extremity laceration, length >5 cm, and contaminated laceration
  - No benefit to prophylactic use of antibiotics for most lacerations


Changes After Massachusetts Health Care Reform

2006 Massachusetts health care reform law attained near-universal insurance coverage and increased access to care
- Mortality of adults in Mass 2001-2005 (pre-reform) vs 2007-2010 (post-reform) compared with changes in counties in other states
  - Reform 2.9% decrease in all-cause mortality with reform vs control group (P=0.005), which is absolute decrease of 8.2 deaths/100 000 adults
  - 4.5% decrease in deaths amenable to health care (P=0.001)
  - Larger changes in counties with lower household incomes and higher pre-reform uninsured rates
  - Number needed to treat: ≈ 830 adults gaining health insurance to prevent 1 death/year

End of Life Care and Hospice Use

Observational Study of Hospice Services 2000-2009

- Utilization increased from 22% to 42% of those who died.
- 60% of cancer patients and almost 50% of dementia patients were enrolled in hospice at time of death.
- Death in acute care hospital decreased from 33% to 25%.
- Deaths at home increased from 31% to 34%.
- Percent of patients with 3 or more hospitalizations during the last 3 months of life stayed the same (≈ 10%).
- More patients had stays in the ICU during the last month of life (24% in 2004 vs 29% in 2009).

Outcomes of Terminally Ill Cancer Patients Receiving Palliative Care

Analysis of 386 terminally ill adults with cancer who died within a median 4 months after study enrollment

Evaluated if chemotherapy within 30 days of death is beneficial

Patients who receive palliative chemotherapy (vs not) more likely to receive:
- "Life extending" care over comfort care (39% vs. 26%)
- CPR or mechanical ventilation or both during last week of life (14% vs. 2%)
- Feeding tubes during last week of life (11% vs. 5%)
- Late hospice referral (< 1 week prior to death) (54% vs. 37%)
- Survival duration did not differ between groups

Patients receiving palliative chemotherapy more likely to undergo invasive treatments but not survive any longer than patients not receiving palliative chemotherapy.

USPSTF Supports Routine HIV Screening

- Recommends HIV screening for all adolescents and adults aged 15-65 years, and younger adolescents and older adults who are at increased risk (i.e. those with new partners)
- Also recommends screening for all pregnant women
- Recommends repeat screening if high risk (i.e. multiple sexual partners or IV drug use).
- 20% of HIV infected people in the US are unaware of their infection

Summary: 2014 Top 10

- Marijuana Use Has Issues, esp Adolescents
- Peds Screening: HIV, CRAFFT, Depression
- Texting in Dangerous
- Viral Syndromes take longer than we think
- Suicide Rate is Up
- Anti-Virals → little benefit; start within 48 Hr
- Macrolides ↑ CV Risk

Summary: 2014 Top 10

- MOVE: After Meals, every 30 Minutes
- Statins & Diuretics ↑ risk: DM, Obesity
- Apples are = to Statins for 1° Prevention
- Ramipril for PAD
- Eggs and DIETARY Fiber ↓ CV Risk
- NO: Ca, MVA, Vitamin E
- No: “Palliative Chemotherapy”