Top 10: EBM Updates From The Medical Literature

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BLOG: http://www.ebpupdate.com/
Objectives:
By the end of this session, the learner will:

• Review a number of recent practice changing publications

• Understand Evidence Based Medicine are changing our methods of care

• Encourage a skeptical mindset toward the medical literature
Randomized trial of peanut consumption in infants at risk for peanut allergy.

• RCT of 640 infants (4-11 months) with Hx: severe eczema, egg allergy, or both
• Skin prick testing: divided by response: no wheal vs 1 to 4 mm wheal
• Consume vs avoid peanuts until 60 months of age.

• RESULTS:
  • Group Prevalence of peanut allergy at 60 months
  • Initially negative: Avoidance group 13.7% vs Consumption group 1.9% (P<0.001).
  • Initially positive: Avoidance group 35.3% vs Consumption group 10.6% (P=0.004).
  • No significant differences in serious adverse events.

• CONCLUSIONS:
  • Early introduction of peanuts significantly decreased the frequency of peanut allergy among high risk children.

↑in Celiac Disease Risk With Gluten Introduction After Age 6 Months: Systematic Review & Meta-Analysis

• SR & MA of 15 studies timing of gluten introduction and breastfeeding on the risk of developing celiac disease.

• CONCLUSION:

• 25% ↑ in Celiac Disease risk with late (>6 months) vs early (4-6 months) gluten introduction (risk ratio [RR], 1.25; 95% CI, 1.08-1.45).

• No effect of breastfeeding on CD risk (OR, 0.55; 95% CI, 0.28-1.10)

Royal Australian College of General Practitioners Feeding 1st year of life

- At ~ 6 months, (but not before 3), introduce solid foods, & continue breastfeeding

- Give allergenic solids: peanut butter, egg, dairy and wheat (US: FISH) in the first year of life, especially those at high risk of allergy

- Hydrolysed formulas are not recommended for prevention of allergic disease.

Infant Animal Exposure reduced Asthma Risk

• Swedish cohort study association between early exposure to dogs and farm animals and the risk of asthma in from 1/1/01 – 12/31/10

• **Dog exposure during the first year of life** → ↓** risk of asthma in school-aged children** (OR, 0.87; 95% CI, 0.81-0.93) and in ≥/≤ 3 years (HR, 0.90; 95% CI, 0.83-0.99) but **not in children < 3 years** (HR, 1.03; 95% CI, 1.00-1.07).

• **Farm animal exposure** → ↓** risk of asthma in both school-aged children and preschool-aged children** (OR, 0.48; 95% CI, 0.31-0.76, and HR, 0.69; 95% CI, 0.56-0.84), respectively.

• Tell Parents DOGS may lower asthma risk

*JAMA Pediatr.* 2015 Nov;169(11):e153219
2014
Child Poverty

“Reporting Nations”
To UNICEF

US 6th

https://www.unicef-irc.org/publications/733
AAP: Clinicians Should Screen Children for "Food Insecurity"

- ~ 20% of U.S. children live without consistent access to adequate food
- Clinicians should screen their patients/families for "food insecurity"
- Food-insecure homes → poorer overall health & more hospitalizations, and is associated with adverse cognitive, behavioral, and emotional outcomes.

A two-question screen
- 1. Within the past 12 mo, we worried whether our food would run out before we got money to buy more. (Yes or No)
- 2. Within the past 12 mo, the food we bought just didn’t last and we didn’t have money to get more. (Yes or No)

Resources for providers who identify food-insecure patients:
- 2-1-1: http://www.211.org/
- Food Hub: http://healthyfoodbankhub.feedingamerica.org/
- Ask your local congressperson

AAP Policy Statement: http://pediatrics.aappublications.org/content/136/5/e1431
“Reddit is an entertainment, social news networking service, and news website.” Reddit's community submits content. Registered users vote on submissions organizing posts to determine position on the pages → submissions with the most positive votes appear on the main page or the top of a category

--Reddit’s “StopDrinking” pages have > 30,000 subscribers, most of whom describe it as “their most helpful tool in their fight against alcohol.”
--StopDrinking has no coherent philosophy on addiction and recovery
--Volunteer led forum, including most important parts of an effective support program: daily check-ins, round-the-clock support, and activities like virtual book clubs that offer alternatives to social drinking.

https://www.washingtonpost.com/news/the-intersect/wp/2016/01/05/the-surprising-internet-forum-some-alcoholics-are-choosing-over-aa/
At what age do you Recommend Aspirin for $1^\circ$ Prevention

1. 40 Years
2. 50 Years
3. 60 Years
2016 USPSTF: Aspirin for Primary Prevention of ASCVD & CRC

• **50-59 Years**: Low-dose aspirin for primary prevention of CVD and CRC who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin for at least 10 years (B; net benefit moderate).

• **60-69 Years**: Low-dose aspirin for primary prevention of CVD and CRC in adults aged 60 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one. (C; net benefit small).

• **Younger than age 50 or over age 70**: The current evidence is insufficient to assess balance of benefits and harms of aspirin use for the primary prevention of CVD and CRC. (I; Insufficient)


To evaluate the benefits and harms of aspirin for the primary prevention of cardiovascular disease and all-cause mortality events in people with diabetes by conducting a systematic review and meta-analysis.

METHODS:
Randomized controlled trials of aspirin compared with placebo (or no treatment) in people with diabetes with no history of cardiovascular disease were identified from MEDLINE, EMBASE, Web of Science, the Cochrane Library and a manual search of bibliographies to November 2015. Study-specific relative risks with 95% CIs were aggregated using random effects models.

RESULTS:
A total of 10 randomized trials were included in the review. There was a significant reduction in risk of major adverse cardiovascular events 0.90 (95% CI 0.81-0.99) in groups taking aspirin compared with placebo or no treatment. Limited subgroup analyses suggested that the effect of aspirin on major adverse cardiovascular events differed by baseline cardiovascular disease risk, medication compliance and sex (P for interaction for all > 0.05). There was no significant reduction in the risk of myocardial infarction, coronary heart disease, stroke, cardiovascular mortality or all-cause mortality. Aspirin significantly reduced the risk of myocardial infarction for a treatment duration of ≤ 5 years. There were differences in the effect of aspirin by dosage and treatment duration on overall stroke outcomes (P for interaction for all < 0.05). There was an increase in risk of major or gastrointestinal bleeding events, but estimates were imprecise and not significant.

CONCLUSIONS:
The emerging data do not clearly support guidelines that encourage the use of aspirin for the primary prevention of cardiovascular disease in adults with diabetes who are at increased cardiovascular disease risk. This article is protected by copyright. All rights reserved.
Aspirin for Primary Prevention App

• Brigham and Women's Hospital: free app calculates risks & benefit of aspirin on 10 year atherosclerotic cardiovascular disease risk.

• This app, called Aspirin-Guide, is free.

• Input: Age, total and HDL-cholesterol, SBP, smoking status, and diabetes

• The app → the patient’s 10 year risk for cardiovascular events and bleeding risk.
Get guidance

Guidance: Advise low-dose aspirin (75-81 mg/d)

ASCVD Risk Score: 11.4% over 10 years without aspirin use.

Bleeding Risk Score: 1.2% over 10 years without aspirin use.

1 risk factor for increased risk of bleeding

• Male

Number Needed to Treat (NNT) with aspirin over 10 years to prevent one ASCVD event: 58

Number Needed to Harm (NNH): number needed to treat with aspirin over 10 years to result in one aspirin-related GI bleeding event: 144

Goal: NNT less than NNH (i.e., benefit is greater than harm)

For patients with this balance of benefits and risks of aspirin and who are willing to take long-term therapy, the decision should be guided by patient preferences and other factors.
Behavioral Activation Equivalent to CBT for Depression

- 221 Randomized to BA vs CBT; Rx controlled
- BA: Identify “LOOPS” of thought → Social Isolation → Depression
- **BA non-inferior to CBT** (PHQ-9: 8.4 vs 8.4, p=0.89)
- Adverse events > in CBT vs BA (non-sig)
- CBT-Advanced degree/training; **BA-no advanced training**

- BA, a simpler psychological treatment than CBT, can be delivered by lower cost providers

www.thelancet.com 7/22/16
Behavioral Activation

• **Methods:**

1. Track activities/mood x 1 week to Identify TRAP
2. "**TRAP**" (Trigger, Response, Avoidance Pattern)
   - ID **Depression Loop**: stressor → coping method →↑ depression → social withdrawal
3. Replace TRAP with **TRAC**
   (Trigger, Response, Alternative Coping Mechanism)
## TRAC
Trigger, Response, Alternative Coping

<table>
<thead>
<tr>
<th>Trigger</th>
<th>Response</th>
<th>Alternative Coping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upsetting event</td>
<td>Thoughts and feelings about the event</td>
<td>What can I do that is better than avoidance in the long term? How can I act in a way that is consistent with my values? What will be the best course of action to increase my wellbeing?</td>
</tr>
<tr>
<td>Boss Angry At Work</td>
<td>I made a mistake, I am worthless, etc.</td>
<td>--My work is normally good --Other reasons my boss is angry --My boss is outspoken; if I made a mistake, would have said so</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>What are the likely SHORT TERM consequences of my Alternative Coping plan?</th>
<th>What are the likely LONG TERM consequences of my Alternative Coping plan?</th>
</tr>
</thead>
<tbody>
<tr>
<td>--Worry Less</td>
<td>--Enjoy Work</td>
</tr>
<tr>
<td>--Sleep Better</td>
<td>--Be Self Sufficient &amp; in control</td>
</tr>
<tr>
<td>--Less Fatigue</td>
<td>--FEEL Better</td>
</tr>
</tbody>
</table>
Behavioral Activation Equivalent to CBT for Depression

- CBT-Advanced degree/training; BA-no advanced training
- 221 Randomized to BA vs CBT; Rx controlled
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www.thelancet.com 7/22/16

BA Apps:

Mood Coach (VA): Motivates + Activities
Moodivate (alone) &
Behavioral Apptivation (Therapist)
MoodTools (uses BA & CBT) → TRAC
iCBT (TRAP → TRAC, voice enabled)
Suicide Rate Increase

• Suicides in the U.S. increased 24% from 1999 to 2014
• National Center for Health Statistics:
  • 1999-2006, ~1%/year; 2006-14 ↑ 2% annually (recession)

• Suicide rate in *males was 3 times > in females* (20.7 vs 5.8 per 100,000).
• **AGE:** Highest in men > aged 75 and in women aged 45–64.
• **Children** (10–14) rates low, but had ↑ (200% in females, 37% in males)
• **Adolescents:** 65.1% Dx behavioral disorder, 26.3% mood disorder, 3.8% psychotic disorder, & 4.8% “other”

• **Most frequent Method**—**Men:** firearms; **Women,** poisoning.

Minority Young Adults Receive Much Less Mental Health Care

- Survey young adults 18-34 covering all 50 states during 2006-2012
- Black and Latino children: fewer psychiatrists visits (37%, 49%), fewer visits to any mental health professional (47%, 58%) than white children.
- Black children's low use of services was not due to lesser need.
  - Black and white children had similar rates of mental health problems, and similar rates of severity (psychiatric hospitalization or emergency visits). Hispanic slightly lower need.
- Substance abuse counseling black young adults 1/7 than whites.

- Groups at highest risk for incarceration -- black and Hispanic young men -- had low mental health visit rates.
  -- Department of Justice data > 50% of inmates suffer from mental illness, most untreated at time of arrest

*International Journal of Health Services; 2016*
DOI: 10.1177/0020731416662736
Text for **Help**: 741741

**Crisis Text Line**

- Non-Profit 24/7 texting service
- Top issues depression, anxiety, suicidal ideation, family issues, and romantic relationships, substance abuse, sexual health, sexual abuse, and eating disorders.

- Text how you feel to 741741 & trained Volunteer Crisis Counselor move “hot moment” to a cool moment

- > 80% of Texters < 25 Years
- ~ 30 Million Texts since 2013
- Ave: 10 “Active Rescues”/day

- Nancy Lubin TED talk
Active Rescue Data

Frequency of Active Rescues, by Month

Frequency of Active Rescues, by Day of Week

Frequency of Active Rescues, by Hour of Day
2009 Oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome

- **31 patients** with moderate OSAS: 3 months of daily (~30 min) sham therapy (n = 15, control) or a set of oropharyngeal exercises (n = 16)
- OP Exercises involving the tongue, soft palate, and lateral pharyngeal wall.

**Outcomes:**
- No significant change occurred in the control group in all variables.
- Oropharyngeal Exercise patients *significant decrease* \((P < 0.05)\) in:
  - Neck Circumference \((39.6 +/- 3.6 \text{ vs. } 38.5 +/- 4.0 \text{ cm})\),
  - Apnea-hypopnea index: \(22.4 +/- 4.8 \text{ vs. } 13.7 +/- 8.5 \text{ events/h}\)
  - Snoring Frequency, Snoring Intensity
  - Daytime Sleepiness, Sleep Quality

2015: Effects of Oropharyngeal Exercises on Snoring

- **RCT** over 3 months of **39 patients**; Control: nasal dilator strips plus respiratory exercises vs. Intervention: oropharyngeal (OP) exercises.
- Both groups were similar at study entry.
- No significant changes occurred in the control group.

- Compared to Control OP Exercise group had significant **decrease** in
  - **Snore Index**: 99.5 (49.6-221.3) vs 48.2 (25.5-219.2); \( P = .017 \) and
  - **Total snore index** (total power of snore/h), 60.4 (21.8-220.6) vs 31.0 (10.1-146.5); \( P = .033 \)

- **CONCLUSIONS**: “Oropharyngeal exercises are effective in reducing objectively measured snoring and are a possible treatment of a large population suffering from snoring.”

- *Chest. 2015;148(3):683-691*
2015 SR & Meta Analysis on Oro-Pharyngeal Exercises for OSA

• 9 studies exercises on snoring and/or sleepiness
• Apnea-hypopnea indices (AHI) ↓ from $24.5 \pm 14.3/h$ to $12.3 \pm 11.8/h$, $P < 0.0001$.
• *Lowest O2 saturations* improved from $83.9 \pm 6.0\%$ to $86.6 \pm 7.3\%$, MD $4.19\%$ (95% CI 1.85, 6.54), $P = 0.0005$.
• Snoring ↓ $14.05\% \pm 4.89\%$ to $3.87\% \pm 4.12\%$ of total sleep time, $P < 0.001$
• *Epworth Sleepiness Scale* decreased from $14.8 \pm 3.5$ to $8.2 \pm 4.1$.

• **CONCLUSION:**
  • Current literature demonstrates that OP exercises ↓ apnea-hypopnea index by ~50%. Low O2 saturation, snoring, and sleepiness outcomes improve in adults.

  • Sleep. 2015 May 1;38(5):669-75. doi: 10.5665/sleep.4652.
Snoring Exercise

1) push the tip of the tongue against the hard palate and slide the tongue backward (20 times)

2) suck the tongue upward against the palate, pressing the entire tongue against the palate (20 times)

3) force the back of the tongue against the floor of the mouth while keeping the tip of the tongue in contact with the inferior incisive teeth (20 times)

4) elevation of the soft palate and uvula (20 times)

5) recruitment of the buccinator muscle against the finger that is introduced in the oral cavity, pressing the buccinator muscle outward (10 times each side)

6) alternate bilateral chewing and deglutition using the tongue in the palate, without perioral contraction, whenever feeding.

Say “AAAAA”
Type 2 Diabetes Mellitus
### Monotherapy
- **Efficacy**: high
- **Hypo risk**: low risk
- **Weight**: neutral/loss
- **Side effects**: GI/lactic acidosis
- **Costs**: low

**Metformin**

If HbA1c target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

<table>
<thead>
<tr>
<th>Metformin</th>
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<tbody>
<tr>
<td>Sulfonlurea</td>
<td>Thiazolidinedione</td>
<td>DPP-4 inhibitor</td>
<td>SGLT2 inhibitor</td>
<td>GLP-1 receptor agonist</td>
</tr>
<tr>
<td>high</td>
<td>high</td>
<td>intermediate</td>
<td>intermediate</td>
<td>high</td>
</tr>
<tr>
<td>moderate risk</td>
<td>low risk</td>
<td>low risk</td>
<td>low risk</td>
<td>highest</td>
</tr>
<tr>
<td>gain</td>
<td>gain</td>
<td>edema, HF, fxs</td>
<td>neutral</td>
<td>high</td>
</tr>
<tr>
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<td>edema, HF, fxs</td>
<td>rare</td>
<td>GU, dehydration</td>
<td>high</td>
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<tr>
<td>low</td>
<td>low</td>
<td>low</td>
<td>low</td>
<td>cost</td>
</tr>
</tbody>
</table>

### Dual Therapy
- **Efficacy**: high
- **Hypo risk**: moderate risk
- **Weight**: gain
- **Side effects**: hypoglycemia
- **Costs**: variable

If HbA1c target not achieved after ~3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

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<td>low</td>
<td>low</td>
<td>low</td>
<td>cost</td>
</tr>
</tbody>
</table>

### Triple Therapy
- **Metformin**
- **Sulfonylurea**
- **TZD**
- **Insulin**

If HbA1c target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables; (2) on GLP-1-RA, add basal insulin; or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-2.

**Basal insulin + Mealtime insulin or GLP-1-RA**

Source: American Diabetes Association
Recommendations for Antihyperglycemic Therapy in Type 2 Diabetes

Lifestyle changes: healthy eating, weight control, increased physical activity, diabetes education

Monotherapy
- Metformin

If A1C target not achieved after 3 months of monotherapy, proceed to:
- Metformin + Sulfonylurea
- Metformin + TZD
- Metformin + GLP-1 RA
- Metformin + DPP-4 inhibitor
- Metformin + SGLT2 inhibitor
- Metformin + Insulin (basal)

Dual therapy

If A1C target not achieved after 3 months of dual therapy, proceed to:
- Metformin + SU + TZD or DPP-4 or GLP-1 or insulin
- Metformin + TZD + SU or DPP-4 or GLP-1 or insulin
- Metformin + GLP-1 RA + SU or TZD or insulin
- Metformin + DPP-4 inhibitor + SU or DPP-4 or TZD or insulin
- Metformin + SGLT2 + SU or DPP-4 or TZD or insulin
- Metformin + Insulin (basal) + TZD or DPP-4 or GLP-1

Triple therapy

If A1C target not achieved after 3 months of triple therapy and patient (1) on oral combination, move to injectables; (2) on GLP-1, add basal insulin; or (3) on optimally titrated basal insulin, add GLP-1 or mealtime insulin. Refractory patients: consider adding TZD or SGLT2.

Combination injectable therapy
- MET + Basal insulin + Mealtime insulin or GLP-1

*Consider initial therapy at this stage with A1C ≥9.0%; †Consider initial therapy at this stage with PG ≥300-350 mg/dL and/or A1C ≥10-12%; ‡Usually a basal insulin

Tight control T2DM & Outcomes

- Meta Analysis of 19 RCT’s (~ 85,000)
- Compared with standard care vs intensive treatment:
  - Intensive -> ↓ risk of Non-fatal MI [(RR) 0.90, CI: 0.83-0.96]
  - BUT NOT:
  - Non-fatal stroke (RR 0.96, CI 0.86-1.07), CV mortality (RR 1.00, CI 0.90-1.11) or All-cause mortality (RR 1.00, CI 0.94-1.06)

2016 Review of Reviews: “No significant impact of tight glycemic control”

• Searched top general medicine and specialty journals on glycemic control 2006 - 2015
• Included all published systematic reviews and meta-analyses of randomized trials of glycemic control & 16 guidelines & 328 “statements”
• “evidence reported no significant impact of tight glycemic control”

Circ Cardiovasc Qual Outcomes. 2016;9:00-00.
Approach to the management of hyperglycemia

<table>
<thead>
<tr>
<th>PATIENT / DISEASE FEATURES</th>
<th>more stringent</th>
<th>HbA$_{1c}$ 7%</th>
<th>less stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks potentially associated with hypoglycemia and other drug adverse effects</td>
<td>low</td>
<td>high</td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>newly diagnosed</td>
<td>long-standing</td>
<td></td>
</tr>
<tr>
<td>Life expectancy</td>
<td>long</td>
<td>short</td>
<td></td>
</tr>
<tr>
<td>Important comorbidities</td>
<td>absent</td>
<td>few / mild</td>
<td>severe</td>
</tr>
<tr>
<td>Established vascular complications</td>
<td>absent</td>
<td>few / mild</td>
<td>severe</td>
</tr>
<tr>
<td>Patient attitude and expected treatment efforts</td>
<td>highly motivated, adherent, excellent self-care capacities</td>
<td>less motivated, nonadherent, poor self-care capacities</td>
<td></td>
</tr>
<tr>
<td>Resources and support system</td>
<td>readily available</td>
<td>limited</td>
<td></td>
</tr>
</tbody>
</table>

Source: American Diabetes Association
Which Drug Class, after Metformin, Produces Lower M/M for T2DM?

1. DPP-4 inhibitors
2. GLP-1 agonists
3. SGLT-2 inhibitors
4. TZD’s
5. Insulin
6. None of Them
2016 AHRQ Review on Efficacy of Medications for T2DM

- **Summary:** Metformin drug of choice for Type 2 DM
  2nd choice: based on your and patient preference
  (no 2nd line agents has M/M outcome benefits)

- **Drugs that had no adverse effect body weight:**
  Metformin, DPP-4 Inhib., GLP-1 agonists, SGLT-2 Inhib

- **Drugs that increased weight:** Sulfonylureas,
  Thiazolidinediones, and insulin (from 1-5 kg.)

- Evidence did not support “substantive conclusions for microvascular outcomes, CHF, cancer, pancreatitis, or other safety concerns from aggressive A1c control.”

- **Ref:** Medications for Adults with Type 2 Diabetes: AHRQ: 2016 April. Report #16-EHCO13-EF

2016 ADA Guidelines

- **Screening for T2DM**: all age \( \geq 45 \), hypertension, on atypical anti-psychotics or HIV medications, those with \( BMI \geq 25 \) or, if of Asian descent, at \( BMI \geq 23 + 1 \text{ CVD RF} \)

- **Hemoglobin A1c frequency**: The ADA “should depend on the clinical situation” and at least twice a year and quarterly if therapy has been changed.

- **Glucose Self Monitoring**: Patients on “intensive insulin regimens” or those on an insulin pump should consider testing pre-prandial. “Evidence is insufficient to determine when to prescribe SMBG.” No evidence on frequency.

- **Lipids**: ADA supports AHA recommendations on statin using 10 year risk calculator.

- **Aspirin**: For both women and men, low dose (82 milligrams per day) of aspirin therapy over the age of 50 for the primary prevention of heart disease when the atherosclerotic cardiovascular risk is greater than 10%. For both T1DM & T2DM.

- **Hypertension**: The ADA’s current goal is a systolic < 140, and a diastolic <90. 1\textsuperscript{st} line: ACEi or ARB (but not both) 2\textsuperscript{nd}: Thiazides. **Lower systolic pressures are not currently evidence based.**

2016 ADA Guidelines: Rx

- **Metformin 1**\(^{st}\) line for all

- **2**\(^{nd}\) Line:
  - **DDP 4 inhibitors** \(\uparrow\) *incretin activity, which \(\downarrow\) glucagon release that leads to \(\uparrow\) insulin secretion, & \(\downarrow\) gastric emptying*; (alogliptin (Nesina), linagliptin (Tradjenta), sitagliptin (Januvia), saxagliptin (Onglyza))

- **GLP 1 agonists** \(\uparrow\) insulin secretion, \(\downarrow\) glucagon secretion, and \(\downarrow\) gastric emptying; (albiglutide (Tanzeum), exenatide (Byetta/Bydureon), dulaglutide (Trulicity), liraglutide* (Victoza)& (Saxenda--for weight loss w/o diabetes)

- **SGLT-2 inhibitors** \(\uparrow\) glucose excretion in the urine; (canagliflozin (Invokana), dapagliflozin (Farxiga), empagliflozin (Jardiance))

- **3**\(^{rd}\) Line: Long acting and regular insulin, sulfonylureas, (SU), and thiazolidinedione (TZD) can be added, but no morbidity and mortality benefit & may \(-\rightarrow\) harm.

- **SURGERY:** “Bariatric surgery considered for adults whose BMI is \(>35\) kg/m\(^2\)”

Hydration (Urine) & Obesity
“Drinking water makes you thin?”

- 9,500 adults BMI & Hydration status using National Health and Nutrition Examination Survey (NHANES) 2009 to 2012; 18 to 64
- Urine osmolality $\geq 800$ mOsm/kg “inadequately hydrated” (~ SG = 1.020).
  Models were adjusted for confounders including age, race/ethnicity, sex, and income-to-poverty ratio.
- 50.8% women, 64.5% non-Hispanic white, mean age 41 years.
- 32.6% of the sample was inadequately hydrated.
- Inadequately hydrated correlated with higher BMIs (1.32 kg/m$^2$; 95% CI, 0.85–1.79; $P < .001$) and higher odds of being obese (OR = 1.59; 95% CI, 1.35–1.88; $P < .001$) compared with hydrated adults.

- Ann Fam Med July/August 2016 vol. 14 no. 4 320-324
2014 World “More dangerous than it has ever been”
Martin Dempsey, Chair Joint Chiefs
Terrorism: the use of violence and intimidation in the pursuit of political aims.

- San Bernardino
- Orlando
- Nice
- Paris
- Syria
Percentage of years in which the ‘Great Powers’ fought one another, 1500-2015 – by Max Roser

Between 1500 and today there were more than 50 wars between ‘Great Powers’. Data are aggregated over 25-year periods.

The Great Powers:
- Entire period – France and England/Great Britain/U.K.
- Since 1949 – China
- Since 1898 – USA
- Since 1740 – Germany/Prussia
- Since 1721 – Russia/USSR
- 1905 to 1945 – Japan
- 1861 to 1943 – Italy
- 17th and early 18th century – the Netherlands and Sweden
- Until 1918 – all entities ruled by the Habsburg dynasty
- Until 1808 – Spain
- Until 1699 – the Ottoman Empire

Wars between Great Powers:
(Complete list includes > 50 wars)

- Thirty Years’ War (1618–48; 6 of the 7 great powers)
- Dutch War of Louis XIV (1672–78; 6 of 7 Great Powers)
- War of the Spanish Succession (1701–13; 5 of 6)
- War of the Austrian Succession (1739–48; 6 of 6)
- Seven Years’ War (1755–63; 6 of 6)
- First World War (1914–18)
- Second World War (1939–45)

A Safer World

The number of people who have died in wars has declined sharply since the 20th century.

Battle-related deaths per 100,000 people*

Sources: U.S., FBI Uniform Crime Reports. England (including Wales): U.K. Office for National Statistics. World: U.N. Office on Drugs and Crime, reported in U.N. Economic and Social Council's "World crime trends and emerging issues and responses in the field of crime prevention and social justice," Feb. 12, 2014, Figure 1. The percentages were converted to homicide rates by setting the 2012 rate at 6.2, the figure reported in the UNODC Global Study on Homicide 2013, Page 12.
Reported violent crime rate in the United States from 1990 to 2014

Source:
FBI
© Statista 2015

Additional Information:
United States: 1990 to 2014
RAPE/SEXUAL ASSAULT AND VIOLENCE AGAINST INTIMATE FEMALE PARTNERS IN THE US
1993-2013

Source: Bureau of Justice Statistics (bjs.gov), using the National Crime Victimization Survey Victimization Analysis Tool
**Perspective**

- **2005-2015:**
  - 71 US Killed Terrorism
  - > 301,000 US Killed by Gun Violence
  - --40% “Crime related”

- **2015:**
  - 7 Children/Teens Killed by guns/DAY
  - A Toddler shoots someone every 7 days
  - 31% Kill self, 5% kill others
  - 40% injure self, 24% injure others

Ref: CDC: 2015

- **Screen Kids, Teens, Encourage Safety**
FDA Updated 2014: Long-Term Clopidogrel Does NOT Affect Mortality Rates in Heart Patients

• DAPT: Dual Anti Platelet Therapy—(clopidogrel (Plavix) + aspirin)

• The incidence of death for clopidogrel plus aspirin for 12 months or longer was ~ same as for \( <= 6 \) months (~7%).

• Long-term treatment on does not change overall risk for death with NO increase in cancer risk with DPAT

American Heart Association & American College of Cardiology Guidelines on Duration Dual AntiPlatelet Therapy (DAPT) in CAD

• DAPT —> “a tradeoff between ↓ ischemic risk and ↑ bleeding risk”

• Stable ischemic heart disease (SIHD) & drug-eluting stent (DES): DAPT x 6 months

• SIHD w/bare-metal stent (BMS), DPAT for a minimum of 1 month

• CABG, DPAT complete 12 months of therapy after ACS

• STEMI treated with fibrinolytic therapy, DPAT for a minimum of 14 days and ideally 12 months

• Aspirin (81 mg daily) should be continued indefinitely in CAD

• *J Am Coll Cardiol.* 2016();. doi:10.1016/j.jacc.2016.03.513
Stress Testing as Effective as CT Angiography

- 10,000 patients with new onset chest pain were evaluated by either **functional testing or CT Angiography (CTA)**; test based up the discretion of the providers.
- **Functional Testing**: 67% underwent nuclear stress testing, 22% under stress echo, and 10% under stress electro-cardiography.
- At 25 months, **primary endpoint** (death, MI, hospitalization for unstable angina or major complication) occurred in 3.3% of the CTA group vs. 3.0% of the functional testing group, a non-significant difference.

**Outcomes:**

<table>
<thead>
<tr>
<th></th>
<th>CTA</th>
<th>Functional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint</td>
<td>3.3%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Invasive angiography</td>
<td>12.2%</td>
<td>8.1%</td>
</tr>
<tr>
<td>Revascularization</td>
<td>6.2%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Normal catheterizations</td>
<td>3.4%</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

Radiation exposure was significantly higher in the CTA group.

*NEJM 2015. March 14*
Which Functional Test to Use? Statistics (ARG)

<table>
<thead>
<tr>
<th>Test Score:</th>
<th>The Truth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Has the disease</td>
</tr>
<tr>
<td></td>
<td>True Positives (TP)</td>
</tr>
<tr>
<td></td>
<td>a</td>
</tr>
<tr>
<td>Negative</td>
<td>False Negatives (FN)</td>
</tr>
<tr>
<td></td>
<td>c</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>TP</td>
<td>TN</td>
</tr>
<tr>
<td>TP + FN</td>
<td>TN + FP</td>
</tr>
<tr>
<td>a</td>
<td>d</td>
</tr>
<tr>
<td>a + c</td>
<td>d + b</td>
</tr>
</tbody>
</table>

PPV = \( \frac{TP}{TP + FP} \)

NPV = \( \frac{TN}{TN + FN} \)
Choosing A Cardiac Test

• Exercise Stress Test (ETT) Sn/Sp = 68/75  **LOW RISK**
  PRO: Assessment of exercise capacity; Cost effective
  CON: Lowest sensitivity of all stress tests; risk of false negative test, lower accuracy in women

• Stress (exercise) Echocardiography Sn/Sp = 83/85  **MODERATE RISK, Female**
  PRO: Assessment of exercise capacity, cardiac structure/function, No radiation, High specificity, better accuracy in women
  CON: False negatives in single vessel/circumflex ischemia

• Nuclear Perfusion Stress Test Sn/Sp = 87/73  **MODERATE RISK**
  PRO: Exercise capacity can be assessed, High sensitivity
  CON: Radiation, False + due to higher sensitivity/ diaphragmatic attenuation

• CT coronary angiography Sn/Sp = 88/85
  PRO: High negative predictive value (especially in low-intermediate risk)
  CON: Radiation, Functional effect of disease & exercise capacity not assessed

Ref:  J Am Soc Echocardiogr. 2011 Mar;24(3):229-67,
Do No Harm
Understanding **Over-diagnosis**

How Mammography Increases Dx of Cancer, But Does Not Decrease Mortality

- **Over-diagnosis**: Screening $\rightarrow$ ↑rate of cancer diagnosis but have no positive effect on patient’s health or mortality.
- Retrospective cohort > 16 million women ≥ 40 years of age.
- 55,000 (0.35%) were diagnosed with breast cancer; 10 year follow-up for 95%.
- Each 10% increase in rate of *breast cancer screening* was associated in an increase in breast cancer diagnosis RR=1.16; 95% CI: 1.13-1.19.
- No decrease in 10 year breast cancer mortality was found.
- The majority of cancers Dx were considered “small” (≤ 2cm); $\rightarrow$ increase in stage 0-2 breast cancer diagnosis
- But no change in stage 3-4 breast cancer.
- Large screening programs do not decrease diagnosis of more dangerous tumors & have no impact on mortality BUT have a significant *increase* in diagnostic morbidity (biopsies, repeat imaging, angst).

*JAMA Inter Med.* 2015; July 6 [epub]
Pain
2012: 259 Million Opioid Rx
1 Rx for every adult in the United States

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016
Recommendations and Reports / March 18, 2016 / 65(1);1–49
2012 CDC: Death from All Substances

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Recommendations and Reports / March 18, 2016 / 65(1);1–49
Opioid Overdose Survivors Receive Repeat Opioid Rx

- 2,848 Adults with nonfatal opioid OD
- Stratified by morphine-equivalent dosage (MED)
  - Large (≥100 mg), Moderate (50 to <100 mg), Low (<50 mg)

- Time to repeated overdose
  - At 299 days, opioids dispensed to 91% of patients after overdose
  - 7% (n = 212) had a repeat opioid overdose.

- At 2 years, the incidence of repeated overdose was:
  - Large MED: 17% (95% CI, 14% to 20%)
  - Moderate MED: 15% (CI, 10% to 21%)
  - Low MED: 9% (CI, 6% to 14%)

True or False?
I know how to Prescribe Naloxone for My Patients on Chronic Opioids

1. True
2. False
# Naloxone

<table>
<thead>
<tr>
<th>Brand name</th>
<th>Injectable (and intranasal- IN) generic&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Intranasal branded&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Injectable generic&lt;sup&gt;3&lt;/sup&gt;</th>
<th>Injectable generic&lt;sup&gt;4&lt;/sup&gt;</th>
<th>Auto-injector branded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Narcan Nasal Spray</td>
<td>X (for IV, IM, SC)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Evzio Auto-Injector</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

## Product comparison

<table>
<thead>
<tr>
<th>FDA approved</th>
<th>Layperson experience</th>
<th>Assembly required</th>
<th>Fragile</th>
<th>Can titrate dose</th>
<th>Strength</th>
<th>Total volume of kit/package</th>
<th>Storage requirements</th>
<th>Cost/kit&lt;sup&gt;4&lt;/sup&gt;</th>
<th>Refills</th>
</tr>
</thead>
<tbody>
<tr>
<td>X (for IV, IM, SC)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>1 mg/mL</td>
<td>4 mg/0.1 mL</td>
<td>Store at 59-86 °F Fragile: Glass.</td>
<td>$</td>
<td>Two</td>
</tr>
<tr>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>4 mg/0.1 mL</td>
<td>4 mg/10 mL</td>
<td>Store at 59-77 °F Excursions from 39-104 °F</td>
<td>$</td>
<td>Two</td>
</tr>
<tr>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>0.4 mg/mL</td>
<td>0.8 mg/2 mL</td>
<td>Store at 68-77 °F Breakable: Glass.</td>
<td>$</td>
<td>Two</td>
</tr>
<tr>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>0.4 mg/0.4 mL</td>
<td>0.8 mg/0.8 mL</td>
<td>Store at 59-77 °F Excursions from 39-104 °F</td>
<td>$</td>
<td>Two</td>
</tr>
</tbody>
</table>

## Prescription variation

- **Cost/kit<sup>4</sup>:**
  - $ for Injectable (and intranasal- IN) generic
  - $ for Intranasal branded
  - $ for Injectable generic
  - $ for Injectable generic
  - $ for Auto-injector branded

- **Refills:**
  - Two for Injectable (and intranasal- IN) generic
  - Two for Intranasal branded
  - Two for Injectable generic
  - Two for Injectable generic
  - Two for Auto-injector branded

---

*PrescribeToPrevent.org*  
**January 21, 2016**
<table>
<thead>
<tr>
<th>Rx and quantity</th>
<th>Injectable (and intranasal-IN) generic¹</th>
<th>Intranasal branded²</th>
<th>Injectable generic³</th>
<th>Injectable generic</th>
<th>Auto-injector branded</th>
</tr>
</thead>
<tbody>
<tr>
<td>#2 2 mL Luer-Jet™ Luer-Lock needleless syringe plus #2 mucosal atomizer devices (MAD-300)</td>
<td>#1 two-pack of two 4 mg/0.1 mL intranasal devices</td>
<td>#2 single-use 1 mL vials OR #1.10 mL multidose vial PLUS #2 3 mL syringe w/ 23-25 gauge 1-1.5 inch IM needles</td>
<td>#2 single-use 1 mL vials PLUS #2 3 mL syringe w/ 23-25 gauge 1-1.5 inch IM needles</td>
<td>#1 two-pack of two 0.4 mg/0.4 mL prefilled auto-injector devices</td>
<td></td>
</tr>
<tr>
<td>Sig. (for suspected opioid overdose)</td>
<td>Spray 0.1 mL into one nostril. Repeat with second device after 2-3 minutes if no or minimal response.</td>
<td>Inject 1 mL in shoulder or thigh. Repeat after 2-3 minutes if no or minimal response.</td>
<td>Inject 1 mL in shoulder or thigh. Repeat after 2-3 minutes if no or minimal response.</td>
<td>Inject into outer thigh as directed by English voice-prompt system. Place black side firmly on outer thigh and depress and hold for 5 seconds. Repeat with second device in 2-3 minutes if no or minimal response.</td>
<td></td>
</tr>
</tbody>
</table>

**Ordering information**

| How supplied | Box of 10 Luer-Jet™ prefilled glass syringes | Two-pack of single use intranasal devices | Box of 10 single-dose flip-top vials (1 mL) OR Case of 25 multi-dose flip-top vials (10 mL) | Box of 10 single-dose flip-top vials | Two pack of single use auto-injectors + 1 trainer |
| Manufacturer | IMS/Amphastar | Telexfl (IN adapter) | Adapt Pharma | Hospira | Mylan |
| Web address | Amphastar.com | Teleflex.com | Narcannasalspray.com | Hospira.com | Mylan.com |
| Customer service | 800-423-4136 | 866-246-6990 | 844-462-7226 | 877-946-7747 | 724-514-1800 |
| NDC | 76329-3369-01 | DME-no NDC | 69547-353-02 | 00409-1215-01 (1 mL) 00409-1219-01 (10 mL) | 67457-0292-02 |
| ¹ IMS/Amphastar has an additional naloxone product, which is not recommended for layperson and take-home naloxone use because it is too strong of a dose by injection only for laypersons. (Naloxone HCl Injection, USP, 2mg/2ml Min-i-Jet Prefilled syringe with 21 Gauge and 1 ½” fixed Needle NDC # 76329-1469-1 (10 pack) and 76329-1469-5 (25 pack))

² As of 1/12/16, Narcan Nasal Spray has been approved by the FDA, but is not yet publicly available.

³ Hospira has an additional naloxone product, which is not recommended for layperson and take-home naloxone use because it is complicated to assemble. (Naloxone Hydrochloride Injection, USP, 0.4 mg/mL Carpuject™ Luer Lock Glass Syringe (no needle) NDC# 0409-1782-69)

⁴ There is considerable price variance for each product- local pharmacists are able to provide specific local pricing.

⁵ Product and co-pay coupons are available- visit manufacturer website for more information.

Image development supported by 1R01DA038082-01 Friedmann/Rich

PrescribeToPrevent.org

January 21, 2016
Antibiotics Given More Than Wanted

- MMWR survey of US consumers & 1500 healthcare providers
- >50% of healthcare providers believe patients expect antibiotics during a visit for a viral illness
- ~25% of consumers actually expect them
- 20% of consumers obtained Antibiotic Rx from source others (grocery stores, friends & family, or leftovers from a previous illness)

MMWR / July 24, 2015 / Vol. 64 / No. 28
CDC: 1/3 of Out Patient Antibiotic Rx “Inappropriate”

- CDC 184,000 ambulatory care visits 2010–2011 national antibiotic Rx rates

- 506 antibiotic Rx/1000 patients annually; 353 were deemed “appropriate”

- Respiratory infections (e.g., URI) accounted for 221 antibiotic Rx/1000, but just 111/1000 were appropriate (1/10)

- Sinusitis (56 antibiotic Rx), otitis media (47 antibiotic Rx), then pharyngitis (43 antibiotic Rx)

- JAMA. 2016;315(17):1864-1873

- HARM: C. diff, Diarrhea, ↑ Rx in Future...
  Children with ABX exposure < 2 Yr have greater risk of childhood obesity and T2DM risk

Gastroenterology; 2016, 151(1): 120–129.e5
Best Evidence Antibiotic Guidelines

• **Sinusitis**: (A.A.of Otolaryngology(AAO-HNSF))
  – Viral rhinosinusitis S/S last < 10 days and do not worsen
  – Acute bacterial rhinosinusitis S/S last > 10 days, or worsen within 10 days after initial improvement (double worsening)

• **Otitis Media** (AAFP Practice Guideline 2013):
  • Pain control
  • **6 - 24 months**: Antibiotics for severe S/S *(moderate or severe otalgia/otalgia for > 48 hours or T >/=39°C [102.2°F])* OR
  • Antibiotic for **bilateral** AOM
  • **For nonsevere unilateral AOM** 6 - 24 months, or non-severe AOM (either unilateral or bilateral) *in >24 months, antibiotic therapy OR observation* offered with close follow up
Pharyngitis: Modified Centor Criteria

• Tonsillar exudate or erythema: +1 point
• Anterior cervical adenopathy: +1 point
• **Cough absent:** +1 point
• Fever present: +1 point
• Age 3 to 14 years: +1 point
• Age 15 to 45 years: 0 points
• Age over 45 years: -1 points
• Just Centor misses < 20% GABHS presence

![AAHHH!!]

**Score**
- 4 to 5: Treat with antibiotics
- 2 to 3: Perform rapid antigen test
  - Antigen positive: Treat w/ antibiotics
  - Antigen negative: → Sympt Tx.
- 0 to 1: Symptomatic Treatment

How to NOT Give Antibiotics

1. **Identify patient’s (parent) concern.** “What are you worried about & what do you think you may need?”

2. **Verbalize your exam.** State out loud: “Ears are normal, throat is a little red, lungs are clear... I suspect you have a viral infection that will resolve in a few days.” (Patient Educ Couns (2010), doi:10.1016)

3. **Delay of antibiotic Rx.** most studied and effective method. Tell your patients: *I suspect you have a viral infection which will get better over next 7-10 days. If you are not **improving** by Friday morning, call office and I **may** call in an Rx.*

How NOT to Give Antibiotics

4. **Symptom control.** Very best evidence offers:

   --Fever/aches: *Acetaminophen* (15 mg/kg) PLUS an *NSAID* like Ibuprofen (10 mg/kg) **together** every 6 hours (alternating doses ↑ risk of overdose)

   --Nasal Congestion & Cough due to post nasal drip:
       Oral or nasal decongestants.

   --Cough not due to post nasal drip:
   Honey alone or mixed w/lemon juice, every hour or two

   --To shorten viral URI Duration:
       Zinc *Acetate* Lozenges q 4 hours
       Pelargonium sidoides (Alcohol based preparations) 30 gtts TID

5. What does NOT work: antibiotics for: URI’s, bronchitis, sinusitis; cough medications (including codeine), Echinacea, Vitamin C, anti-histamines
Zinc Lozenges: Meta Analysis

- 3 RCTS on zinc acetate (75 mg/d) lozenges for common cold
- Zinc acetate lozenges shortened duration of:
  - Illness by > 24 hours
  - Nasal discharge by RRR=34% (95% CI: 17% to 51%),
  - Nasal congestion 37% (15% to 58%), Scratchy throat 33% (8% to 59%), Cough by 46% (28% to 64%), Myalgia by 54% (18% to 89%)
  - There was no difference in the duration of headache and fever.
  - Zinc Lozenge at least 4/day, dissolved in mouth

BMC Fam Pract. 2015; 16: 24
doi: 10.1111/bcp.13057
Cochrane DSR; 2013
Jun 18;(6):CD001364
Practice Changers
Stop ICS’s in COPD

• **Methods:** > 100,000 patients w/COPD on inhaled corticosteroids (ICS) x 5 five years
• Compared “severe pneumonia” and ICS use.

• **Outcomes:** 14,000 developed “severe pneumonia”

• **Patients who stop their ICS had ↓ rate Pneumonia**
  (rate ratio [RR], 0.63; 95% CI, 0.60-0.66) vs those on ICS.
• Stopping ICS → Risk ↑ 4 months after stopping

• **Conclusions:** COPD patients on chronic ICS were at higher risk of developing pneumonia than those not; **Stop if able**

Ref: Chest 2015; 148: 1177
Single Dose Dexamethasone Not Inferior to Prednisone in Mild to Moderate Asthma

• **Methods:** RCT~ 380 adult patients
  Dexamethasone 12 mg (two 6 mg tablets) x 1 dose vs
  Prednisone 60 milligrams/day x 5 days.
  Outcomes evaluated by telephone at 2 weeks.

• **Outcomes:**
  • Relapse in Dex 12.1% vs 9.8% in Pred (non-inferior)
  • Hospitalization relapse 3.4% in Dex vs 2.9% Pred (NS)
  • Adverse effects were the same in both groups.

• **Conclusion:** Single dose of oral Dext 12 mg not
  inferior to 5 days of prednisone at 2 weeks

Prednisone for Gout

• **Design:** RCT indomethacin (50 tid) or prednisolone (30 mg/d) for acute Gout PAIN in ED/Hong Kong (Colchicine not used)

• **Results:** Equivalent & significant reductions in mean pain score @rest & w/Activity w/indomethacin and prednisolone in ED & on Days 1 to 14

• No major adverse events

• **Conclusion:** Oral prednisolone and indomethacin had similar pain relief in acute gout.

Mean pain scores and 95% CIs at each assessment (n=376).

Data were analyzed per protocol. The means and 95% CIs of the coefficients (slopes) of change in pain over unit time for patients in each group were compared using the t test. A. Pain score at rest in the emergency department phase. We found no statistically or clinically significant differences between groups (P = 0.69). The mean decrease in pain score was 6.54 mm/h (95% CI, 5.02 to 8.06 mm/h) for indomethacin and 5.05 mm/h (CI, 3.56 to 6.55 mm/h) for prednisolone (mean difference, −1.49 mm/h [CI, 0.64 to −3.61 mm/h]). B. Pain score with activity in the emergency department phase. We found no statistically or clinically significant differences between groups (P = 0.56). The mean decrease in pain score was 11.69 mm/h (CI, 10.10 to 13.28 mm/h) for indomethacin and 11.38 mm/h (CI, 9.98 to 12.79 mm/h) for prednisolone (mean difference, −0.31 mm/h [CI, 1.80 to −2.42 mm/h]). C. Pain score at rest from days 1 to 14. We found no statistically or clinically significant differences between groups (P = 0.80). The mean decrease in pain score was 1.80 mm/d (CI, 1.46 to 2.13 mm/d) for indomethacin and 1.68 mm/d (CI, 1.39 to 1.97 mm/d) for prednisolone (mean difference, −0.12 mm/d [CI, 0.32 to −0.55 mm/d]). D. Pain score with activity from days 1 to 14. We found no statistically or clinically significant differences between groups (P = 0.20). The mean decrease in pain score was 2.96 mm/d (CI, 2.62 to 3.30 mm/d) for indomethacin and 3.19 mm/d (CI, 2.85 to 3.52 mm/d) for prednisolone (mean difference, 0.22 mm/d [CI, 0.70 to −0.25 mm/d]).

Figure Legend:
Vitamin B3 and Skin Cancer

- RCT 386 immune competent with ≥ 2 NMSC of oral nicotinamide 500mg bid (NIC) or placebo (PBO) for 12 months in Australia
- Mean age 66 years, and 63% were men.
- Outcomes:
  - NMSC rate sig lower for NIC (1.77) vs PBO (2.42).
  - RR = 0.27 (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)
Active monitoring has similar 10-year mortality outcomes as prostatectomy and radiotherapy in men aged 50-69 years with newly diagnosed localized prostate cancer

- Reference - Prostate Testing for Cancer and Treatment (ProtecT) trial (N Engl J Med 2016 early online) (level 1 [likely reliable] evidence)
- It is unclear how to best manage newly diagnosed localized prostate cancer first identified by prostate-specific antigen (PSA) screening.
- The recent ProtecT trial randomized 1,643 men (98% white, aged 50-69 years) with newly diagnosed localized prostate cancer detected by PSA screening to one of three groups: active monitoring versus radical prostatectomy versus radiotherapy, and followed them for a median of 10 years.
- Cancer-specific and all-cause mortality were similar among the three groups. Prostatectomy and radiotherapy decreased rates of clinical progression, including metastatic disease, compared to active monitoring. However, treatment-related complications are significant, with prostatectomy, in particular, having a sizable and lasting effect on sexual and urinary function.
- Prostate cancer has a lifetime risk in the United States of about 15% (CA Cancer J Clin 2014 Jan-Feb;64(1):9), but localized prostate cancer identified by PSA screening generally has a slow progression. It is unclear how to best weigh the possible beneficial effects of prostatectomy or radiotherapy against their complications. The recent National Comprehensive Cancer Network (NCCN) guidelines recommend active surveillance for many men with low-risk prostate cancer, but this recommendation is based on lower-level evidence, albeit with uniform consensus (NCCN website).

The recent ProtecT trial, conducted in the United Kingdom, randomized 1,643 men (98% white, aged 50-69 years) with localized prostate cancer diagnosed after PSA screening to active monitoring versus radical prostatectomy versus radiotherapy (with neoadjuvant androgen deprivation therapy), and followed them for a median of 10 years with regular PSA monitoring. The diagnosed cancers were mostly low-risk: 76% had stage T1c, 77% had a Gleason score = 6, and 90% had PSA levels < 10 ng/mL. Patients in the active monitoring group with a 50% or greater increase in the PSA level over one year during follow-up were managed at physician’s discretion (54% eventually had treatment).

Death due to prostate cancer occurred in 1%, and death of any cause occurred in 10% of the entire cohort. Incidences of both outcomes were not significantly different among groups. However, incidence of any clinical progression was greater with active monitoring (22.9 per 1,000 person-years vs. 8.9 with prostatectomy vs. 9 with radiotherapy, p < 0.001 for difference across groups), as was incidence of metastatic disease (6.3 per 1,000 person-years vs. 2.4 vs. 3, p = 0.004 for difference across groups). Patient-reported outcomes over 72 months post-randomization (reported in a companion article) showed significant treatment-related complications in sexual function, as well as bladder and bowel continence. Men allocated to treatment groups had a decreased likelihood of preserved sexual function shortly after randomization: erection was firm enough for intercourse at 6 months in 51.6% with active monitoring, but in only 12% with prostatectomy and 22.2% with radiotherapy. At 72 months, rates were similar between active monitoring (29.6%) and radiotherapy (27.4%), and both were superior to prostatectomy (16.5%). Rates of complete urinary continence at 6 months were 61% with active monitoring, 29% with prostatectomy, and 61.8% with radiotherapy, and decreased or remained low over time to 49.9%, 31.3%, and 50.8% at 72 months. Bowel dysfunction was mostly infrequent and mild, but generally worse with radiotherapy. Interpretation of these complication rates is limited, however, as statistical tests at specific time points were not reported.

Although allocation to treatment after localized prostate cancer diagnosis did not decrease 10-year mortality compared to active monitoring in this trial, the decreased risk of disease progression raises the possibility that a longer follow-up may reveal a benefit. Only 2% of the men were non-white, which limits the generalization of the findings. Decreased disease progression must be balanced with treatment-related complications, particularly with prostatectomy, when considering whether to treat newly diagnosed PSA-detected localized prostate cancer.
Therapeutics US for OA Knee

- SR of 10 RCT’s (645 patients) of Therapeutic Ultrasound on OA
- TU: Use of sound waves above human hearing; “stimulating” or provoking tissue

  - **Pain**: TU → ↓ Pain (SMD = -0.93, 95%, CI = -1.22 to -0.64).
  - **Physical function**, TU → improved WOMAC physical function score (SMD = -0.37, 95% CI = -0.73 to -0.01)
  - No adverse events caused by TU in any trial.

- Therapeutic ultrasound is beneficial & safe for reducing knee pain and improving physical functions in patients with knee osteoarthritis
- Home Rx ($75-150) 15 minutes/day

Consumption of spicy food inversely associated with risk for death

• Prospective cohort of ~500,000 men & women U.S. & China over 7 years: consumption of Spicy Foods on Total and Cause Specific Mortality

• After adjusting for variables, hazard ratios for death:

  \[
  \begin{align*}
  &HR \\
  1-2 \text{ days per week} &- 0.90 (95\% \text{ CI}, 0.84 \text{ to } 0.96) \\
  3-5 \text{ days per week} &- 0.86 (0.80 \text{ to } 0.92) \\
  6-7 \text{ days per week} &- 0.86 (0.82 \text{ to } 0.90)
  \end{align*}
  \]

• This inverse association was also true for ischemic heart disease, cancer and lung disease.

BMJ. 2015 Aug 4;351:h3942
Watching cooking shows correlates with obesity

- Survey of 501 **females** (20–35) how obtained information on new recipes, cooking habits, weight and height.

- Obtaining information from print, online, or in-person sources was not associated with ↑ BMI.

- Obtaining information from cooking shows and social media correlated with higher BMI ($p < 0.05$)

- **Watching** cooking shows & **cooking from scratch** ("doers") was associated with higher BMI ($p < 0.05$) vs "viewers"

- Promoting healthy foods on cooking shows may be one way to positively influence the weight status of “doers” as well as “viewers.”

*Appetite; 2015; 90: 131–135*
Summary

• Introduce nuts, gluten, eggs, fish & pets early

• Screen for Food Insecurity & Where to Refer

• Use Tech: Alcohol Abuse, Behavioral Activation, ASA

• Child/Teen Safety: Gun, Text for Crisis (741741)

• Snoring Exercises
Summary

• DM: Screen BMI >/= 25/23, Metformin 1st
• DAPT ~ 1 Yr, Cardiac Test Appropriately
• Understand Over Diagnosis
• Prescribe Naloxone
• Appropriate Antibiotic Use; Zinc Acetate
• Hold ICS in COPD, Steroid in Asthma & Gout
• Add Some Hot Sauce at least 3 times a week
Top 10: EBM Updates From The Medical Literature

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