Articles that could change your practice

Jill Endres, MD
Jason Wilbur, MD
Mark A. Graber, MD, FACEP
MMR and fever/seizures


- 840,348 kids 12-23 mos received MMR or MMR-V vaccine between 2001-2011 in VSD clinics.
MMR and Fever, seizures

- Increased risk of seizures in 7-10 day high risk interval for kids who received the vaccine at 16-23 (vs 12-15) mos of age.
  - RR 6.5 (95% CI 5.3-8.1) vs RR 3.4 (95%CI 3-3.9)
  - Attributable risk 9.5 vs 4 cases per 10,000 doses

- Increased risk of fever and seizures in kids receiving MMR-V vs MMR +/- separate Varicella vaccine
  - 1.4-fold increase in fever
  - 2-fold increase in seizures
Why?

- Kids have higher immune responsiveness in 16-18 month age range
  - Peak incidence of febrile seizures
So what?

- Stick to recommended childhood vaccine schedule.
- Discuss additional risk when parents want to follow alternate schedules.
- Don’t use MMR-V combination vaccine.
How do we manage blood pressure in ischemic stroke?

Randomized 4700 Chinese to antihypertensive therapy (140/80) goal or no antihypertensive.

Initiated with 24 hours of presentation (but stroke could be 48 hours before)

Excluded if BP >= 220/120, thrombolytic, a reason to lower BP (CHF)

Average BP at entry 167/97
- Used ACE, Calcium channel blocker and diuretics
- Goal: 10-25% within 24 hours
- At 24 hours
  - Systolic decreased by 22mmHg treatment group
  - Systolic decreased by 13mm Hg control group
- Outcome of death or disability:
For both groups...

- Death or disability same at 14 days: odds ratio, 1.00 [95%CI, 0.88 to 1.14]; \( P = .98 \)

- Death or disability same at 3 months: odds ratio, 0.99 [95%CI, 0.86 to 1.15]; \( P = .93 \)

- Death the same....so not just driven by disability.
- 220/120 unless evidence of end organ problems
- Reduce by only 15% in 24hrs.
- You *can* reduce the BP and not make them worse.
- But, go have a coffee instead.
Special Case

- If thrombolytic candidate:
  - <185/110

- Recommendation:
  - Labetalol IV
  - Nicardipine infusion
How about in hemorrhagic stroke?
Blood Pressure Control

Study

- Acute, spontaneous, bleeds
- Randomized within 6 hours to SBP<140mmHg
- Or conventional (<180mm hg).
- 2794 patients, 90 day outcomes
- No difference in outcomes and no change in size of hematoma!!
Wait a minute. Didn’t they conclude there was reduced morbidity and an improved Rankin score?
Table 3. Primary, Secondary, and Safety Outcomes at 90 Days.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Blood-Pressure Lowering (N=1399)</th>
<th>Guideline-Recommended Blood-Pressure Lowering (N=1430)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome: death or major disability — no./total no. (%)†</strong></td>
<td>719/1382 (52.0)</td>
<td>785/1412 (55.6)</td>
<td>0.87 (0.75–1.01)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
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</tr>
<tr>
<td>Score on the modified Rankin scale — no./total no. (%)‡</td>
<td></td>
<td></td>
<td>0.87 (0.77–1.00)</td>
<td>0.04</td>
</tr>
<tr>
<td>0: No symptoms at all</td>
<td>112/1382 (8.1)</td>
<td>107/1412 (7.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: No substantive disability despite symptoms</td>
<td>292/1382 (21.1)</td>
<td>254/1412 (18.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2: Slight disability</td>
<td>259/1382 (18.7)</td>
<td>266/1412 (18.8)</td>
<td></td>
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</tr>
<tr>
<td>3: Moderate disability requiring some help</td>
<td>220/1382 (15.9)</td>
<td>234/1412 (16.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4: Moderate–severe disability requiring assistance with daily living</td>
<td>250/1382 (18.1)</td>
<td>268/1412 (19.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5: Severe disability, bed-bound and incontinent</td>
<td>83/1382 (6.0)</td>
<td>113/1412 (8.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6: Death by 90 days</td>
<td>166/1382 (12.0)</td>
<td>170/1412 (12.0)</td>
<td>0.99 (0.79–1.25)</td>
<td>0.96</td>
</tr>
<tr>
<td>Death — no./total no. (%)</td>
<td>166/1394 (11.9)</td>
<td>170/1421 (12.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Here is the table from the “supplementary material”…hmm why are there two more columns?

<table>
<thead>
<tr>
<th>Characteristic of mRS outcome scores</th>
<th>Blood pressure lowering</th>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intensive (N=1399)</td>
<td>Guideline (N=1430)</td>
<td>OR (95% CI)</td>
<td>P Value</td>
<td>OR adjusted (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td><strong>Primary outcome - no. (%)†</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>0 to 2</td>
<td>663 (48.0)</td>
<td>627 (44.4)</td>
<td>0.87 (0.75 to 1.01)</td>
<td>0.059</td>
<td>0.87 (0.73 to 1.04)</td>
<td>0.122</td>
</tr>
<tr>
<td>3 to 6</td>
<td>719 (52.0)</td>
<td>785 (55.6)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Key secondary outcome, shift on scores – no. (%)†</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>0 (no symptoms at all)</td>
<td>112 (8.1)</td>
<td>107 (7.6)</td>
<td>0.87 (0.77 to 1.00)</td>
<td>0.044</td>
<td>0.89 (0.78 to 1.02)</td>
<td>0.105</td>
</tr>
<tr>
<td>1 (no significant disability despite symptoms)</td>
<td>292 (21.1)</td>
<td>254 (18.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (slight disability)</td>
<td>259 (18.7)</td>
<td>266 (18.8)</td>
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<td></td>
<td></td>
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</tr>
<tr>
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</tr>
<tr>
<td>4 (moderate-severe disability much help)</td>
<td>250 (18.1)</td>
<td>268 (19.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 (severe disability, requiring full care)</td>
<td>83 (6.0)</td>
<td>113 (8.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 (death by 90 days)</td>
<td>166 (12.0)</td>
<td>170 (12.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other outcomes – no. (%)</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>0 to 1</td>
<td>404 (29.2)</td>
<td>361 (25.6)</td>
<td>0.83 (0.70 to 0.98)</td>
<td>0.030</td>
<td>0.85 (0.70 to 1.03)</td>
<td>0.092</td>
</tr>
<tr>
<td>2 to 6</td>
<td>978 (70.8)</td>
<td>1051 (74.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0, 1, 2, and 3, shift in scores‡</td>
<td>883 (63.9)</td>
<td>861 (61.0)</td>
<td>0.87 (0.76 to 0.99)</td>
<td>0.038</td>
<td>0.88 (0.76 to 1.02)</td>
<td>0.079</td>
</tr>
<tr>
<td>4 to 6 combined</td>
<td>499 (36.1)</td>
<td>551 (39.0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or major disability at 7 days – no./total no. (%)§</td>
<td>1056 (76.5)</td>
<td>1087 (77.3)</td>
<td>0.95 (0.80 to 1.14)</td>
<td>0.597</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or major disability at 28 days – no./total no. (%)¶</td>
<td>913 (66.0)</td>
<td>965 (68.1)</td>
<td>0.91 (0.77 to 1.06)</td>
<td>0.219</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

What the heck?
Blood transfusions in GI bleeders

Study of 898 patients with GI bleeding admitted to hospital

Randomized to restrictive-strategy vs liberal-strategy

Exclusions: most commonly for “low risk of rebleeding”. Also excluded “exsanguinous bleeding”.

Included: all types of upper GI bleed, but predominantly ulcer and variceal
- Deviations from protocol occurred in < 10% of patients

- Restrictive:
  - Transfuse at Hgb < 7 g/dl
  - Target Hgb 7 – 9 g/dl

- Liberal:
  - Transfuse at Hgb < 9 g/dl
  - Target Hgb 9 – 11 g/dl
Restrictive group:
- 51% received NO transfusion
- Mean units transfused – 1.5

Liberal group:
- 14% received NO transfusion
- Mean units transfused – 3.8

Hemoglobin concentrations at 45 days were about the same.
Bottom line

- Lower mortality at 45 days post-hospitalization in the restrictive group
- A restrictive transfusion strategy in patients with acute upper GI bleeding is safe and effective compared to a liberal transfusion strategy
  - Consistent with studies of critically ill patients (non-GI bleeds)
Enhancing the Benefits of Fruit Intake

- **Primary prevention**
  - Type 2 DM
  - Stroke
  - Heart disease
  - Cancers

- Greater variety, rather than quantity may be more important

Muraki I et al. BMJ 2013; 347
Fruit intake and DM2

Data from

- Nurses Health Study I, II (121,700; 116,671)
- Health Professional Follow-up Study (51,529)
- Excluded
  - Preexisting diabetics, heart disease, cancer
  - Missing data for fruits or fruit juice
- Food frequency questionnaires, diet records
- Specific fruits
- Fruit juices

Muraki I et al. BMJ 2013; 347
Fruit intake and DM2

- Total whole fruit intake weak reduction in risk
  - HR 0.98 (0.96-0.99) for every 3 servings/week

- Fruit juice consumption associated with increased risk

- Results were not dependent on glycemic index of fruits
Fruit intake and DM2

- Whole fruit intake and risk of DM
- Linear trend estimated based on 3 serving/week

<table>
<thead>
<tr>
<th>Fruit Type</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total whole fruits</td>
<td>0.98 (0.96-0.99)</td>
</tr>
<tr>
<td>Blueberries</td>
<td>0.74 (0.66-0.83)</td>
</tr>
<tr>
<td>Grapes/raisins</td>
<td>0.88 (0.83-0.93)</td>
</tr>
<tr>
<td>Apples/pears</td>
<td>0.93 (0.90-0.96)</td>
</tr>
<tr>
<td>Bananas</td>
<td>0.95 (0.91-0.98)</td>
</tr>
<tr>
<td>Grapefruit</td>
<td>0.95 (0.91-0.99)</td>
</tr>
<tr>
<td>Oranges</td>
<td>0.99 (0.95-1.03)</td>
</tr>
<tr>
<td>Peaches/plums/apricots</td>
<td>0.97 (0.92-1.02)</td>
</tr>
<tr>
<td>Prunes</td>
<td>0.89 (0.79-1.01)</td>
</tr>
<tr>
<td>Strawberries</td>
<td>1.03 (0.96-1.10)</td>
</tr>
<tr>
<td>Cantaloupe</td>
<td>1.10 (1.02-1.18)</td>
</tr>
</tbody>
</table>
Fruit intake and DM2

- Replacing 3 servings/wk juice with whole fruit
If life gives you lemons, 

Do whatever you like.

But, if life gives you apples, don’t make apple juice; just eat them.

...or, better yet, trade them for blueberries.
And yet more BP....


([http://dx.doi.org/10.1097/01.AOG.0000437382.03963.88](http://dx.doi.org/10.1097/01.AOG.0000437382.03963.88))
Proteinuria no longer required for pre-eclampsia if other findings

- Instead can have:
  - thrombocytopenia,
  - impaired liver function,
  - new-onset renal insufficiency,
  - pulmonary edema,
  - new development of cerebral or visual disturbances
Other stuff...

- Treat only if BP >160/110 (!!)
  - If sx (hypertensive emergency) treat at lower BP
  - Lowering BP may effect fetal perfusion
  - Lowering BP does not change the course of preeclampsia.
Chronic HTN

- Treat **chronic** HTN in pregnancy if BP 160/105 with goal < 160/105 and > 120/80

- But.....treat early to avoid hypospadias: OB & GYN, 2014;123:309 (some problems with study....like they didn’t define HTN!!)
Magnesium intrapartum/postpartum

- Only for patients with severe preeclampsia including:
  - SBP > 160 mmHg,
  - low platelets,
  - impaired liver function,
  - AKI, pulmonary edema
  - CNS changes

- No bedrest for preeclampsia
New Recommendation from USPSTF

USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults ages 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Why screen?

- Lung cancer is the leading cause of cancer deaths in the U.S. – 27% of cancer deaths
- 75% of patients with lung cancer present with symptoms due to incurable or advanced local or metastatic disease
- Early stage lung cancer is potentially curable
<table>
<thead>
<tr>
<th>Study, Recruitment Years (Reference)</th>
<th>Population*</th>
<th>Baseline Smoking Status*</th>
<th>Screening Rounds, n</th>
<th>Screening Intervals, y</th>
<th>Total Median Follow-up</th>
<th>Follow-up After Screening Ended</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LDCT vs. chest radiography</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>NLST, 2002–2004 (53)</td>
<td>n = 26,722 vs. 26,732 Age: 55–74 y Men: 59%</td>
<td>Current: 48% vs. 48% Former: 52% vs. 52% Mean pack-years: 56</td>
<td>3</td>
<td>0, 1, 2</td>
<td>6.5 y (maximum, 7.4 y)†</td>
<td>NR but presumably 4.5 y</td>
<td>Good</td>
</tr>
<tr>
<td><strong>LDCT vs. no LDCT</strong></td>
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</tr>
<tr>
<td>DANTE, 2001–2006 (39, 40)†</td>
<td>n = 1,276 vs. 1,196 Age: 60–74 y Men: 100%</td>
<td>Current: 56% vs. 57% Former: NR Mean pack-years: 47.3 vs. 47.2</td>
<td>5</td>
<td>0, 1, 2, 3, 4</td>
<td>33.7 mo (range, 1.8–79.2)</td>
<td>NR (final results pending)</td>
<td>Fair§</td>
</tr>
<tr>
<td>DLCST, 2004–2006 (60)</td>
<td>n = 2,052 vs. 2,052 Age: 50–70 y Men: 55%</td>
<td>Current: 75% vs. 77% Former: 25% vs. 23% Mean pack-years: 36.4 vs. 35.9</td>
<td>5</td>
<td>0, 1, 2, 3, 4</td>
<td>4.8 person-years</td>
<td>NR</td>
<td>Fair‖</td>
</tr>
<tr>
<td>MILD, 2005–2011 (57)</td>
<td>n = 2,376 (1,190 annual, 1,186 biennial) vs. 1,723 Age: ≥49 y Men: 66%</td>
<td>Current: 68% vs. 68% Former: 31% vs. 32% Median pack-years: 39 vs. 39 vs. 38† Median number of CTs, annual vs. biennial: 5 vs. 3</td>
<td>Median number of CTs, annual vs. biennial: 5 vs. 3</td>
<td>Annual vs. biennial: every 12 mo (0, 1, 2, 3, 4 y) vs. every 24 mo (0, 2, 4 y)</td>
<td>4.4 y (maximum, 6 y)</td>
<td>Recruitment ended January 2011; follow-up until November 2011</td>
<td>Poor**</td>
</tr>
</tbody>
</table>
Figure 1. Trial results for lung cancer mortality.

<table>
<thead>
<tr>
<th>Author, Year (Reference)</th>
<th>Male, %</th>
<th>Follow-up, y</th>
<th>Deaths per 100 000 Person-Years, n</th>
<th>Mean Age, y</th>
<th>Pack-Years, n</th>
<th>Screening Intervals, y</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aberle et al, 2011 (53)</td>
<td>59</td>
<td>6.5</td>
<td>247</td>
<td>61</td>
<td>56</td>
<td>0, 1, 2</td>
<td>0.80 (0.73–0.93)</td>
</tr>
<tr>
<td>Infante et al, 2009 (39, 40)</td>
<td>100</td>
<td>2.8</td>
<td>527</td>
<td>65</td>
<td>47</td>
<td>0, 1, 2, 3, 4</td>
<td>0.83 (0.45–1.54)</td>
</tr>
<tr>
<td>Saghri et al, 2012 (60)</td>
<td>56</td>
<td>4.8</td>
<td>154</td>
<td>58</td>
<td>36</td>
<td>0, 1, 2, 3, 4</td>
<td>1.37 (0.63–2.97)</td>
</tr>
<tr>
<td>Pastorino et al, 2012 (57)*</td>
<td>66</td>
<td>4.4</td>
<td>216</td>
<td>57↓</td>
<td>39↓</td>
<td>0, 1, 2, 3, 4</td>
<td>1.99 (0.80–4.96)</td>
</tr>
</tbody>
</table>

* Annual screening group compared only with control group; biennial screening group not shown. † Median

Figure 2. Trial results for all-cause mortality.

<table>
<thead>
<tr>
<th>Author, Year (Reference)</th>
<th>Male, %</th>
<th>Follow-up, y</th>
<th>Deaths per 100 000 Person-Years, n</th>
<th>Mean Age, y</th>
<th>Pack-Years, n</th>
<th>Screening Intervals, y</th>
<th>Relative Risk (95% CI)</th>
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<tbody>
<tr>
<td>Aberle et al, 2011 (53)</td>
<td>59</td>
<td>6.5</td>
<td>1142</td>
<td>61</td>
<td>56</td>
<td>0, 1, 2</td>
<td>0.93 (0.86–0.99)</td>
</tr>
<tr>
<td>Infante et al, 2009 (39, 40)</td>
<td>100</td>
<td>2.8</td>
<td>1212</td>
<td>65</td>
<td>47</td>
<td>0, 1, 2, 3, 4</td>
<td>0.85 (0.56–1.27)</td>
</tr>
<tr>
<td>Saghri et al, 2012 (60)</td>
<td>56</td>
<td>4.8</td>
<td>625</td>
<td>58</td>
<td>36</td>
<td>0, 1, 2, 3, 4</td>
<td>1.46 (0.99–2.15)</td>
</tr>
<tr>
<td>Pastorino et al, 2012 (57)*</td>
<td>66</td>
<td>4.4</td>
<td>558</td>
<td>57↓</td>
<td>39↓</td>
<td>0, 1, 2, 3, 4</td>
<td>1.80 (1.03–3.13)</td>
</tr>
</tbody>
</table>
NLST

- 6.5 year follow up
- 3 annual low-dose CT scans
- Compared to annual CXR
- Showed:
  - 20% RRR in lung cancer specific mortality
  - Absolute risk of lung cancer death:
    - Screened group: 1.3%
    - Control group: 1.6%
  - Reduction in overall mortality of 6.7%
    (2000 deaths vs 1877)
NNT

- Number needed to treat (or screen)

- NNS = 1/ARR
- ARR = 1.6 – 1.3 = 0.3%
- NNS = 1/0.003 = 333

- So, to avert 1 lung cancer death, 333 would need to be screened using the NLST method.
Risks?

- The number needed to harm for “abnormal finding” is only 4
  - More testing
  - More biopsies
  - More surgeries
  - More anxiety
What should we do?

- This dilemma will arise multiple times per day in my clinic!
Limiting Screen Time

- <2 hour AAP guideline is over 10 years old

- Outcomes
  - Obesity
  - Poor sleep
  - Inactivity
  - Academic underachievement
1550 parents, nationally represented sample
- Parents’ daily TVV = 4.07 hrs
- TV’s in home = 3
- TV’s in parent bedroom = 70%
- TV’s in child bedroom = 46% (increased w age)
- Parent restricted TVV = 2.67 (1 never, 4 often)

Parent TVV strongest association with child TVV across all ages
- Each hour corresponds with add’l 23 min child TVV

Parents underestimated adolescents TVV by 47 min

What can we do?

- Factors known to increase screen time
  - Enforce parental restrictions
  - Limit co-viewing with parents
  - No TV in bedroom
  - Limit number of TVs in home
  - Don’t eat meals in front of TV

- And, of course, role model desired behaviors...
Does cognitive rest improve post-concussion syndrome?

- Prospective cohort at concussion clinic at Boston Children’s Hospital (spectrum bias??)
- Within 3 weeks of injury
- Used a validated “Post Concussion Symptom Scale”
1124 screened: 335 included age 8 to 23 years
- Mean age 15

All had sports related concussion

62% were male

19% reported a loss of consciousness

37% reported experiencing amnesia
- Rated their cognitive activity on scale of 0-4 at each visit.
- Cognitive activity included reading, homework, video games, etc.
- Non-cognitive activity included TV (yup!), movies or music.
<table>
<thead>
<tr>
<th>Level</th>
<th>Cognitive Activity</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Complete cognitive rest</td>
<td>No reading, homework, text messaging, video game playing, online activity, crossword puzzles, or similar activities. The most stimulating activities at this level would be watching television, watching movies, or listening to music.</td>
</tr>
<tr>
<td>1</td>
<td>Minimal cognitive activity</td>
<td>No reading, homework, crossword puzzles, or similar activities. Less than 5 text messages per day, less than 20 min per day combined of online activity and video games.</td>
</tr>
<tr>
<td>2</td>
<td>Moderate cognitive activity</td>
<td>Reading less than 10 pages per day, less than 20 text messages per day, and doing less than 1 h combined of homework, online activity, and video games per day.</td>
</tr>
<tr>
<td>3</td>
<td>Significant cognitive activity</td>
<td>Reading less, doing less homework, working less online, text messaging less, and doing crossword or other activities than you would normally do, but more than listed in level 2.</td>
</tr>
<tr>
<td>4</td>
<td>Full cognitive activity</td>
<td>You have not limited cognitive activity at all.</td>
</tr>
</tbody>
</table>
Mean duration of sx: 43 days

Only associations with recovery were:

- Initial symptom score
- Cognitive activity

But........
Kaplan-Meier Curve of Symptoms

- Proportion still symptomatic
- Time in days

Lines represent:
- 1st quartile activity score
- 2nd quartile activity score
- 3rd quartile activity score
- 4th quartile activity score
Initial Score: 95% CI 0.9738-0.9856
Cognitive activity: 95% CI 0.9924-0.9960

When you have to carry your CI out to 4 decimal points there is not much of an association
Round them off to 2 decimal points and they lose!
Maybe there is something else not being measured?
Other stuff

- Not randomized but you would expect the people with more sx to do less activity just 'cos
- Those with more sx had more activity
- So likely not biased.
- (see next two slides for guidelines...I will not review these slides)
Another J-curve?

- Depression historically linked to alcohol intake
- PREDIMED study- prospective cohort
  - 5505 adults 55-80 yo without depression or CAGE +
  - Annual food freq questionnaire over 7 years
  - Depression= clinical diagnosis or antidepressant drugs
- Moderate intake (5-15 g/day) associated with lower risk of incident depression
  - HR 0.72, 95% CI (0.53-0.98)
- Wine intake (2-7 glasses per week)
  - HR 0.68, 95% CI (0.47-0.98)

Gea A et al. BMC Medicine 2013, 11:192
Always caveats...

- Heavier drinkers at higher risk
- Not consistent results between studies
  - Excluding problem drinkers could explain
- Other confounding lifestyle factors
Dentists and Doctors disagree...

Should parents suck on pacifiers to “clean” them?

Dentists say “NO!”

...but are there some benefits?
Parents sucking pacifiers

- 184 infant birth cohort (Sweden)
  - At least one parent with allergies
  - 4 month salivary microbiota
  - 6 month parental survey about pacifier practices
  - 18, 36 month allergy assessment
  - Respiratory infections in first 6 mos
  - Relationship to mode of delivery
Parents sucking pacifiers

- 36% of parents suck on pacifiers to clean them
  - Salivary microbiota differed
  - No difference in respiratory infections in first 6 mos
  - Reduced allergic disease at 18 mos - Odds Ratios (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>18 months</th>
<th>36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>0.12 (0.01-0.99)</td>
<td>Hazard Ratio 0.51 (p=0.04)</td>
</tr>
<tr>
<td>Eczema</td>
<td>0.37 (0.15-0.91)</td>
<td></td>
</tr>
<tr>
<td>Sensitization</td>
<td>0.37 (0.10-1.27)</td>
<td></td>
</tr>
</tbody>
</table>

TB screening

- What happens when you apply a highly sensitive test to a population with low disease prevalence?
TB Screening

TB Screening

- Single-center study at Stanford University Medical Center
- Retrospectively evaluated the application of QuantiFERON-TB Gold In-Tube (QFT) for screening ~ 10,000 health-care workers annually for TB, and compared to historical control
- Used the manufacturer recommended cut-off (/>=0.35IU/mL)
<table>
<thead>
<tr>
<th>Category</th>
<th>No. (%)</th>
<th>Mean Age (±SD)*</th>
<th>Females No. (%)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative tests</td>
<td>17,094 (85.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive tests</td>
<td>2,774 (13.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indeterminate tests</td>
<td>113 (0.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCWs persistently negative</td>
<td>7,496 (81.9%)</td>
<td>42 (12.7)</td>
<td>5,465 (72.9%)</td>
</tr>
<tr>
<td>HCWs persistently positive</td>
<td>828 (9.0%)</td>
<td>44 (11.7)</td>
<td>562 (67.9%)</td>
</tr>
<tr>
<td>HCWs with conversion</td>
<td>361 (4.4%)</td>
<td>43 (11.6)</td>
<td>260 (72.1%)</td>
</tr>
<tr>
<td>HCWs with reversion</td>
<td>613 (38.7%)</td>
<td>42 (12.0)</td>
<td>427 (69.6%)</td>
</tr>
</tbody>
</table>
So...

- In the initial testing, 13.4% of HCW’s had a positive test!
- For those testing negative initially, the conversion rate was 4.4%.
- Historically, at Stanford, the conversion rate was 0.4%.
What’s going on here?

- Overall TB rates in the area of the study were low:
  - Incidence of TB at Stanford Med averages 14 cases
  - Incidence of TB in Santa Clara County during the period was 10.8/100,000 persons
- Incidence of TB in the U.S. is in decline
- There is no gold standard to detect latent TB
- A positive test result alone is not enough to diagnose latent TB—consider history and epidemiology
How about “Low-T”
Is treatment safe?

(http://dx.doi.org/10.1001/jama.2013.280386)

(http://dx.doi.org/10.1001/jama.2013.280387)
NPR and CBS beat me to this one. So....
Well what about my erections, doc?

- 140 men (age 40-70) with erectile dysfunction.
- Testosterone low <330ng/dl or free testosterone of <50pg/ml

Run in phase...

- Optimized sildenafil dose (don’t ask)
- Then...randomized to either placebo or testosterone
- Testosterone 649ng/dl v. 347ng/dl
- Erectile Dysfunction Domain of the International Index of Erectile dysfunction (which I did not know existed!)
Exclusion

- Prostate or breast cancer
- Structural abnormalities
- Major psychiatric disease
- Elevated creatinine
- HbA1c > 8.5%
- MI or stroke < 6 months
- BP > 160/100
Good power to find a difference
What did they find?

- Sildenafil: EFD score (mean, 7.7 [95% CI, 6.5 to 8.8]) increase
- Testosterone: 2.2 [CI, -0.8 to 5.1]; $P=0.150$). (same in both groups)
Difference Between Testosterone and Placebo Groups in Mean On-Treatment Changes (95% CI)

- Erectile Function Score: Favors Testosterone, $P = 0.150$
- Orgasmic Function Score: Favors Testosterone, $P = 0.43$
- Sexual Desire Score: Favors Testosterone, $P = 0.42$
- Intercourse Satisfaction Score: Favors Testosterone, $P = 0.30$
- Overall Satisfaction Score: Favors Testosterone, $P = 0.85$
- Composite IIEF Score: Favors Testosterone, $P = 0.198$
To D or not to D…
The age-old question

- Meta-analysis for D (without calcium) in adults
  - 23 studies, 4032 participants, 92% female
  - BMD measured at 1-5 sites
  - 10 studies with <800 IU per day
Vitamin D supplements and bone density

- Vit D levels increased from 53-92 nmol/L
- No difference at
  - Spine
  - Total hip
  - Trochanter
  - Total body
  - Forearm
- Small benefit at femoral neck (0.8%, 95%CI 0.2-1.4%)-heterogeneous data
- Evidence of bias toward positive results

Reid IR et al. Lancet 2013
Soooo, what do we do?

- Don’t
  - Vitamin D appears to confer little added benefit over calcium supplements alone in patients who are not deficient and high-risk.

- IOM recommendation
  - 40 nmol/L is adequate concentration
Which NSAID is safest?

The article

Meta-analysis
- 280 trials of NSAID vs placebo
- 474 trials of NSAID vs NSAID
- Over 350,000 participants
- Over 230,000 person-years

Outcomes
- Major vascular event (non-fatal MI, non-fatal stroke, vascular death)
- Major coronary event (non-fatal MI, coronary death)
- Stroke
- Mortality
- Heart failure
- Upper GI complications (perforation, obstruction, bleed)
For major vascular events:
- Coxibs RR 1.37
- Diclofenac RR 1.41

For vascular death:
- Coxibs RR 1.58
- Diclofenac 1.65

HF ~ risk doubled for all NSAIDs

For upper GI complications:
- Coxibs RR 1.81
- Diclofenac RR 1.89
- IBU RR 3.97
- Naproxen RR 4.22
Bottom line

- For patients at risk for vascular disease, naproxen appears safest
- For patients at risk for upper GI complications, coxibs appear safest
- Anybody know patients at risk for vascular disease and upper GI complications?
  ...yeah, we don’t either!
  • But seriously, there’s still acetaminophen
Does time to suturing change infection rate?


(http://dx.doi.org/10.1136/emj.2012-202143)
3957 of whom 2663 had complete follow-up data.
  • Maybe the rest died of sepsis??

Lacerations NOT caused by bites.

Consecutive patients
Followed up at 30 days to determine infection rate.

Infection defined as need to visit a health practitioner and treated with ABX (one weakness here).
2.6% overall infection rate

Multivariate analysis showed infection rate increased by:

- Diabetes OR 3.1
- Length of wound >5cm OR 2.4
- Wound contamination OR 1.9

Time didn’t seem to make a difference (<12h or >12h)...some wounds left open, though.
Table 4  Lacerations repaired before and after 12 h from injury

<table>
<thead>
<tr>
<th></th>
<th>Injury &lt;12 h (N=2176)</th>
<th>Injury &gt;12 h (N=72)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>34</td>
<td>41</td>
<td>0.02</td>
</tr>
<tr>
<td>Male sex</td>
<td>61%</td>
<td>58%</td>
<td>0.42</td>
</tr>
<tr>
<td>Infection (95% CI)</td>
<td>2.9% (2.3% to 3.8%)</td>
<td>1.4% (0.3% to 6.4%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Hours from injury (median IQR)</td>
<td>2 (1–3)</td>
<td>16 (12–24)</td>
<td></td>
</tr>
<tr>
<td>Length of wound (mean cm)</td>
<td>2.6</td>
<td>2.4</td>
<td>0.31</td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Head and neck</td>
<td>55%</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Extremity/torso</td>
<td>45%</td>
<td>69%</td>
<td></td>
</tr>
<tr>
<td>Repair type</td>
<td></td>
<td></td>
<td>0.96</td>
</tr>
<tr>
<td>Simple</td>
<td>82%</td>
<td>86%</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>9%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Complex</td>
<td>4%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Prophylactic antibiotics</td>
<td>2.2%</td>
<td>2.9%</td>
<td>0.93</td>
</tr>
<tr>
<td>Cosmetic outcome 100 mm VAS</td>
<td>86</td>
<td>85</td>
<td>0.67</td>
</tr>
<tr>
<td>Considering scar revision</td>
<td>10%</td>
<td>5%</td>
<td>0.40</td>
</tr>
</tbody>
</table>

13/85 Wounds left open after 12 h (72 closed and analysed) 81/2257 (2176 closed and analysed). Four of 13 include delayed primary closure left open up to 96 h before closure. Nine left open. VAS, visual analogue scale.
All estrogens are not created equal

- Two studies looking at risk of venous thrombosis with different hormonal therapies
Postmenopausal HRT: CEE vs Estradiol

- Smith, et al.
  - Case-control study of 384 postmenopausal women on HRT
    - 68 VT (primary outcome)
    - 67 MI
    - 48 Ischemic stroke
  - Group Health Cooperative
    - Preferred drug used by 87%
      - CEE until Jan 1, 2003-Jan 31, 2005
      - Estradiol in Feb 1, 2005-Dec 31, 2009
Postmenopausal HRT: CEE vs Estradiol

- Venous Thrombosis risk greater in CEE-users
  - OR 2.08 (1.02-4.27) p=0.045
- MI risk greater
  - OR 1.87 (0.91-3.84) p=0.09
- Ischemic stroke risk not significantly different
- Biologic plausibility:
  - nAPCsr median levels were higher in the CEE group than in the estradiol group
- Not randomized assignment, but systemwide recommendations (eliminates some bias?)
Combination OCPs and VT risk

<table>
<thead>
<tr>
<th></th>
<th>Non-use</th>
<th>First</th>
<th>Second</th>
<th>Third</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-use</strong></td>
<td>1</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td><strong>First generation</strong></td>
<td>3.2 (2.0-5.1)</td>
<td>1</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>(lynestrenol, norethisterone)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Second generation</strong></td>
<td>2.8 (2.0-4.1)</td>
<td>0.9 (0.6-1.4)</td>
<td>1</td>
<td>--</td>
</tr>
<tr>
<td>(norgestrel, levonorgestrel)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Third generation</strong></td>
<td>3.8 (2.7-5.4)</td>
<td>1.2 (0.8-1.9)</td>
<td>1.3 (1.0-1.8)</td>
<td>1</td>
</tr>
<tr>
<td>(gestodene, desogestrel, norgestimate)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>0.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(drospirenone, Cyproterone acetate)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dose dependent effects occurred with gestodene, desogestrel, levonorgestrel
Combination OCPs and VT risk

- Baseline VT risk 1.9-3.7 per 10,000 py
- ALL combination OCP’s increased VT risk
  - RR 3.5 (2.9-4.3)
- Higher doses of EE related to increased risk
  - Depends on progestin (desogestrel, but not levonorgestrel)
Recommendations

- Although more studies are needed for postmenopausal HRT,
  - Consider using estradiol instead of CEE in women who take HRT for symptoms
  - Consider using OCP containing 30 mcg EE and levonorgestrel as first line
All that dwindles is not Alzheimer’s…

The study

- Subjects recruited for longitudinal studies, with no dx of dementia (Rush Memory and Aging Project and Religious Orders Study)
- 850 subjects
- Annual cognitive assessments for average of 75 years (range 2-18)
- Autopsy with brain pathological exam
The study

- Calculated the rate of change of cognitive decline (2\textsuperscript{nd} order derivative—ouch, is that calculus?)
- Also determined the range of variability accounted for by pathologic differences between subjects
No surprise here...
FIGURE 3: Variation in cognitive decline explained by the pathologic indices (gray) and the residual, unexplained variation in cognitive decline (white) derived from fully adjusted models. AD = Alzheimer disease; CVD = cerebrovascular disease; LBD = Lewy body disease.
Bottom line

- In the majority of subjects (59%), the variability in cognitive decline could not be predicted by the pathologic burden of dementing diseases (Alzheimer's, vascular events, Lewy bodies)

- So...we don't really understand dementia.
PCOS treatment

- Randomized trial: 198 women with PCOS
  - 56 Metformin alone (M) 1000 mg / day
  - 51 Spironolactone alone (S) 50 mg/day
  - 62 Metformin+spironolactone (M+S)

- Outcomes of interest at 0,3,6 mos
  - BMI
  - Total T
  - Glucose and insulin sensitivity
  - LH, FSH
  - Menstrual cycle pattern
  - Waist-hip ratio (WHR)
  - BP
  - Ferriman-Gallwey Score (FG score)

Ganie MA et al. J Clin Endocrinol Metab 2013:
PCOS treatment

- All groups
  - No significant change in weight, BMI, WHR, BP
  - Increased menstrual cycles per year
  - Improved FG score
  - Decreased Total T
  - Improved insulin sensitivity
PCOS treatment

- Combination (M+S) group
  - No increase in adverse events
  - Better compliance
  - Decreased FG score, total T, LH, FSH, glucose and insulin
PCOS treatment

- Outcomes (mean, baseline) at 6 mos

<table>
<thead>
<tr>
<th></th>
<th>Metformin</th>
<th>Spironolactone</th>
<th>M+S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menstrual cycles/yr</td>
<td>10.02 (5.95)</td>
<td>10.35 (6.45)</td>
<td>10.86 (6.13) b,y</td>
</tr>
<tr>
<td>FG score</td>
<td>9.67 (13.27)</td>
<td>9.56 (13.65)</td>
<td>9.09 (13.11) b,y,z</td>
</tr>
<tr>
<td>Total serum T</td>
<td>1.89 (3.03)</td>
<td>1.80 (2.98)</td>
<td>1.58 (3.10) b,y,z</td>
</tr>
<tr>
<td>AUC glucose</td>
<td>14841.0 (15671.6)</td>
<td>14720.0 (15960.0)</td>
<td>14400.5 (15665.8) b,z</td>
</tr>
<tr>
<td>AUC insulin</td>
<td>5034.91 (6466.81)</td>
<td>5396.60 (6568.14)</td>
<td>4051.46 (6497.81) b,y,z</td>
</tr>
</tbody>
</table>

b = 0 vs 6 month
y = M vs M+S
z = S vs M+S
Quick Pearls
Quick pearls

- 5 days of prednisone is fine for COPD as well as for asthma.

- ACE + ARB does not help anyone

Renal stenting does not work for atherosclerotic renal artery disease as a treatment for hypertension.

PPIs can lead to Vit B-12 deficiency (as can metformin).
References for quick pearls


- Lam JR et al. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B<sub>12</sub> deficiency. JAMA 2013 Dec 11; 310:2435. (http://dx.doi.org/10.1001/jama.2013.280490)
Dogma overturned?


- Showed that migraine patients do not display any demonstrable vascular changes while having their headaches.
The fungus amongus


The short version: washing socks in 40 degree C water eliminates most fungi; using 60 degree C water kills all of the usual pathogens.
Are beta blockers safe in those with COPD?

1069 patients with COPD and myocardial infarction.

Study was retrospective.

23% on beta blockers at baseline.

22% received beta blockers around their MI.

55% did not get any beta blockers.

Observed for 2.9 years.
- Adjusted the best they could for confounders.
- Hazard ratio for death: 0.6 for those on beta-blockers at study start.
- Hazard ratio: 0.5 for those who started beta blockers as inpatient.
- So, beta-blockers are safe in COPD and inhalers are safe in the setting of MI
Not first study to find this.

In community patients beta-blockers were safe in those with severe COPD.

Actually better survival


See also:

- BMJ 2011 May 10; 342:d2549. (http://dx.doi.org/10.1136/bmj.d2549)