Methodology

- Clinically important for practicing internists
- Methodologically sound
- Review in ACP Journal Club or Journal Watch in addition to primary journal
- Topics: Dementia, vitamins, zoledronic acid, osteoarthritis, constipation, HTN

Does This Patient have Dementia?

**JAMA 2007; 297: 2391-2404**

- Review of Performance of MMSE, brief instrument, comprehensive instruments, and instruments for special situations

Primary Care Screen for Early Dementia

**JAGS 2008; 56: 206-213**

- Compared MMSE to ADS - PC

You want to begin to screen all of your patients for dementia. You practice in a clinic that serves many immigrants and people with low education level. The best brief screen for your clinic is:

1. The Mini-mental state exam
2. The Hopkins Verbal learning test
3. The Clock Draw Test
4. Ask a family member about whether patient has memory loss

**Table:**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini-mental state exam</td>
<td>13%</td>
<td>65%</td>
</tr>
<tr>
<td>Hopkins Verbal learning test</td>
<td>22%</td>
<td>0%</td>
</tr>
<tr>
<td>Clock Draw Test</td>
<td>22%</td>
<td>0%</td>
</tr>
</tbody>
</table>

5. Does This Patient have Dementia?
Why Screen?
- Dementia often unrecognized in primary care settings (67% - Valcour 2000 Arch Intern Med)
- Early detection allows opportunity for:
  - Advance care planning
  - Promotion of safety (driving, firearms, financial security, elder abuse)
  - Look for potentially reversible causes
  - Treat with medications, which may help modestly
- USPSTF recommendations: “The concept of detecting dementia at an early stage to allow interventions is a good one” Annals of Internal Medicine 2003

Authors’ Summary of Most Practical Approach for Primary Care Practitioners
- Want to find Cognitive Impairment of at Least Moderate Severity
  - Use MMSE
- Suspicion of Mild Impairment or Highly Educated Patient
  - Hopkins Verbal Learning Test or Word List Acquisition Test
- Little Time Available
  - Memory Impairment Screen or Clock Draw Test (or mini-cog)
  
Clinical Bottom Line
- Dementia Screening is reasonable for patients over age 65 or 70
- The mini-cog (clock draw plus the 3 item recall) is probably the most reasonable screen
  - Takes little time, easy to use
  - Less education/language dependent than MMSE
- MMSE reasonable for patients who do not pass mini-cog
  - Currently copyrighted
  - 24 is usual cutoff, performs best with age/education norms
- Might consider other screens in special practices

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>LR +</th>
<th>LR-</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>7-10</td>
<td>6.3</td>
<td>1.9</td>
</tr>
<tr>
<td>Memory Impairment Screen</td>
<td>4</td>
<td>33</td>
<td>0.08</td>
</tr>
<tr>
<td>Clock Draw Test</td>
<td>1-2</td>
<td>1.2-7.8</td>
<td>.13-.3</td>
</tr>
<tr>
<td>Mini-Cog</td>
<td>3-4</td>
<td>13</td>
<td>0.25</td>
</tr>
<tr>
<td>Hopkins Verbal Learning Test</td>
<td>30</td>
<td>4.8</td>
<td>.05-.21</td>
</tr>
</tbody>
</table>

Materials must be purchased

Holsinger et al JAMA June 6, 2007
Which of the following vitamins has been shown to reduce mortality?

1. Vitamin E
2. Vitamin D
3. Vitamin B complex
4. Vitamin E, vitamin C, beta-carotene, selenium complex
5. None of the above

Vitamin D Meta-analysis

- **Rationale:** Associations have been found between latitude, seasonality, and mortality from various conditions
- Vitamin D expressed in many tissues
- Activation of Vitamin D receptors induces cell differentiation, inhibits proliferation, invasiveness, and metastatic potential
- Theoretical, in vitro, and other evidence suggests that vitamin D might play a protective role in many chronic diseases

*Autier et al Arch Intern Med September 10, 2007 & Editorial*

**Vitamin D Meta-analysis**

- 18 independent RCTs
- 57311 patients, 4711 deaths analyzed
- Average study duration of 5.7 year
- Average Vitamin D dose of 300-200IU
- Most, but not all, performed in frail elders
- **Results:** All cause mortality reduced by 7% (CI 0.87-0.99)
- Trends for decrease in CV and cancer deaths, but not definitive or statistically significant

Clinical Bottom Line

- Vitamin D supplementation now linked to decreased falls, fractures, and mortality
- Multiple other vitamin studies published in past 10 years have been negative

_Autier et al. Arch Intern Med September 10, 2007 & Editorial_

Clinical Bottom Line

For elders, two approaches

- Check 25-OH vitamin D levels in all patients over 65
- Target levels of 30-40ng/ml
- For those with low levels (<15ng/ml), give loading dose of 50,000 IU weekly for 2-8 weeks
  OR
- Treat everyone with 800IU vitamin D plus 1000-1500 mg of calcium
- Check 25-OH vitamin D in patients with osteoporosis or otherwise at high risk

Zoledronic Acid, when given with 90 days of hip fracture, can improve which of the following outcomes?

1. Hip fractures
2. Vertebral fractures
3. Mortality
4. All of the above

Zoledronic Acid and Clinical Fractures and Mortality after Hip Fracture

- RCT double blind placebo controlled
- 2127 patients randomized to receive 5mg IV zoledronic acid (n=1065) vs placebo (n=1062) within 90 days after hip fracture
- All received calcium and vitamin D (if levels low, vitamin D loaded X1)
- Follow up ~ 2 years
- Primary outcome: New clinical fxs

Patient Characteristics

- All patients unable or unwilling to take oral bisphosphonate (those previously on bisphosphonate or PTH could enroll after washout)
- Mean age 75, 75% women
- 41% had T score < -2.5
- 35% had T score of -2.5- -1.5
- 12% were receiving other osteoporosis therapy

Results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo</th>
<th>Zoledronic acid</th>
<th>HR</th>
<th>P value</th>
<th>NNT over 2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fractures</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>13.9%</td>
<td>8.6%</td>
<td>0.65</td>
<td>0.001</td>
<td>19</td>
</tr>
<tr>
<td>Non-Vertebral</td>
<td>10.7%</td>
<td>7.6%</td>
<td>0.73</td>
<td>0.03</td>
<td>32</td>
</tr>
<tr>
<td>Vertebral</td>
<td>3.8%</td>
<td>1.7%</td>
<td>0.70</td>
<td>NS</td>
<td>-</td>
</tr>
<tr>
<td>Hip</td>
<td>3.5%</td>
<td>2.0%</td>
<td>0.54</td>
<td>0.02</td>
<td>67</td>
</tr>
<tr>
<td>Death</td>
<td>13.3%</td>
<td>9.6%</td>
<td>0.72</td>
<td>0.01</td>
<td>27</td>
</tr>
</tbody>
</table>

Adverse Events

- Adverse events were similar in the two groups
  (38% ZDA group, 41% in placebo)
- More common in ZDA group:
  - pyrexia (9% v 3%)
  - myalgia (5% v 3%)
  - bone pain (3% v 1%)
  - no incidents of jaw osteonecrosis
Bottom Line

- IV zolendronic acid given within 90 days of hip fracture reduces fractures and mortality at 2 years with no increase in adverse events
- Zoledronic Acid ~ $970 for 1 – 4mg vial (in this trial 5mg was given)
- Alendronate Cost = ~ $400 for 12 months of 70mg weekly

Source: Drugstore.com

Clinical Bottom Line

- Would I change patients from other bisphosphonates to zoledronic acid?
  I would at least offer, let patients decide based on cost and convenience
- Would I give 5mg as in the trial, or 4mg (cheaper and more convenient)?
  4mg
- Remember Vitamin D!

(Also of interest: Black DM et al. NEJM 2007: 356: 1809-22.)

Your patient is an 80 year old man with Parkinson’s disease and chronic constipation. A colonic transit study confirmed the diagnosis of slow transit constipation. Based on recent literature, which of the following regimens would most likely to be safe and effective as a first line treatment?

1. Increased fiber
2. Docusate sodium
3. Polyethylene glycol
4. Bisacodyl

Treatment of Chronic Constipation

- Despite high prevalence of chronic constipation, relatively few long term studies to guide our treatments
- Recent trial published in Am J. Gastroenterology suggested that use of polyethylene glycol for up to 6 months was safe and effective
- Recent guidelines on chronic constipation published by AGA Institute [www.MyGuidelinesCenter.com]
Treatment of Chronic Constipation

Methods
- RCT of patients with constipation for at least 3 months (ROME criteria)
- 2:1 randomization design
- 17gm PEG (Miralax) or identical placebo in 8oz juice once daily

Outcomes:
- 3 or more stools week, ROME criteria, and use of rescue laxatives

DiPalma Am J. Gastroenterology 2007

Results

<table>
<thead>
<tr>
<th></th>
<th>PEG N=202</th>
<th>Placebo N=100</th>
<th>P Value</th>
<th>NNT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Response</td>
<td>52%</td>
<td>11%</td>
<td>&lt;0.001</td>
<td>2–3</td>
</tr>
<tr>
<td>% of weeks with no constipation</td>
<td>61%</td>
<td>22%</td>
<td>&lt;0.001</td>
<td>2-3</td>
</tr>
<tr>
<td>% of weeks with ROME criteria not met</td>
<td>66%</td>
<td>25%</td>
<td>&lt;0.001</td>
<td>2-3</td>
</tr>
<tr>
<td>Bowel movements/wk</td>
<td>7.9</td>
<td>5.6</td>
<td>&lt;0.001</td>
<td>NA</td>
</tr>
<tr>
<td>Adverse Events: &quot;GI complaints&quot;</td>
<td>40%</td>
<td>25%</td>
<td>0.015</td>
<td>NNH = 7</td>
</tr>
</tbody>
</table>

DiPalma Am J. Gastroenterology 2007

In Summary

- Polyethylene glycol was safe and effective for chronic constipation over 6 months
- 2 cases of “severe” diarrhea were reported – one resolved spontaneously, other after d/c of medication
- No electrolyte problems reported
- Costs: about $20-30/mo (@drugstore.com)

DiPalma Am J. Gastroenterology 2007

Clinical Bottom Line

- Chronic Constipation: 59% of cases
  Would use polyethylene glycol or lactulose (osmotic laxatives) as second line agents for chronic constipation not responsive to lifestyle (diet, exercise, fluid) and fiber
- Slow Transit Constipation: 13% of cases
  Would use polyethylene glycol or lactulose as first line in patients with “slow transit” constipation
- Pelvic Floor Dysfunction or mixed – 25% of cases
  More individualized approach needed

AGA Institute Chronic Constipation Guidelines
www.MyGuidelinesCenter.com
Your patient has severe osteoarthritis of the right hip. She is already taking acetaminophen, ibuprofen, and occasional opioids. She is otherwise well. She grades her pain as 6/10 on most days. What would be the best next step in her treatment?

1. Glucosamine/chondroitin sulfate
2. Total hip replacement
3. Fluoroscopic-guided intra-articular injection of corticosteroid
4. Fluoroscopic-guided intra-articular hyaluronic acid

Methods

- RCT of 52 patients with symptomatic OA for at least 6 months
- Daily pain despite maximum doses of conventional drugs
- Intervention: Fluoroscopic guidance of either bupivacaine 10mg and triamcinolone hexacetonide 40mg, bupivacaine alone, or saline placebo
- Outcomes 20% improvement in WOMAC scores
- SF-36 QOL score

Lambert et al Arthritis and Rheumatism July 2007

<table>
<thead>
<tr>
<th>Outcomes at 2 months</th>
<th>Steroid</th>
<th>Placebo</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20% improvement in pain (WOMAC)</td>
<td>68%</td>
<td>24%</td>
<td>3 (2-7)</td>
</tr>
<tr>
<td>50% improvement in pain (WOMAC)</td>
<td>61%</td>
<td>14%</td>
<td>3 (2-5)</td>
</tr>
</tbody>
</table>

P value

| Global Assessment of health | -22 | +1.2 | 0.005 |
| Physical function score | -431 | -22 | <0.0001 |
| SF-36 physical | +1.0 | +5.3 | p<0.05 |
Clinical Bottom Line

- Intra-articular steroid injection under fluoroscopic guidance is a reasonable intervention for reducing pain and function in patients with OA hip
- We may need to do some education with our IR colleagues

Hypertension in the Oldest Old

- Despite the known benefits of blood pressure reduction in almost all clinical situations, whether control of HTN in the oldest old confers a mortality risk is unclear
- In observational studies, patients over age 85 with the lowest blood pressure had the highest mortality rates  
  Bulpitt 2003
- In the past, reduction in blood pressure in patients over age 80 has been shown to decrease CHF and Stroke, but not mortality
- A study was published this year in the NEJM that adds to our knowledge

Which of the following is true about treatment of BP in patients older than age 80?

1. There are no RCTs that inform this question
2. Lower blood pressure is associated with an increase in mortality
3. Treatment of HTN reduces stroke, but no other outcomes
4. At least in healthier elders, treatment of HTN reduces mortality in addition to other CV outcomes

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**Hyvet**  
Beckett et al NEJM 2008

- 3845 patients from Europe, China, Australia, Tunisia who were 80+ with systolic blood pressure of 160mm HG or more
- Multiple exclusion criteria
- Randomized to indapamide SR 1.5 mg or placebo
- If target blood pressure of 150/80 not reached, perindopril or placebo added
- Outcomes:
  - Primary: Stroke (fatal or non-fatal)
  - Secondary: Mortality, CV mortality, heart failure, CV events

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**Results**

*NNT to prevent one event over 4 years

<table>
<thead>
<tr>
<th>Event</th>
<th>Tx</th>
<th>Placebo</th>
<th>P Value</th>
<th>NNT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality</td>
<td>47%</td>
<td>60%</td>
<td>0.02</td>
<td>~8</td>
</tr>
<tr>
<td>Stroke</td>
<td>51%</td>
<td>69%</td>
<td>0.06</td>
<td>NS</td>
</tr>
<tr>
<td>Fatal Stroke</td>
<td>27%</td>
<td>42%</td>
<td>0.046</td>
<td>~7</td>
</tr>
<tr>
<td>CHF</td>
<td>22</td>
<td>57</td>
<td>&lt;0.001</td>
<td>~3</td>
</tr>
<tr>
<td>CV Event</td>
<td>34</td>
<td>51</td>
<td>&lt;0.001</td>
<td>~6</td>
</tr>
</tbody>
</table>

Beckett et al NEJM 2008
Clinical Bottom Line

- This adds evidence that treating hypertension in the oldest old is beneficial
- This group was VERY healthy
- Would still use caution in applying results to frailer elders
- Unclear how indapamide +/-perindopril compared to other regimens

The oldest Americans are also the happiest, research finds

CHICAGO Apr 19, 2008 (AP)
By Lindsey Tanner AP Medical Writer

“Overall, about 33 percent of Americans reported being very happy at age 88, versus about 24 percent of those age 18 to their early 20s”

“Overall, baby boomers were the least happy”


Happy Life Expectancy to You!

Edna Parker, age 115