Don’t just do something, Stand There: Brief topics in Care of the Elderly

G. Michael Allan

Faculty/Presenter Disclosure

• Faculty: G Michael Allan
• Relationships with commercial interests >19 yrs:
  – Grants/Research Support: None
  – Speakers Bureau/Honoraria: None
  – Consulting Fees: None
  – Other: None
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  – I get pay from Alberta Health, University of Alberta, & College of Family Physicians of Canada
  – I get grants and KT funding from a variety of non-profit sources like ACFP and TOP.
Jeopardy: Audience Choices

1. Cholinesterase Inhibitors
2. Vitamins (general)
3. Vitamin D
4. Risky Medicines
5. Agitation (anti-psychotics)
6. Agitation (other)
7. Osteoporosis (Medicine Basics)
8. Osteoporosis (How to Prescribe)

RISKY MEDICINES
**Cooks in the Kitchen**

- Average ≥65 year old patient has 6 chronic conditions
  - Often lots of medicines and lots of prescribers

- Each additional prescriber is associated with 29% increase in Adverse Drug Reactions
  - If your patient sees someone else, Take a good drug history.


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**Criteria for Drug Use in Elderly**

- Beers: 12 experts.\(^1\) Updated in 2003.

- >10 types\(^2\): Beers, STOPP, START, Canadian Criteria, IPET, French Consensus, Australian Prescribing indicator, Japanese Beers, NORGEP, & Italian, + Drug Burden Index (DBI)\(^3\), + PRISCUS\(^4\)
  - All are consensus based
  - Overlap as little as 30%

## Guides to safe prescribing

- **Beers, the most popular:** weak evidence\(^1\)
  - Assoc with hospitalization in community elderly,
    - No other consistent associations
- **Drug Burden Index (DBI)**
  - DBI assoc decreased physical function & falls,\(^2\)
    - Beers not\(^3\)
- **STOPP\(^5\) may be better**
  - STOPP slightly better to predict ADE & hospitalization

**Best Study to date?**

- Hospitalization\(^1\) for Drug related Adverse Events,
- In people ≥65
  - Half happened in ≥80
  - 66% were unintentional overdose.
- 67% were: warfarin, insulins, oral antiplatelet agents, and oral hypoglycemic agents.
  - Prescribing rules would identify 1-6% of meds.


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**Some Associations Are**

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Falls</th>
<th>Fractures</th>
<th>Delirium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Anti-depressants</td>
<td>✔</td>
<td>✔</td>
<td>?</td>
</tr>
<tr>
<td>Anti-psychotic</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Anti-epileptic</td>
<td>✔ (?)</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive</td>
<td>✔ (?)</td>
<td></td>
<td></td>
</tr>
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</table>

Studies of Unsafe Prescribing

• Mainly benzodiazepines, antidepressants, antipsychotics, anticholinergics, BP meds, etc.¹

• Benzodiazepine in age ≥80 associated with falls
  – Perhaps 2.8% increase falls/year (9% fatal)²

• Systematic Rev: 29 studies (28 cohort, 1 RCT)³
  – Mainly benzodiazepine, antidepressants, antipsychotics
  – Also BP meds & anti-epileptic (weaker association)

• Med associated with falls⁴
  – Consistent: Sedative/hypnotics, Benzodiazepines, & antidepressants
  – Less consistent: Neuroleptics/antipsychotics & anti-hypertension


Studies of Unsafe Prescribing

• Systematic review¹: meds associated with fracture
  – 1.34 (1.24, 1.45) for benzodiazepines (23 studies),
  – 1.60 (1.38, 1.86) for antidepressants (16 studies),
  – 1.54 (1.24,1.93) for antiepileptic drugs (13 studies)
  – 1.59 (1.27, 1.98) for antipsychotics (12 studies)
  – 1.38 (1.15, 1.66) for opioids (six studies).

• NSAIDS may also be associated with falls.²

OSTEOPOROSIS: HOW TO PRESCRIBE

Understanding The Risk of Fracture

Acceptance of Osteoporosis medications

- Physicians estimate ~70% adhere to osteoporosis meds
  - However, only ~50% even fill their scripts

- When physicians & patients are given absolute fracture risk (versus simply high/mod/low)
  - Prescribing rates go down 7-10%

- What hip fracture risk should someone have before you offer bisphosphonate therapy?

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<tr>
<td>3%</td>
<td>10%</td>
<td>50%</td>
</tr>
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</table>


What if they have had a fragility fracture?

- Systematic review of 23 sys reviews: select 14 RCTs with
  - Past fracture (vertebral): bisphosphonate vs placebo (~3 yrs)

<table>
<thead>
<tr>
<th>RR Fracture</th>
<th>Overall Event Rates</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMD for Inclusion</td>
<td>No BMD for Inclusion</td>
</tr>
<tr>
<td>Non vertebral Fracture</td>
<td>0.77 (0.63-0.93)</td>
<td>0.73 (0.58-0.91)</td>
</tr>
<tr>
<td>Vertebral Fracture</td>
<td>0.64 (0.47-0.87)</td>
<td>0.62 (0.50-0.77)</td>
</tr>
</tbody>
</table>

- **Bottom-Line:** Once a fracture has happened,…
  1. You don’t really need a BMD (fracture risk ~30% in 10 yrs)
  2. Just offer therapy: NNT is 36 for non-vertebral fracture in 3 yrs.
Who needs a BMD?

- 8 systematic reviews, 108 studies, 208,738 patients
- No tool clearly superior, but OST performs ≥ other tools:
  - FRAX missed ~9% femoral neck osteo vs OST missing 6%.
  - OST validated in both sexes and differing races.
- **OST: Weight (kg) – Age (years).**
- If <10, risk of osteoporosis, BMD is needed. Example:
  - A 55 year old woman weighing 70 kg: OST=70-55=15,
  - She is low risk for osteoporosis and does not need a BMD.
- **Bottom-Line:** You want to weigh 10 kg more than your age, or you need a BMD.

https://osteoporosisdecisionaid.mayoclinic.org/index.php/osteo/index
Retesting BMD

• Alendronate yearly increase = variation in BMD\(^1\)
  – Variation in BMD= 2.4% to 5% (over 2 weeks)
  – On Treatment, BMD improves 1-6% over 3 years,
  – Not on Treatment, BMD worsens 1.5%-6% over 3 years
  – Note: Alendronate “sufficient” BMD for 97.5% at 3 yrs & even decreased BMD still reduced fracture risk.

• New Guidelines recommend against repeat BMD on Tx\(^2\)

• **Bottom-Line:** If on therapy, no need to repeat BMD. If not on therapy, consider at ~5 years.

Drug Holiday

• FLEX: 1,099 women, 60% past fracture, alendronate x5 yrs. After 5 years more:
  – No difference: non-vertebral # & total vertebral #
    • 1 subgroup - clinical vertebral #, (2.4% v 5.3%). NNT = 36

• HORIZON: RCT, 1,233 pts, stop vs continue zoledronic acid x additional 3 yrs
  – No different in clinical fractures.

• FDA requires label that duration unknown

• **Bottom-Line:** “ACP recommends that clinicians treat osteoporotic women with pharmacologic therapy for 5 years.” Maybe continue in high risk but that unclear. No other guidance.
Osteoporosis: MEDICINE BASCIS

Comparing Relative Reduction in Fracture with Different Treatments

<table>
<thead>
<tr>
<th>Drug</th>
<th>Sys Reviews</th>
<th>RCTs</th>
<th>RR Vertebral</th>
<th>RR Non vertebral</th>
<th>RR Hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etidronate</td>
<td>NR</td>
<td>11</td>
<td>0.53</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Alendronate</td>
<td>9</td>
<td>17</td>
<td>0.36-0.60</td>
<td>0.51-0.89</td>
<td>0.45-0.79</td>
</tr>
<tr>
<td>Risedronate</td>
<td>10</td>
<td>14</td>
<td>0.31-0.54</td>
<td>0.40-0.81</td>
<td>0.60-0.74</td>
</tr>
<tr>
<td>Zoledronic Acid</td>
<td>0</td>
<td>4</td>
<td>0.23-0.54</td>
<td>0.72-0.73</td>
<td>0.56-0.69</td>
</tr>
<tr>
<td>Denosumab</td>
<td>0</td>
<td>8</td>
<td>0.34-0.44</td>
<td>0.80</td>
<td>0.59</td>
</tr>
<tr>
<td>Teriparatide</td>
<td>2</td>
<td>5</td>
<td>0.31-0.36</td>
<td>0.60-0.65</td>
<td>NS</td>
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<tr>
<td>Raloxifene</td>
<td>3</td>
<td>NR</td>
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Often no clear distinction between 1 and 2 prevention

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### 10 Year Fracture Risk (on FRAX & Bisphosphonate Benefits (T-score = -2.5))

<table>
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<th>Age</th>
<th>Risk of All Fracture</th>
<th>Risk of Hip Fracture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Without Meds</td>
<td>With Meds (30% RRR)</td>
</tr>
<tr>
<td>50</td>
<td>11%</td>
<td>8%</td>
</tr>
<tr>
<td>60</td>
<td>16%</td>
<td>11%</td>
</tr>
<tr>
<td>70</td>
<td>23%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Approximate values*60kg women, No other risk factors

MORE ON HARMS:

**Prolonged bisphosphonates**
- Observational evidence - atypical fractures: minimal absolute risk\(^1,2\)
- First 5 years of therapy:
- Total Fractures Prevented: 2,590/100,000\(^3\)
  - (175 hip, 1470 vertebral, 945 wrist)
- Atypical Fractures: 16/100,000
- **Benefit**: 162 fractures prevented / 1 caused
- Risk of AF and ONJ may \(\uparrow\) with prolonged exposure.

**Denusomab**:
- \(\uparrow\) risk bacterial cellulitis (1.3% vs 0.6%), \(\uparrow\) risk rash/eczema (RR 1.96)
- Rare atypical fracture and ONJ


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**What about Mortality?**

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>Relative Risk [95% Confidence Interval]</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>24/1022</td>
<td>21/1005</td>
<td>1.12 [0.63, 2.01]</td>
<td>3</td>
</tr>
<tr>
<td>Black 1996</td>
<td>37/2214</td>
<td>49/2218</td>
<td>0.93 [0.56, 1.44]</td>
<td>5</td>
</tr>
<tr>
<td>Risedronate</td>
<td>61/3236</td>
<td>61/3223</td>
<td>1.00 [0.70, 1.41]</td>
<td>P=0.98</td>
</tr>
<tr>
<td>Harris 1999</td>
<td>15/813</td>
<td>15/815</td>
<td>0.94 [0.47, 1.89]</td>
<td>2</td>
</tr>
<tr>
<td>Reginster 2000</td>
<td>11/407</td>
<td>12/416</td>
<td>0.94 [0.47, 1.89]</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>140/4382</td>
<td>142/4382</td>
<td>1.00 [0.70, 1.41]</td>
<td>P=0.98</td>
</tr>
<tr>
<td>Strontium</td>
<td>171/3352</td>
<td>171/3352</td>
<td>0.90 [0.63, 1.29]</td>
<td>P=0.54</td>
</tr>
<tr>
<td>Muenier 2004</td>
<td>29/826</td>
<td>31/826</td>
<td>0.90 [0.63, 1.29]</td>
<td>P=0.54</td>
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<td>Reginster 2005</td>
<td>142/2526</td>
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<tr>
<td>Black 2007</td>
<td>101/1054</td>
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<tr>
<td>Cummings 2008</td>
<td>70/3602</td>
<td>90/3606</td>
<td>0.78 [0.57, 1.06]</td>
<td>P=0.11</td>
</tr>
<tr>
<td>Total</td>
<td>673/19788</td>
<td>744/19761</td>
<td>0.90 [0.81, 1.00]</td>
<td>P=0.044</td>
</tr>
</tbody>
</table>

Test for heterogeneity: \(P=0.27\), \(I^2=0.2%\)

**IF REAL, NNT ~300 Over ~3 years**

\[ J \text{ Clin Endocrinol Metab. 2010 Mar} \]
Vitamins

Multivitamins: Living longer

- Meta-analysis 21 RCTs with 91,074 patients (54% males) multivitamins vs placebo x3.5 yrs. Primary prevention RCTs, Europe or North America.
  - Overall mortality RR=0.98 (0.94-1.02).
  - Cancer mortality: RR=0.96 (0.88-1.04).
  - CVD mortality: RR=1.01 (0.93-1.09).

- **Bottom-Line**: Tons studied, no effect!

TFP #87, August 5, 2016.
Macular Degeneration: Ocular Vitamins

- Ocular Vitamins: Antioxidants/zinc vs placebo. Category 3 & 4 (more advanced), over 6.3 yrs.
  - Preventing 15 letter visual loss: antioxidants/zinc (23%) vs placebo (29%), NNT 17.
  - Preventing progression: NNT 13
  - Newer formulation Equal placebo.

- **Bottom-Line**: For patients with more advanced age-related macular degeneration, ocular vitamins reduce progression & visual loss with NNT ~15 over 6 years.

Antioxidant vitamin cure-alls

- Meta-analysis of 78 RCT (but others find similar)
  - 296,707 (75% healthy, 25% pre-existing).
- Focusing on high-quality RCTs:
  - Antioxidants increase mortality: RR 1.04 (1.01-1.07), NNH=240.
  - Beta carotene, A and E each significant
  - Vitamin C or selenium not.

- **Bottom-Line**: Daily use of anti-oxidant vitamins cause one more death for every 250 over ~5 years.
Iron: A Plug for Therapy

- RCT, 90 elderly anemic x2m (150, 50, 15mg)
  - Hgb ↑ significantly (1.4 or 14), no diff between doses
  - AE ↑ significantly as dose ↑, Dropout 15mg vs 150mg
    NNH = 5
- 30mg of elemental iron = Ferrous sulphate 150mg
  - 15mg elemental iron = 2.5 ml's of Fer-In-Sol
- **Bottom-Line:** Low dose iron for replacement in the elderly (with appropriate work-up)

Calcium: It does a body harm?

- 5 systematic reviews: a few statistical significant (some with subgroups)
  - MI (RR 1.16 to 1.27)
  - Generally Ca+ supplementation (≥500mg/d) vs placebo
- Ca+ (88% Vit D) reduces fracture, NNT 63 x3.5 yrs
  - Ca+ alone just failed to reach statistical significance.
- **Bottom-line:** If real, the increase risk is likely <1% for most but similar to benefit.
Getting the most of your vitamins

1) Take the vitamins to a friends' house ~5 km from your house. If you want to take your vitamin, walk to their house, pop the pill, walk home.

2) If you believe in higher dose vitamins, choose a home 10 km from your house, run there at a comfortable pace, take two pills, and run home.
   • Note: You can just take one and get the same effect
   • Note 2: You can also take none

3) Place your vitamins on your dinner plate. Surround them with fresh and well seasoned/flavored vegetables, fruit, grains and fish/poultry. If compelled to try a vitamin, pick it up, lick it. Does it compare to food?

4) Your body is equipped with a tremendous filtering system called “kidneys.” So when you ingest more than the small amount of vitamins required for health, you pee out the excess. To avoid possible strain on your kidneys, place your vitamins directly into the toilet and flush.

5) Finally, if you really want your vitamins to work, package them up and send them to countries where vitamin deficiency are a serious health concern. The effect generosity may be the only supplement you need.