Geriatric Medicine: 2018 Updates

Rocky Mountain Geriatrics Conference
September 24, 2018

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University of Colorado Hospital
Disclosures

- No financial relationships with commercial interests to disclose
The Agenda/Learning Objectives

• Nutrition related issues
  ➢ meds that impact nutrition
  ➢ iron replacement pearls
  ➢ CHF management

• New agents/approaches to consider?
  ➢ DVT prophylaxis after THA/TKA
  ➢ For Bladder

• Reducing polypharmacy “deprescribing”
Meds & Nutritional issues in older adults: Case Vignette

• A 78 yo F is seen in f/u for DM, HTN, GERD, OA & depression. She c/o knee pain & mood being down, o/w stable. **Meds:** metformin, lisinopril, omeprazole, sertraline, APAP

• You recognize that 2 of her meds ↑ her risk for a relevant micronutrient deficiency and order a - ?

A) Vitamin B12 level
B) Vitamin D level
C) Magnesium level
D) Calcium level
Nutritional issues in older adults: Case Vignette

• You recognize that 2 of her meds ↑ her risk for a relevant micronutrient deficiency and order a -?
  A) Vitamin B12 level – d/t metformin and PPI
     - low B12 level 2x ↑ risk of depression
  B) Vitamin D level
  C) Magnesium level
  D) Calcium level

Am J Psychiatry 2000;157:715-21
Metformin & B12 Deficiency

• B12 deficiency common in older adults: 5-15%

• Metformin may double prevalence low B12
  - Impairs B12 absorption
  - Risk ↑ with duration use, likely also dose effect

• Diabetes prevention program met vs plb, at 5 yrs
  - B12 ≤ 200 pg/mL: Met 4.3% vs PLB 2.3%, $P = .02$
  - B12 ≤ 300 pg/mL: 19.1% vs 9.5%, $P < .01$

J Clin Endocrinol Metab 2016;101:1754-61
PPIs & B12 Deficiency

- **MOA:** achlorhydria $\rightarrow \downarrow$ absorption food-cbl

- **PPI > H2 block, w/dose & duration effect**
  - 2+ yr PPI $\uparrow$ risk: OR 1.65 (95% CI, 1.58-1.73)
  - 1.5+ PPI pills/d $\uparrow$ risk: OR 1.95 (95% CI, 1.77-2.15)
  - 2+ yr H2RAs $\uparrow$ risk: OR 1.25 (95% CI, 1.17-1.34)

- **BTW, ideally avoid chronic PPI use**
  - $\downarrow$ absorption B12, iron, mg++, ca++, LT4
  - $\uparrow$ C Diff, fractures, CKD, dementia?
  - PPI deprescribing – more later

B12 Deficiency Dx Pearls

- **Rec screen** at least once age 65+

- **Signs/sxms** subtle, non-specific, eg fatigue, ↓ mood or memory, ↓ balance

- **Lab Dx** B12 150-350pg/ml unreliable (as is ↑ MCV)
  - B12 level 200 pg/ml → sens/spec 50%
  - Methylmalonic acid level best, renal cleared, $50
  - Best to treat all low/borderline low levels < 350 ?

B12 Deficiency Tx Pearls

• **Tx** 1000µg oral daily works as well as IM/mo

• **Oral repletion**
  - B12 diffusion → 1% intake absorbed
  - Physiologic requirements 1-2 µg/d
  - 1000µg/d → clinical, heme, serum response

• **Caveats** compliance, initial tx, clinical dz

Nutrition & Prescribing Practices: The issue of iron supplementation

A 75-year-old woman falls and suffers a hip fracture. S/P hip repair her Hgb drops from 12 pre-op to 8. PHM: HTN & DM w/o known cardiovascular dz. She feels fine save for mild fatigue. What do you recommend for her anemia?

A) Fe So4 325 mg QD
B) Fe So4 325 mg BID
C) Fe Gluconate 325 mg QD
D) Transfuse 1 U PRBC
Excessive iron supplementation: one of my pet peeves

What do you recommend for her anemia?

A) Fe So4 325 mg QD – 65mg elemental iron (EI)
B) Fe So4 325 mg BID – marginal benefit BID dose
C) Fe Gluconate 325 mg QD – 37.5mg EI
D) Transfuse 1 U PRBC – no s/s to warrant txn
   - 2016 US guideline: txn threshold Hgb 8g/dL for pts having orthopedic or cardiac surgery or preexisting cardiovascular dz (o/w 7g/dL)

AABB RBC Txn Guidelines JAMA 2016;316:2025-35
Is Low Dose Elemental Iron the Way to Go in Older Adults?

- RCT 90 inpts age 80+ w/iron deficiency anemia
- Elemental iron*: 15 mg or 50 mg of liquid ferrous gluconate, or 150 mg ferrous calcium citrate daily
- 60 day f/u: Hgb ↑ x 1.4 g/dL, Ferr ↑ x 40
- No difference in rise in hemoglobin or ferritin levels between groups over 60 days

* Elemental iron (EI): FeSo4 325mg = 65mg EI, FeGluconate 325mg = 37.5mg EI, MVI = 0-18mg

Variable dose iron effect on ferritin

![Graph showing ferritin levels over time for different iron dosages.](image-url)
Is Low Dose Iron The Way to Go in Older Adults? → YES!

- Significantly less adverse effects with lower dose

- **Dose**
  - 15mg vs 50mg vs 150mg

<table>
<thead>
<tr>
<th>Condition</th>
<th>15mg</th>
<th>50mg</th>
<th>150mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abd discomfort</td>
<td>20%</td>
<td>60%</td>
<td>70%</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>13%</td>
<td>36%</td>
<td>67%</td>
</tr>
<tr>
<td>Constipation</td>
<td>0%</td>
<td>10%</td>
<td>23%</td>
</tr>
<tr>
<td>Black Stool</td>
<td>0%</td>
<td>30%</td>
<td>67%</td>
</tr>
<tr>
<td>Dropout</td>
<td>7%</td>
<td>17%</td>
<td>27%</td>
</tr>
</tbody>
</table>

Iron Repletion in the Elderly

• Side effects of iron may lead to noncompliance
• QOD morning dosing nearly as effective as QD
• ↓ absorption if on PPI, take w/OJ or Vit C may ↑
• If can’t take/tolerate oral iron → IV rx of choice may be ferric carboxymaltose (injectafer, ferinject)
  - can dose 750mg single dose over 15 minutes
  - may repeat in 7+ days if needed
  - simpler than iron sucrose (venofer) 200mg qd x 5d

*Lancet Haematol* 2017;4: 524–33
CHF Case

• 78 yo M w/2yr hx HFrEF (EF 25%), NYHA class III, inpt x1 past 6 mo is seen in f/u
• Meds: aspirin, carvedilol, furosemide, losartan, spironolactone, escitalopram, APAP
• Labs: Cr 1.4, K+ 4.6, Hgb 10.5, Ferr 150, iron sat 14%, 25-Vit D level 24, TSH 6, B12 425

Which of the following is most likely to improve clinical s/s of CHF in this pt?
A) Vitamin D supplementation
B) Levothyroxine 25ug, titrate to TSH 2-4
C) Iron supplementation
D) Vitamin B12 supplementation
CHF Case

Which of the following is most likely to improve clinical s/s of CHF in this pt?

A) Vitamin D supplementation

B) Levothyroxine 25ug, titrate to TSH 2-4

C) Iron supplementation

D) Vitamin B12 supplementation
Heart Failure: Iron-Deficiency Adverse Effects

Eur Heart J. 2013;34:816-29

Cellular
- Mitochondrial dysfunction
- Deranged activity of enzymes
- Abnormal transport and structural proteins
- Apoptosis

Tissue
- Tissue remodelling
- Impaired organ efficacy

Function
- Impaired exercise capacity
- Reduced work efficacy
- Impaired cognitive performance and behaviour
- Increased morbidity and mortality
Mortality with Iron-Deficiency (ID) in HF

- Common comorbid condition in 1/3 pts
- Independent assoc w/mortality: adj HR 1.58

Eur Heart J. 2013;34:816-29
Iron-Deficiency Anemia: Defn & Dx

- 2 types of iron deficiency
  - **Absolute** depleted iron stores w/intact iron homeostasis
    - causes: low-diet intake, impaired GI absorp, blood loss
  - **Functional** nl or ↑ iron stores, but iron trapped inside cells of reticuloendothelial system, unavailable

- Serum ferritin
  - **Low** <100 ng/mL = absolute iron deficiency
  - **Normal** 100-300 ng/mL but could be functional defic

- Iron binding panel (iron/TIBC, Tsat < 20% low)
  - **Functional iron deficiency** Transferrin sat < 20% w/nl ferr

## Clinical studies of Iron Rx for CHF

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>INCLUSION CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FAIR-HF 2009</strong></td>
<td>Ferr &lt;100 ng/mL or 101-299ng/mL w/ TSat &lt;20%; Hb 9.5-13.5 NYHA II-III, HFrEF with LVEF ≤40-45%</td>
</tr>
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<td><strong>CONFIRM-HF 2015</strong></td>
<td>Ferr &lt;100 ng/mL or 100-300ng/mL w/ TSat &lt;20%; Hb &lt;15 Symptomatic HFrEF w/LVEF ≤45%, NYHA II-III, &amp; high BNP</td>
</tr>
<tr>
<td><strong>IRONOUT-HF 2017</strong></td>
<td>Ferritin &lt;100 ng/mL or 101-299ng/mL w/ TSat &lt;20%; NYHA II-III, LVEF ≤40%</td>
</tr>
<tr>
<td><strong>EFFECT-HF 2017</strong></td>
<td>Ferr &lt;100 ng/mL or 100-300ng/mL w/TSat &lt;20%; Hb &lt;15 NYHA II-III, HFrEF w/EF ≤45%; VO₂ max 10-20 mL/kg/min</td>
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Eur Heart J 2015;36:657  
JAMA 2017;317:1958  
Circulation 2017;136:1374-1383
Clinical studies of Iron Rx for CHF

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<th>N</th>
<th>DRUG REGIMEN</th>
</tr>
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<tbody>
<tr>
<td>FAIR-HF 2009</td>
<td>459</td>
<td><em>IV</em> ferric carboxymaltose (FCM) 200mg weekly, then Qmo starting at wk 8 or 12; or placebo</td>
</tr>
<tr>
<td>CONFIRM-HF 2015</td>
<td>304</td>
<td><em>IV</em> FCM 500-1000 mg based on weight/Hb at weeks 0, 6; 500mg at wks 12, 24, &amp; 36 depending upon Tsat and ferritin; or placebo</td>
</tr>
<tr>
<td>IRONOUT-HF 2017</td>
<td>225</td>
<td><em>Oral</em> iron polysaccharide 150mg BID or placebo</td>
</tr>
<tr>
<td>EFFECT-HF 2017</td>
<td>174</td>
<td><em>IV</em> FCM 500-1000 mg based on weight/Hb at weeks 0, 6 and 12; or placebo ± oral iron</td>
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Clinical studies of Iron Rx for CHF

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<tr>
<td>FAIR-HF</td>
<td>• Sig ↑ in pt global assessment (50% much or moderately improved vs 28%, OR 2.51)</td>
</tr>
<tr>
<td></td>
<td>• Significant ↑ in functional class (47% class I or II vs 30% at wk-24, OR 2.40), ↑ 6MW test and QOL</td>
</tr>
<tr>
<td></td>
<td>• Results similar in patients with anemia/no anemia</td>
</tr>
<tr>
<td></td>
<td>• No difference in death or adverse events</td>
</tr>
<tr>
<td></td>
<td>Sig ↑ in 6MW, NYHA class, QOL &amp; fatigue starting at week 24 in all subgroups through wk52</td>
</tr>
<tr>
<td></td>
<td>• Significant ↓ in hospitalization for worsening HF (HR 0.39), trend ↓ hosp any CV reason (HR 0.63)</td>
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<td>IRONOUT-HF</td>
<td>• Signif ↑ Tsat (2 pts); Nonsig ↑ ferritin (18 pts)</td>
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<tr>
<td>16 wk f/u</td>
<td>• No difference in change in VO(_2) max</td>
</tr>
<tr>
<td>Oral iron</td>
<td>• No difference in 6MW distance, NT-proBNP levels or KCCQ QOL score</td>
</tr>
<tr>
<td>150mg BID</td>
<td></td>
</tr>
<tr>
<td>EFFECT-HF</td>
<td>• ↑ Hb (by 0.74), ↑ ferritin (by 189), ↑ Tsat (by 5)</td>
</tr>
<tr>
<td>24 wk f/u</td>
<td>• Significant ↑ VO(_2)max with or without anemia</td>
</tr>
<tr>
<td>Mean IV</td>
<td>• Significantly improved functional class &amp; patient global assessment</td>
</tr>
<tr>
<td>iron dose</td>
<td></td>
</tr>
<tr>
<td>1204 mg</td>
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*JAMA 2017;317:1958  Circulation 2017;136:1374-1383*
Meta-Analysis: IV Iron for Pts with HFrEF and Iron Deficiency

Eur J Heart Fail 2016;18(7):786-95
## Meta-Analysis: IV Iron for Pts with HFrEF and Iron Deficiency

### 6MWT distance

**6 min walk**

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean difference</th>
<th>MD</th>
<th>95%-CI</th>
<th>P-value</th>
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<td>-1.77</td>
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<td>0.193</td>
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<td>20</td>
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<td>0.228</td>
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<td>Anker et al. 2009</td>
<td>294 -0.306</td>
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<td>121</td>
<td>-0.28</td>
<td>-0.49</td>
<td>-0.05</td>
<td>0.276</td>
</tr>
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Heterogeneity: I-squared = 55.2%, tau-squared = 0.0904, p = 0.0001

Q = 20.66

### NYHA class

**NYHA**

<table>
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<tr>
<th>Study</th>
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<td>-0.05</td>
<td>0.276</td>
</tr>
</tbody>
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Heterogeneity: I-squared = 85.5%, tau-squared = 0.0904, p = 0.0001

Q = 9.17

### LVEF

**LVEF**

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean difference</th>
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<th>95%-CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toblli et al. 2007</td>
<td>20 -4.4</td>
<td>20</td>
<td>-6.4</td>
<td>-9.32</td>
<td>-3.48</td>
<td>0.514</td>
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<tr>
<td>Okonko et al. 2008</td>
<td>20 -2.0</td>
<td>10</td>
<td>1.0</td>
<td>-2.8</td>
<td>4.80</td>
<td>0.486</td>
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</table>

Heterogeneity: I-squared = 89.1%, tau-squared = 24.39, p = 0.0025

Q = 9.17

Eur J Heart Fail 2016;18(7):786-95
2016 Eur Soc of Cardiology Guidelines

Recommendations for the treatment of other co-morbidities in patients with heart failure

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron deficiency</td>
<td>IIA</td>
<td>A</td>
<td>469, 470</td>
</tr>
</tbody>
</table>

- Based upon FAIR-HF and CONFIRM-HF
- Intravenous ferrous carboxymaltose (FCM)
  - Improve self-reported global assessment
  - Improve QOL
  - Improve NYHA class
  - Improve exercise capacity
  - Reduce HF hospitalizations

Eur J Heart Fail 2016;18(7):786-95
### 2017 AHA/ACC Guideline Recs

#### Recommendations for Anemia

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
<th>Comment/Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>B-R</td>
<td>In patients with NYHA class II and III HF and iron deficiency (ferritin &lt;100 ng/mL or 100 to 300 ng/mL if transferrin saturation is &lt;20%), intravenous iron replacement might be reasonable to improve functional status and QoL(173, 174).</td>
<td>NEW: New evidence consistent with therapeutic benefit.</td>
</tr>
</tbody>
</table>

- **Routine eval of HF pts should include eval for anemia**
- **When iron deficiency is dx’ed and after full eval for cause, IV iron may ↑ exercise capacity and QoL**
- **“a strong rec for IV iron repletion must await the results of an appropriately powered trial on M&M”**

http://circ.ahajournals.org/content/early/2017/04/26/CIR.0000000000000000509
The Agenda/Learning Objectives

✓ Nutrition related issues
  ➢ meds that impact nutrition
  ➢ iron replacement
  ➢ CHF management

• New agents/approaches to consider?
  ➢ DVT prophylaxis after THA/TKA
  ➢ For bladder

• Reducing polypharmacy “deprescribing”
New info re: DVT prophylaxis
s/p elective orthopedic surgery
Your 74 yo pt with obesity (BMI 33), DM, HTN, CKD 3 (eGFR 40mL/min) and osteoarthritis undergoes elective total hip replacement surgery. Which of the following should you recommend for venous thromboembolism (VTE) prophylaxis?

A) Low molecular weight heparin SQ x 35 days

B) LMWH x 10 d then ASA 325mg qd x 25 d

C) Rivaroxaban 10mg qd x 14 days

D) Rivaroxaban 10mg x 5d then ASA 81mg x 30d
Which of the following should you recommend for venous thromboembolism prophylaxis?

A) Low molecular weight heparin SQ x 35 days
- LMWH no better than DOAC, ↑ cost, injection

B) LMWH x 10 d then ASA 325mg qd x 25 d
- studied, effective, but w/ASA 81mg (325mg ↑ risk)

C) Rivaroxaban 10mg qd x 14 days
- 14d for TKA, standard for THA 35 days

D) Rivaroxaban 10mg x 5d then ASA 81mg x 30d
- New study worth knowing about

VTE Prophylaxis s/p Hip or Knee Arthroplasty

- **Premise**
  - DOAC safe and effective: 14d TKA, 35d THA
  - ASA effective r/t placebo but ? vs DOAC

- **RCT:** ~ 3400 pts s/p *elective* TKA or THA

- **Compare:** rivaroxaban 10mg x 5d then ASA 81 vs rivaroxovvan 10mg qd x 9 (TKA) or 25 (THA) days

- **Outcome:** symptomatic VTE & bleeding

*Chest 2012:141(2);e278S*  
*NEJM 2018;378:699*
VTE Prophylaxis s/p Hip or Knee Arthroplasty

- Similar low VTE and bleeding rates

Table 2. Primary Effectiveness and Safety Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rivaroxaban (N = 1717)</th>
<th>Aspirin (N = 1707)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous thromboembolism</td>
<td>12 (0.70)</td>
<td>11 (0.64)</td>
<td>0.84*</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>6 (0.35)</td>
<td>5 (0.29)</td>
<td></td>
</tr>
<tr>
<td>Proximal deep-vein thrombosis</td>
<td>4 (0.23)</td>
<td>4 (0.23)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism and proximal deep-vein thrombosis</td>
<td>2 (0.12)</td>
<td>2 (0.12)</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>5 (0.29)</td>
<td>8 (0.47)</td>
<td>0.42</td>
</tr>
<tr>
<td>Any bleeding†</td>
<td>17 (0.99)</td>
<td>22 (1.29)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

* P<0.001 for noninferiority, as defined by the upper boundary of the 95% confidence interval for the absolute between-group difference.
† This category includes major bleeding and clinically relevant nonmajor bleeding.
**VTE Prophylaxis s/p Hip or Knee Arthroplasty**

- Concomitant ASA < 100mg PTA if anything increased bleed risk w/o additional benefit

<table>
<thead>
<tr>
<th>Table 4. Subgroup Analysis of Primary Outcomes, According to Use of Long-Term Aspirin Therapy.</th>
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<tbody>
<tr>
<td><strong>Outcome</strong></td>
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<tr>
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<td>Venous thromboembolism</td>
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<tr>
<td>Major bleeding</td>
</tr>
<tr>
<td>All bleeding†</td>
</tr>
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*P<0.001 for noninferiority.
†This category includes major and clinically relevant nonmajor bleeding.
VTE Prophylaxis s/p Hip or Knee Arthroplasty

Conclude

- After 5 day DOAC subsequent VTE prophylaxis w/ASA vs DOAC had similar efficacy & safety

- Caveats: Elective surgery, most NOT high risk pts
  - Study pt mean age 63, BMI 31
  - cancer 2%, hx VTE 2%
  - no recent fracture (may not apply to hip fx pts)
  - RFs: age, BMI > 40, hypercoag state, CHF, COPD

- If ↑ VTE risk extending DOAC likely appropriate

**NEJM 2018;378:699**
An 82 yo F c/o frequent (3-4x) night time voiding. She drinks 6 glasses H20 by day but limits intake after dinner, no coffee or soda. She has HTN, early Alzheimers dz, lumbar stenosis & mild depression. She takes her meds w/dinner: hctz, donepezil, APAP, citalopram. Exam & labs unremarkable save for Na+ 134

Which of the following is the next best step for reducing her nocturia?
A) Stop donepezil
B) Stop hctz
C) Start mirabegron
D) Start desmopressin acetate nasal spray
Whats new for the bladder?

Which of the following is the next best step for reducing her nocturia?

A) **Stop donepezil** – can ↑ both bowel and bladder contractility. Common “prescribing cascade” problem: rx Chol-I for AD, then bladder antispasmodic for “overactive bladder”

B) Stop hctz

C) Start mirabegron – reasonable if pt/family want to continue donepezil

D) Start desmopressin acetate nasal spray → NEW and probably never a good idea for older adults!
What’s new for incontinence?
Low dose nasal desmopressin (Noctiva)
Low dose nasal desmopressin acetate

- Oral desmopression 0.1-0.2mg has been used off-label to reduce nocturnal polyuria
- Some efficacy: may ↓ nocturnal voids by 0.5 to 1.5
- Sig risk: hyponatremia ~ 4% (Na+ < 130mmol/L)
- Hyponatremia RFs: age, other meds that ↑ risk low Na+ (SSRI, diuretics), ↓ renal funx
- FDA approved desmopression acetate nasal spray in 2017 for tx nocturia d/t nocturnal polyuria ≥ 2x/night

Low dose nasal desmopressin acetate

- Two *non-published* RCTs: ~1000 pts age 50+, mean baseline 3.3 night time voids

- Effects
  - # voids \(\downarrow\) /night: -1.5 active tx vs -1.2 placebo
  - # pts \(\downarrow\) voids by 50+: 48% active tx vs 28% placebo

- Adverse effects
  - Boxed warning for hyponatremia
  - Serum Na+: 14% < 135 mmol/L, 1% < 125 mmol/L
  - ADEs: nasal discomfort, nasopharyngitis, epistaxis, other

Low dose nasal desmopressin acetate

Other considerations

- Studies excluded pts with
  - eGFR < 50 mL/min
  - CHF II-IV, on loop diuretics, systemic or inhaled steroids, hx low Na+ or SIADH, uncontrolled HTN

- No non-pharm tx, eg ↓ fluids after dinner, ↓ caffeine

- Conclusion: marginal efficacy, significant safety concern, just say no! (vs placebo nasal saline!)
The Agenda/Learning Objectives

✓ Nutrition related issues
  ➢ meds that impact nutrition
  ➢ iron replacement
  ➢ CHF management

✓ New agents/approaches to consider?
  ➢ DVT prophylaxis after THA/TKA
  ➢ For bladder

• Reducing polypharmacy “deprescribing”
Polypharmacy in Older Adults

“One of the first duties of the physician is to educate the masses not to take medicine”
- Sir William Osler

DRUGS
Polypharmacy In Older Adults

- Over 1/3 (39 %) pts age 65+ on ≥ 5 meds
- 12% Medicare beneficiaries on ≥ 10 meds
- Of 11,000 pts age 100 in UK
  - 73% on 1+ med
  - median # meds → 7!

Polypharmacy in Older Adults

- Polypharmacy & inappropriate meds common
- Results in
  - ↑ Adverse Drug Events (ADEs)
  - ↑ Drug-drug interactions
  - ↑ Drug-disease interactions
  - ↑ risk med errors and ↑ cost
  - ↓ adherence

Polypharmacy & Adverse Drug Reactions

“any noxious, unintended, & undesired effect of a drug”

- ADRs ↑ as meds > 4-5
- Aim at < 5 meds

Reducing Inappropriate Polypharmacy
The Process of Deprescribing

- **Deprescribing**: The systematic process of identifying & discontinuing drugs when existing or potential harms outweigh existing or potential benefits within the context of an individual’s care goals, current level of functioning, life expectancy, values and preferences”

- Consider individual rx as well as cumulative rx risk

- How can this best be accomplished?

JAMA Intern Med 2015;175:827
Reducing Polypharmacy

Tools to identify potentially inappropriate meds

- Beers Criteria  
  J Am Geriatr Soc 2015; 63:2227

- STOPP/START  
  Int J Clin Pharmacol Ther 2008; 46:72

- “Good Palliative-Geriatric Practice Algorithm”  
  Arch Intern Med Oct 2010; 170:1648
Reducing Polypharmacy in the Elderly

“Good Palliative-Geriatric Practice algorithm”

- **NH:** n=119, x age 83, x 7 meds ↓ by 3
  - 10% resumed stopped med
  - hosp ↓ (30 v 12%) vs matched controls
  - mort ↓ (45 v 21%)

- **Outpt:** n 70, x age 83, x 8 meds ↓ by 4, 19 mo f/u
  - 2% failed rx d/c & resumed d/t sxms
  - no ↑ M&M

Discuss the following with the patient/guardian

An evidence-based consensus exists for using the drug for the indication given in its current dosing rate in this patient's age group and disability level, and the benefit outweighs all possible known adverse effects

Yes

No/Not sure

Indication seems valid and relevant in this patient's age group and disability level

Yes

No

Do the known possible adverse reactions of the drug outweigh possible benefit in old, disabled patients?

Yes

No

Any adverse symptoms or signs that may be related to the drug?

Yes

No

Is there another drug that may be superior to the one in question?

Yes

No

Can the dosing rate be reduced with no significant risk?

Yes

Reduce dose

No

Continue with the same dosing rate
Start with verifying what medications your pt is taking
1. Accurately ascertain all current drug use
   - ‘brown paper bag’ medication reconciliation

2. Identify patients at risk of, or suffering, ADR
   - at risk: ≥8 medications
     - advanced age (> 75 years)
     - high-risk medications
   - assess for current, past or highly likely future toxicity

3. Estimate life expectancy
   - clinical prognostication tools or lifespan calculators

4. Define overall care goals
   - consider current functional status and quality of life with reference to estimated life expectancy

5. Verify current indications for ongoing treatments
   - perform diagnosis-medication reconciliation
   - confirm diagnostic labels against formal diagnostic criteria
   - ascertain, for each confirmed diagnosis, drug appropriateness
   - Be informed of criteria for identifying the required clinical evidence of past, current or future toxicity (eg triple whammy of NSAID, diuretic, ACE inhibitor)

   - If life expectancy less than 2 years, preservation of function and quality of life predominate over prolonging life and avoiding future complications as goals of care

   - Discontinue drugs for which the diagnosis is wrong or totally unsubstantiated or where, for a confirmed diagnosis, the drug is ineffective

   - Evid Based Med 2013;18(4):121
6. Determine need for disease-specific preventive medications
   - estimate clinical impact and time to future treatment benefit
   - compare this estimate with expected lifespan

7. Determine absolute benefit-harm thresholds of medications
   - reconcile estimates of absolute benefit and harm using prediction tools (see http://www.mdcalc.com)

8. Review the relative utility of individual drugs
   - rank drugs according to the relative utility from high to low based on predicted benefit, harm, administration and monitoring burden

9. Identify drugs to be discontinued and seek patient consent
   - reconcile drugs for discontinuation with patient preferences

10. Devise and implement drug discontinuation plan with close monitoring

   Discontinue preventive drugs whose time until benefit exceeds expected lifespan

   Discontinue drugs whose absolute level of harm exceeds absolute level of benefit; in ‘line-ball’ cases elicit patient preferences

   Discontinue drugs of low utility

   Discontinue drugs patients are not in favour of taking

Evid Based Med 2013;18(4):121
Deprescribing Barriers

• 10 step EBM too long? → see 5 step version

• Both pts & providers fear adverse drug withdrawal effects even though these occur much less often than adverse drug effects

• We likely don’t hesitate as much as we should when we initiate an rx and likely hesitate more than we should to stop an rx

• Dz-specific guidelines ↑ pressure to prescribe

JAMA Intern Med 2015;175:827
EBM to Optimize Care of the Elderly?

Apply clinical practice guidelines with caution

- Almost all existing guidelines have single dz focus
- Application of CPGs to hypothetical 79yo pt w/COPD, DM, HTN, OP, OA
  → 12 medications, complicated regimen
  → $406 monthly cost
- Studies rarely include frail elderly, mult comorbid dz
- Risks (drug-drug, drug-dz interactions) likely are ↑
- Do CPGs address short & long term goals?
- Pt preferences?

JAMA 2005;294:716
EBM for the Frail Older Adult

Does the Emperor have any clothes?

- Evidence for the best care of frail older pts w/multimorbidity is often lacking

- “Guidelines are meant to inform but not dictate, guide but not enforce, support but not restrict”

JAMA 2014;311(14):1403
DAMMIT, JIM, I'M A DOCTOR

--- not just a guideline follower!
DEPREPRESCRIBING – JUST DO IT!

Recognize opportunities to stop meds

- Review existing meds before starting new rx
- Annual/semiannual medication review
- Care transitions are key opportunities
  - Is pt managing current care plan?
  - Is complexity impacting adherence & safety?
  - Have pt preferences changed?
- Be aware of deprescribing tools
Deprescribing Resources

Proton Pump Inhibitor (PPI)
- PPI evidence-based deprescribing guideline
- PPI deprescribing algorithm

Antihyperglycemic
- Antihyperglycemic deprescribing guideline & algorithm

Benzodiazepine receptor agonist deprescribing algorithm

Antipsychotic deprescribing guidelines & algorithm

Chol-I & memantine deprescribing guideline & algorithm
MedStopper is a deprescribing resource for healthcare professionals and their patients.

1. Frail elderly?  

2. Generic or Brand Name: amlod

3. Select Condition Treated:

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Condition Treated</th>
<th>Add to MedStopper</th>
</tr>
</thead>
<tbody>
<tr>
<td>amlodipine</td>
<td>Norvasc</td>
<td>blood pressure</td>
<td>ADD</td>
</tr>
</tbody>
</table>

MedStopper Plan

Arrange medications by: Stopping Priority

http://medstopper.com/
<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>RED=Highest</td>
<td>amlodipine (Norvasc) / Calcium antagonist dihydropyridine / blood pressure</td>
<td>🎁</td>
<td>🌻</td>
<td>😞</td>
<td><strong>If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.</strong></td>
<td>chest pain, pounding heart, heart rate, blood pressure (re-measure for up to 6 months), anxiety, tremor</td>
<td></td>
</tr>
</tbody>
</table>

http://medstopper.com/
Deprescribing Website: Be a deprescriber!

http://medstopper.com/about.php
ANY Questions!
Can I tell you about a few medication issues in older adults that really get under my skin?
Things I hate to see in older pts

- Muscle relaxants
  - Sedating, anticholinergic, falls/fx ↑, ?’able efficacy

- Megestrol acetate (Megace)
  - minimal wt ↑, thrombotic event ↑, mortality ↑

- ASA continued when warfarin or Xa-inhib started for new indication (AF, VTE) in stable CAD pts
  - Warf & Xa-inhib cardioprotective, ASA 2x ↑ bleed risk w/o conferring additional cardioprotection

- Polypharmacy ≥ 5 prescriptions – more later

Beers Criteria for Potentially Inappropriate Medication Use in Older Adults  J Am Geriatr Soc 2015:63:2227
Extra slides follow
EBM to Optimize Care of the Elderly?

Apply clinical practice guidelines with caution

- CHF Guidelines: based on excellent RCT data
- Issue: Older Adults w/CHF often w/comorbid dz
- Characteristics 2.5 million Medicare Beneficiaries Hospitalized for Heart Failure, 2001-2005
  - mean age 80 years old, nearly 60% women
  - 2/3 of pts w/chronic atherosclerosis
  - 67% HTN
  - 42% COPD
  - 42% diabetes mellitus
  - 30% renal failure
  - 14% dementia

Arch Intern Med 2008;168(22):2481-8
Meta-Analysis: IV Iron for Patients with HFrEF and Iron Deficiency

Meta-Analysis: IV Iron for Patients with HFrEF and Iron Deficiency