Deprescribing in CKD patients: Is less more?

Speaker: Dr. Judith G. Marin, PharmD
Case

Mr. Kid Ney is a 75 y/o patient who has been on dialysis for the last 4 years (PD, then HD).

- PMHx: HTN, DM, CAD, osteoarthritis
- BP pre HD: 135/80; BP post HD: 120/70; HR stable between 70-80
- His functional status has been decreasing in the past 6 months
- Patient complaining that he feels like his stomach is always full with meds
Case

Medications:

- **Acetaminophen OA**, 1.3 g PO BID
- **EC ASA**, 81 mg PO daily
- **Metoprolol**, 50 mg PO BID
- **Ramipril**, 10 mg PO daily
- **Atorvastatin**, 40 mg PO daily
- **Gliclazide MR**, 30 mg PO daily
- **Linagliptin**, 5 mg PO daily
- **Insulin lantus**, 20 units SC at HS
- **Alfacalcidol**, 0.25 mcg PO 3 times/week
- **Tums Ultra**, 2 tabs PO TID
- **Renavite**, 1 tab PO daily
- **Epoietin α**, 3,000 units IV 2 times/week
- **Ferrlicit**, 125 mg IV Q2weeks
- **Quinine**, 300 mg PO Qdialysis
- **Hydroxyzine**, 20 mg PO TID PRN
<table>
<thead>
<tr>
<th>Labs (Normal values)</th>
<th>6 weeks ago</th>
<th>Today</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb (120-155 g/L)</td>
<td>100</td>
<td>104</td>
</tr>
<tr>
<td>A1C (4.5-6%)</td>
<td>7.0</td>
<td>6.8</td>
</tr>
<tr>
<td>K (3.5-5 mmol/L)</td>
<td>5.0</td>
<td>4.6</td>
</tr>
<tr>
<td>Ca (2.1-2.55 mmol/L)</td>
<td>2.25</td>
<td>2.45</td>
</tr>
<tr>
<td>PO4 (0.8-1.45 mmol/L)</td>
<td>1.11</td>
<td>1.3</td>
</tr>
<tr>
<td>iPTH (&lt; 7 pmol/L)</td>
<td>35</td>
<td>22</td>
</tr>
<tr>
<td>Albumin (34-50 g/L)</td>
<td>38</td>
<td>35</td>
</tr>
<tr>
<td>BUN (2-8.2 mmol/L)</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>Creatinine (40-95 mmol/L)</td>
<td>450</td>
<td>480</td>
</tr>
</tbody>
</table>
Outline

1. Polypharmacy

2. Prescription patterns in BC

3. Deprescribing tools

1. New initiatives
A few questions...

What is the average number of medication prescribed to BC dialysis patients?

A. 8  
B. 12  
C. 15  
D. 18
A few questions...

What are the risk related to polypharmacy?
A. Increases risk of adverse drug reactions
B. Increases risk of ER visits and hospital admission
C. Increases risk of fall
D. Increases risk of mortality
E. All of these options
A few questions...

Which of these medications are Potentially Inappropriate Medications (PIMs), according to Beers list in elderly patients?

A. Hydroxyzine
B. Insulin Regular sliding scale
C. Glyburide
D. Zopiclone
E. All of these options
Background

Polypharmacy is defined by > 5 regular medications prescribed

- Every 12 months, 1/3 people taking > 5 meds/d suffers of ADRs, with more than 25% being preventable.
- 18% of all inpatients death related to ADRs
- 44% of all discharge prescription contains at least 1 unnecessary medication

Number of meds taken is one of the most important predictor of harm, especially in elderly patients

Background

• Drivers for polypharmacy
  • Multiple disease specific clinic guidelines
  • Quality indicators and performances indicators
  • Patient and family’s expectations
  • Focus on treating acute disease without reassessing treatment for chronic disease
  • Misinterpreting ADRs for new diagnosis
  • Dialysis patients have the highest pill burden of all chronically ill patients

Background

• Dialysis patients are at higher risk of ADRs
  • Impaired drug clearance
  • Polypharmacy
  • Comorbidities
  • PK/ PD change
  • Rarely included in trials → efficacy and safety uncertain

Deprescription

The systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient’s care goals, current level of functioning, life expectancy, values, and preferences.

- Cumulative risk with multiple drugs and their pharmacokinetic/pharmacodynamic interactions.

_Evid Based Med 2013; 18(4): 121-4._
Deprescription

Potentially Inappropriate Medications (PIMs)
Medication with no clear evidence-based indication, with risk of adverse drug reactions, or not cost-effective.

2012 AGS Beers PIMs list for older adults

- Anticholinergic meds (TCA, 1st gen. antihistamine, antispasmodic)
- Ticlodipine and dypiridamole
- Nitrofurantoin
- α-blockers, Central α-agonists, Anti-arrythmics, digoxin, spironolactone
- Barbiturates, antipsychotics, benzo, hypnotics
- Hormone thx, megestrol, LA sulfonylurea, insulin SS
- Metoclopramide
- NSAIDs, meperidine, muscle relaxants

Deprescription in elderly

- In Canada, it is estimated that 37% of people > 65 years old and 47% of patients > 85 years old received at least 1 PIM prescription in 2013.
- The cost for the PIMs is equivalent to $75 per Canadian older than 65 years old or $419 millions in total outside of other hospital cost.
- 47% of women aged > 85 years old had a PIM prescription.
- Benzo and hypnotics were the leading PIMs prescribed.

_CMAJ Open 2016; 4: E346-51._
PIMs in HD patients

  - Data from J-DOPPS II and III on Japanese hemodialysis patients
    - Included patients > 65 years old and on chronic hemodialysis
  - Identified 47 PIMs based on expert opinions and modified Beers criteria for elderly Japanese populations
  - PIM only considered if still ordered 1 year after enrollment
### PIMs in HD patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>J-DOPPS II (2002) (n = 595) (%)</th>
<th>J-DOPPS III (2005) (n = 772) (%)</th>
<th>Overall (n = 1367) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>57</td>
<td>60</td>
<td>59</td>
</tr>
<tr>
<td><strong>Primary cause of ESRD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DM</td>
<td>32</td>
<td>34</td>
<td>33</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65–69</td>
<td>31</td>
<td>36</td>
<td>34</td>
</tr>
<tr>
<td>70–74</td>
<td>34</td>
<td>27</td>
<td>30</td>
</tr>
<tr>
<td>75–79</td>
<td>20</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>80–84</td>
<td>9</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>≥85</td>
<td>5</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td><strong>Vintage (year)</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;1</td>
<td>15</td>
<td>23</td>
<td>19</td>
</tr>
<tr>
<td>1–4</td>
<td>45</td>
<td>34</td>
<td>39</td>
</tr>
<tr>
<td>≥5</td>
<td>40</td>
<td>43</td>
<td>42</td>
</tr>
<tr>
<td><strong>Number of comorbidities</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>0</td>
<td>6</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>1–2</td>
<td>18</td>
<td>37</td>
<td>29</td>
</tr>
<tr>
<td>3–4</td>
<td>42</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>≥5</td>
<td>33</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td><strong>Number of medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6</td>
<td>33</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td>6–7</td>
<td>18</td>
<td>26</td>
<td>23</td>
</tr>
<tr>
<td>8–9</td>
<td>24</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>≥10</td>
<td>25</td>
<td>24</td>
<td>24</td>
</tr>
</tbody>
</table>

PIMs in HD patients

- 57% of patients had at least 1 PIMs prescribed
  - 31% of patients were on H2 blockers
  - 19% of patients on antiplatelets
  - 16% on ticlopidine
  - 13% on α-blockers

- Diabetic patients with a longer vintage on dialysis, with more comorbidities and higher number of medications are at higher risk of having a PIM prescribed

- Pt receiving HD at facility with multidisciplinary rounds and at a teaching hospital were less frequently prescribed PIMs.

BC Prescribing patterns data

• Part of a national initiative on deprescribing in dialysis patients

• PROMIS database for BC dialysis patients between June 3rd to October 1st 2015
  • > 18 years old
  • Same dialysis modality for > 120 continuous days
  • PD vs. Hemodialysis
## BC Prescribing patterns data

<table>
<thead>
<tr>
<th></th>
<th>All dialysis patients (n=3,017)</th>
<th>HD (n=2,243)</th>
<th>PD (n=774)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD)</td>
<td>66.2 (14.8)</td>
<td>67.7 (14.7)</td>
<td>64.2 (14.4)</td>
</tr>
<tr>
<td>Male Sex, n (%)</td>
<td>1,824 (60.5)</td>
<td>1,336 (59.6)</td>
<td>488 (63)</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td>1,741 (57.7)</td>
<td>1,335 (59.5)</td>
<td>406 (52.5)</td>
</tr>
<tr>
<td>DM</td>
<td>2,098 (69.5)</td>
<td>1,588 (70.8)</td>
<td>510 (65.9)</td>
</tr>
<tr>
<td>Race (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>1,730 (57.3)</td>
<td>1,285 (57.3)</td>
<td>445 (57.5)</td>
</tr>
<tr>
<td>Asian</td>
<td>1,006 (33.3)</td>
<td>741 (35)</td>
<td>265 (34.3)</td>
</tr>
<tr>
<td>Native</td>
<td>125 (4.1)</td>
<td>96 (4.3)</td>
<td>29 (3.7)</td>
</tr>
<tr>
<td>Others</td>
<td>156 (5.6)</td>
<td>121 (3.4)</td>
<td>35 (4.5)</td>
</tr>
<tr>
<td>Median Dialysis vintage [IQ]</td>
<td>3.3 [1.7-6.1]</td>
<td>3.8 [1.8-7.1]</td>
<td>2.4 [1.3-3.9]</td>
</tr>
</tbody>
</table>
### BC Prescribing patterns data

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<th>PD (n=774)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of meds (SD)</td>
<td>17.7 (5.7)</td>
<td>18.1 (5.9)</td>
<td>16.7 (5.0)</td>
</tr>
<tr>
<td>Mean number of reg. meds (SD)</td>
<td>12.4 (4.2)</td>
<td>12.3 (4.2)</td>
<td>12.5 (4.2)</td>
</tr>
<tr>
<td>Mean number of meds (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiology</td>
<td>3.5 (2.0)</td>
<td>3.5 (2.0)</td>
<td>3.6 (2.0)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.6 (0.8)</td>
<td>0.6 (0.8)</td>
<td>0.7 (0.9)</td>
</tr>
<tr>
<td>Renal</td>
<td>4.7 (1.4)</td>
<td>5.0 (1.3)</td>
<td>3.9 (1.2)</td>
</tr>
<tr>
<td>Symptoms</td>
<td>5.8 (3.0)</td>
<td>6.0 (3.2)</td>
<td>5.2 (2.2)</td>
</tr>
<tr>
<td>Others</td>
<td>3.1 (2.2)</td>
<td>3.0 (2.3)</td>
<td>3.5 (2.1)</td>
</tr>
<tr>
<td>Mean number PIMs (SD)</td>
<td>5.0 (2.8)</td>
<td>5.4 (2.8)</td>
<td>4.0 (2.4)</td>
</tr>
<tr>
<td>Number of pts on PIMs (%)</td>
<td>2,936 (97.3)</td>
<td>2,200 (98.1)</td>
<td>736 (95.1)</td>
</tr>
</tbody>
</table>
### BC Prescribing patterns data

<table>
<thead>
<tr>
<th>Age Group</th>
<th>All dialysis patients (n=3,017)</th>
<th>HD (n=2,243)</th>
<th>PD (n=774)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of meds by age group (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 to 39 years old</td>
<td>15.4 (6.1)</td>
<td>16.1 (6.4)</td>
<td>13.4 (4.8)</td>
</tr>
<tr>
<td>40 to 64 years old</td>
<td>17.7 (5.8)</td>
<td>18.1 (6.1)</td>
<td>16.5 (4.8)</td>
</tr>
<tr>
<td>65 to 79 years old</td>
<td>18.4 (5.6)</td>
<td>18.7 (5.8)</td>
<td>17.3 (5.0)</td>
</tr>
<tr>
<td>≥ 80 years old</td>
<td>17.2 (5.4)</td>
<td>17.2 (5.4)</td>
<td>17.3 (5.1)</td>
</tr>
<tr>
<td>Mean number of PIMs by age group (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 to 39 years old</td>
<td>3.6 (2.9)</td>
<td>4.2 (3.0)</td>
<td>2.1 (2.0)</td>
</tr>
<tr>
<td>40 to 64 years old</td>
<td>4.9 (2.9)</td>
<td>5.4 (3.0)</td>
<td>3.9 (2.3)</td>
</tr>
<tr>
<td>65 to 79 years old</td>
<td>5.3 (2.6)</td>
<td>5.7 (2.7)</td>
<td>4.4 (2.2)</td>
</tr>
<tr>
<td>≥ 80 years old</td>
<td>5.1 (2.7)</td>
<td>5.2 (2.7)</td>
<td>4.3 (2.7)</td>
</tr>
<tr>
<td>Medication</td>
<td>All dialysis patients (n=3,017)</td>
<td>HD (n=2,243)</td>
<td>PD (n=774)</td>
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<tr>
<td>----------------------------</td>
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<td>------------</td>
</tr>
<tr>
<td>Allopurinol</td>
<td>537 (17.8%)</td>
<td>359 (16.0%)</td>
<td>178 (23%)</td>
</tr>
<tr>
<td>1st gen. antihistamines</td>
<td>1,117 (37%)</td>
<td>1,005 (44.8%)</td>
<td>112 (14.5%)</td>
</tr>
<tr>
<td>ASA</td>
<td>1,392 (46.1%)</td>
<td>1,049 (46.8%)</td>
<td>343 (44.3%)</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>554 (18.4%)</td>
<td>458 (20.4%)</td>
<td>96 (12.4%)</td>
</tr>
<tr>
<td>Hypnotics</td>
<td>665 (22.0%)</td>
<td>523 (23.3%)</td>
<td>142 (18.4%)</td>
</tr>
<tr>
<td>Loop diuretic</td>
<td>896 (29.7%)</td>
<td>526 (23.5%)</td>
<td>370 (47.8%)</td>
</tr>
<tr>
<td>Narcotics</td>
<td>832 (27.6%)</td>
<td>708 (31.6%)</td>
<td>124 (16.0%)</td>
</tr>
<tr>
<td>PPI</td>
<td>1,210 (40.1%)</td>
<td>944 (42.1%)</td>
<td>266 (34.4%)</td>
</tr>
<tr>
<td>Statin</td>
<td>1,427 (47.3%)</td>
<td>996 (44.4%)</td>
<td>431 (55.7%)</td>
</tr>
</tbody>
</table>
Where do we go from here?

- General tools
  - Guide an overall reassessment of all medications a patient is taking
  - Tools only validated in the elderly population

- Specific tools
  - Target re-assessment of specific medication within a population
  - Specific medication algorithms geared toward deprescribing
  - START/STOP tool for elderly patients
Deprescribing in HD pts

• McIntire et al. *In press*
  • Prospective observational study at UHN hemodialysis unit
• 3 phases
  • Development of deprescribing tools
    • Quinine
    • Loop diuretics
    • Alpha-blockers
    • Proton pump inhibitors
    • Statins
  • Validation of deprescribing tools
  • Implementation and evaluation of deprescribing tools
Deprescribing in HD

Table 3. Number of target medications throughout the deprescribing study

<table>
<thead>
<tr>
<th>Target Medication</th>
<th>Total in unit, prior to study (171 patients)</th>
<th>Flagged by algorithm (71 patients)</th>
<th>Enrolled in the trial (35 patients)</th>
<th>Successfully deprescribed (27 patients)</th>
<th>Successfully deprescribed 6 months after trial (19 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinine</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Diuretics</td>
<td>31</td>
<td>31</td>
<td>10</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Alpha-1 blockers</td>
<td>14</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Statins</td>
<td>95</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>PPI</td>
<td>86</td>
<td>40</td>
<td>24</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>231</strong></td>
<td><strong>80</strong></td>
<td><strong>40</strong></td>
<td><strong>31</strong></td>
<td><strong>24</strong></td>
</tr>
</tbody>
</table>

- Pts didn’t report any concerns
Deprescribing in HD pts

• Qualitative study to explore perception of HD pts on polypharmacy and deprescribing and identify patient-specific barrier
  • 12 patients interviewed
  • Factors related to polypharmacy
    • Patients likely unwilling initially to stop or change meds on first approach. However, if given clear explanation of why this might be beneficial to them, then are willing to reconsider
    • Challenges associated with dialysis and need for certain medications.
  • Factors enabling med optimazation
    • Awareness of the risk of polypharmacy
    • Confidence in healthcare providers
Future projects

• Canadian initiative to evaluate polypharmacy and deprescribing in dialysis patient
  • Part of the Can-SOLVE CKD
• 3 phases projects
  • Evaluate prescription patterns in dialysis patients and associated cost
  • Developing evidence-based deprescribing algorithms in dialysis patients
  • Modified Delphi Approach to reach agreement on the content of the deprescribing algorithms and the how to use of these algorithms in practice
Conclusion

• Deprescribing is a new process
  • Improve safety in different populations
  • Opportunity to reassess therapy and have a discussion about therapeutic goals
  • Time consuming, but reduce ADRs, waste and may improve compliance to essential medications

• New Canadian initiative to produce evidence-based deprescribing algorithm to the dialysis population...

Stay tuned!
Acknowledgement

BC team
Gabriela Espino
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Zainab Sheriff
Dr. Adeera Levin

Canadian Team
Dr. Marisa Battistella
Dr. Marcello Tonelli
Cali Orsulak
Dr. Jo-Anne Wilson
Dr. Clara Bohm
Dr. Amit Garg
Just to go back to the case...

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C. Glyburide
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E. All of these options