Therapeutic Challenges IN Managing Heart Failure

Heart Failure Management 2019
Amelia Island, FL

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Case 1

- **CC:** “Short of breath and legs are swelling”
- LS is a 68-year-old male, presents to clinic.
- **PMH:** HFrEF (EF= 30%), persistent NVAF, CAD, hypertension, dyslipidemia, Type 2 diabetes, rheumatoid arthritis
- **Allergies:** NKDA
- **Meds:** Metoprolol XL 100 mg QD, Entresto 49/51mg BID, Spironolactone 25 mg qd, Torsemide 20mg QD Rivaroxaban 20 mg QD, Digoxin 125 mcg QD, Simvastatin 20 mg QD, Gabapentin 800 mg BID, Metformin 1000mg BID
- **FH:** Noncontributory
- **SH:** Drinks 2-3 cocktails/week
Case 1

- **HPI/ROS:** Beginning 2–3 weeks ago, L.S. reported gradually worsening shortness of breath, fatigue, and swelling in his legs. He does not miss any doses of torsemide. He has been drinking more lately (about two 2-L jugs of water daily) and eating a lot of watermelon from Texas. He denies any PND, CP, palpitations, presyncope or syncope.

- **Exam:**
  - **VITAL SIGNS:** BP 110/76 mmHg | Pulse 88 | Wt 180 lb | BMI 27 kg/m2 | SpO2 96%
  - **GENERAL:** NAD
  - **NECK:** No JVD
  - **CARDIOVASCULAR:** RRR, s1s2, no audible murmurs
  - **RESPIRATORY:** Normal respiratory effort, Slight crackles
  - **ABDOMEN:** + bowel sounds, est. liver 14 cm by percussion
  - **EXTREMITIES:** 2+ ankle edema
  - **SKIN:** Warm, dry
  - **NEUROLOGIC:** Appropriate mood and affect. A & O x 3
Case 1

- **Labs:**
  - Mg: 2
  - Pro-BNP: 600
  - A1c: 8.2%
  - Hgb: 16
  - Hct: 47
  - Alb: 3
  - AST: 80
  - ALT: 102
  - **Concentrations:**
    - Sodium: 140
    - Potassium: 102
    - Creatinine: 20
    - Hemoglobin: 95

- **Tests:**
  - **Echocardiogram** - Moderate LV dilatation. LV wall thickness moderately increased. Global hypokinesis. LVEF estimated to be 35%. Dilated left atrium. Normal RV size and function. Mild mitral regurgitation.
  - **ECG** – Atrial Fibrillation, ventricular response rate = 95 bpm
  - **6MWT** – 300 meters
  - **KCCQ** – 74
  - **MoCA** – 24

- **Assessment:** Patient is fluid overloaded
PD of Loop Diuretics

![Graph showing the response of urinary sodium concentration to different doses of Furosemide. The graph illustrates the diuretic threshold and how it changes with increasing doses of Furosemide (40 mg, 80 mg, 160 mg).]
Diuretic Resistance

• Threshold Dose
• Drug Compliance
• Dietary Compliance (sodium, H2O intake)
• Bioavailability, absorption
  o ↓ absorption with furosemide as pts decompensate
• Drug interactions (NSAID)
• Distal tubular hypertrophy
Patient Info -

Additional background data to obtain?

• How is your water pill (name of drug) working? – Assessing Diuretic Threshold
• Have you recently missed any doses of your water pill recently? – Assessing Compliance
• Have you changed your diet recently – have you been eating out more? – Assessing Compliance
• Have you taken anything like ibuprofen or naproxen for anything recently? – Assessing Drug Interactions
• Have you recently increased your dose of beta blocker or ACE-inhibitor? – Assessing Dose Change
Patient Info -

Additional background data to obtain?

• How is your water pill (name of drug) working? – Assessing Diuretic Threshold

• If urinating – at threshold dose, may need to increase frequency to get more fluid off not increase dose

• If not working well minimal urine response
  o May need to increase dose to get to threshold (especially if patient is at a low dose)
  o May need to switch to a better absorbed drug like torsemide.
  o May need to add thiazide diuretic (especially if patient is already on a high dose of diuretic)
Question 3

Which one of the following is best to recommend for lowering L.M.’s A1C to less than 8% and improving outcomes?

A. Increase metformin to 1500 mg twice daily.
B. Add empagliflozin 10 mg once daily.
C. Add saxagliptin 2.5 mg once daily.
D. Add alogliptin 5 mg once daily.
CV Outcomes

Major Adverse CV Events

- Lixisenatide (ELIXA)
- Liraglutide (LEADER)
- Semaglutide (SUSTAIN-6)
- Exenatide (EXSCEL)
- Saxagliptin (SAVOR TIMI 53)
- Alogliptin (EXAMINE)
- Sitagliptin (TECOS)
- Empagliflozin (EMPA-REG)
- Canagliflozin (CANVAS)

Heart Failure Hospitalization

- Lixisenatide (ELIXA)
- Liraglutide (LEADER)
- Semaglutide (SUSTAIN-6)
- Exenatide (EXSCEL)
- Saxagliptin (SAVOR TIMI 53)
- Alogliptin (EXAMINE)
- Sitagliptin (TECOS)
- Empagliflozin (EMPA-REG)
- Canagliflozin (CANVAS)

Hazard ratio (95% CI)
### DECLARE-TIMI 58

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dapaglifoxin (N=8582)</th>
<th>Placebo (N=8578)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. (%)</td>
<td>rate/1000 patient-yr</td>
<td>no. (%)</td>
<td>rate/1000 patient-yr</td>
</tr>
<tr>
<td>Cardiovascular death or hospitalization for heart failure</td>
<td>417 (4.9)</td>
<td>12.2</td>
<td>496 (5.8)</td>
<td>14.7</td>
</tr>
<tr>
<td>MACE</td>
<td>756 (8.8)</td>
<td>22.6</td>
<td>803 (9.4)</td>
<td>24.2</td>
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<tr>
<td>≥40% decrease in eGFR to &lt;60 ml/min/1.73 m^2, ESRD, or death from renal or cardiovascular cause</td>
<td>370 (4.3)</td>
<td>10.8</td>
<td>480 (5.6)</td>
<td>14.1</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>529 (6.2)</td>
<td>15.1</td>
<td>570 (6.6)</td>
<td>16.4</td>
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<tr>
<td>Hospitalization for heart failure</td>
<td>212 (2.5)</td>
<td>6.2</td>
<td>286 (3.3)</td>
<td>8.5</td>
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<tr>
<td>Myocardial infarction</td>
<td>393 (4.6)</td>
<td>11.7</td>
<td>441 (5.1)</td>
<td>13.2</td>
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<tr>
<td>Ischemic stroke</td>
<td>235 (2.7)</td>
<td>6.9</td>
<td>231 (2.7)</td>
<td>6.8</td>
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<tr>
<td>Death from cardiovascular cause</td>
<td>245 (2.9)</td>
<td>7.0</td>
<td>249 (2.9)</td>
<td>7.1</td>
</tr>
<tr>
<td>Death from noncardiovascular cause</td>
<td>211 (2.5)</td>
<td>6.0</td>
<td>238 (2.8)</td>
<td>6.8</td>
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<tr>
<td>≥40% decrease in eGFR to &lt;60 ml/min/1.73 m^2, ESRD, or death from renal cause</td>
<td>127 (1.5)</td>
<td>3.7</td>
<td>238 (2.8)</td>
<td>7.0</td>
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<tr>
<td>Effect</td>
<td>Consequence</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>-------------------------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuresis</td>
<td>Reduced filling pressures, pre-/afterload reduction</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Natriuresis</td>
<td>Reduced filling pressures, pre-/afterload reduction</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Blood pressure lowering</td>
<td>Reduced myocardial work, reduced filling pressures, pre-/afterload reduction</td>
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<td></td>
<td></td>
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<tr>
<td>Weight loss</td>
<td>Improved CV risk profile, lower blood pressure</td>
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<tr>
<td>Reduction in/prevention of albuminuria, slowing of kidney function decline</td>
<td>Reduction in kidney risk profile, possibly fewer incident CV events, including less HF</td>
<td></td>
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<tr>
<td>Effects on myocardial and kidney metabolism: shift to more efficient ketone-based metabolism</td>
<td>Improved metabolic efficiency, less myocardial workload</td>
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<tr>
<td>Blockade of sodium-hydrogen cotransporter</td>
<td>Tissue protection: reduction in kidney and myocardial injury</td>
<td></td>
<td></td>
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<tr>
<td>Reduction in sympathetic tone</td>
<td>Reduce blood pressure and arrhythmia</td>
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</tbody>
</table>

CV = cardiovascular; HF = heart failure; SGLT2 = sodium-glucose cotransporter 2.
L.S.’s prescriber decides to initiate empagliflozin. Which one of the following is most important to monitor for in L.S. upon initiation of therapy?

A. Diuresis  
B. Hypoglycemia  
C. UTI  
D. Ketoacidosis
Case 2

• 66 year-old Caucasian woman with HTN was admitted for STEMI and received PCI to proximal LAD with DES, her echo showed EF 25% and she developed atrial fibrillation during the admission.

• Vitals: BP 124/88, HR 94, Ht 68”, Wt 121.8 kg, BMI 40.3

• Medications: aspirin 81 mg QD, clopidogrel 75 mg QD, atorvastatin 80 mg QD, valsartan 40 mg QD, carvedilol 6.25 mg BID

• Labs: Na 130, K 4.8, SCr 1.1, Mg 2, LFTs wnl
2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

Stroke Prophylaxis

- \( \text{CHA}_2\text{DS}_2\text{-VASc: 0} \)
  - Men: No Therapy
  - Women: DOAC > warfarin “reasonable” or ASA or No therapy

- \( \text{CHA}_2\text{DS}_2\text{-VASc: 1} \)
  - Men: DOAC > warfarin “recommended”
  - Women: DOAC > warfarin “reasonable” or ASA or No therapy

- \( \text{CHA}_2\text{DS}_2\text{-VASc: } \geq 2 \)
  - Men: DOAC > warfarin “recommended”
  - Women: DOAC > warfarin “reasonable” or ASA or No therapy

- \( \text{CHA}_2\text{DS}_2\text{-VASc: } \geq 3 \)
  - Men: DOAC > warfarin “recommended”
  - Women: DOAC > warfarin “reasonable” or ASA or No therapy

Circulation. 2019;139:e000–e000. DOI: 10.1161/CIR.0000000000000665.
## ACS + AF Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Population</th>
<th>Arms</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOEST</td>
<td>Long-term OAC + indication for PCI</td>
<td>clopidogrel + warfarin vs clop. + ASA + warfarin</td>
<td>Bleeding events lower in DAPT vs triple therapy group</td>
</tr>
<tr>
<td>ISAR-TRIPLE</td>
<td>Any indication for OAC + tx w/ PCI and DES</td>
<td>DAPT x6 weeks vs DAPT x6 months</td>
<td>$1^0$ endpoint of bleeding + ischemia no different, lower bleeding in shorter use of clopidogrel arm</td>
</tr>
<tr>
<td>PIONEER AF-PCI</td>
<td>NVAF x 1 yr. +, OAC 3 mo.+ before PCI + stent</td>
<td>Rivaroxaban 15 mg QD + P2Y$_{12}$, riva. mg 2.5 BID + DAPT, VKA + DAPT</td>
<td>Clin. sig. bleeding and bleed req. med. attn. both lower in group 1, no difference in CV events among grps.</td>
</tr>
<tr>
<td>RE-DUAL</td>
<td>NVAF on long-term OAC, PCI w/ BMS or DES w/in 120 h</td>
<td>Dabigatran 110 mg BID + clop./ticagrelo, dabi. 150 BID + clop./ticag. or VKA + DAPT</td>
<td>Bleeding lower in dabigatran + P2Y$<em>{12}$ vs VKA groups (superior), TE events lower in dabi. +P2Y$</em>{12}$ vs triple therapy</td>
</tr>
<tr>
<td>AUGUSTUS</td>
<td>NVAF on long-term OAC, PCI w/ P2Y$_{12}$ x at least 6 mo.</td>
<td>Apixaban + DAPT, apixa.+ clopidogrel, VKA + clop., VKA + DAPT</td>
<td>Bleeding lower in apixaban vs VKA and incr. in ASA vs placebo groups, death or hosp reduced in apixa group</td>
</tr>
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### Ongoing Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Study Arm</th>
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<tbody>
<tr>
<td>ENTRUST-AF PCI</td>
<td>Edoxaban 60 mg daily + P2Y$_{12}$ vs VKA + DAPT</td>
</tr>
<tr>
<td>APPROACH-ACS-AF</td>
<td>Apixaban + P2Y$_{12}$ vs VKA + DAPT</td>
</tr>
<tr>
<td>COACH-AF PCI</td>
<td>Triple antithrombotic therapy x 1 mo. -&gt; Dabi + P2Y$<em>{12}$ vs VKA + P2Y$</em>{12}$</td>
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AFib Complicating ACS

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
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<tbody>
<tr>
<td>I</td>
<td>B-R</td>
</tr>
<tr>
<td>IIa</td>
<td>B-NR</td>
</tr>
<tr>
<td>IIa</td>
<td>B-R</td>
</tr>
<tr>
<td>IIb</td>
<td>B-R</td>
</tr>
</tbody>
</table>

- Anticoagulation recommended in ACS + AFib w/CHA$_2$DS$_2$VASc > 2 (LOE updated from C to B-R)
  - If triple therapy (OAC, ASA, P2Y$_{12}$ inhibitor) prescribed, reasonable to choose clopidogrel over prasugrel
  - Double therapy (OAC + P2Y$_{12}$ inhibitor) with clopidogrel or ticagrelor + VKA or clopidogrel + rivaroxaban 15 mg QD or clopidogrel + dabigatran 150 mg BID is reasonable to reduce bleeding risk vs triple therapy
- If triple therapy is prescribed, may consider transition to double therapy at 4 to 6 weeks

OAC = oral anticoagulant, VKA = vitamin K antagonist

Circulation. 2019;139:e000–e000. DOI: 10.1161/CIR.0000000000000665.
Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation

Renato D. Lopes, M.D., Ph.D., Gretchen Heizer, M.S., Ronald Aronson, M.D., Amit N. Vora, M.D., M.P.H., Tyler Massaro, Ph.D., Roxana Mehran, M.D., Shaun G. Goodman, M.D., Stephan Windecker, M.D., Harald Darius, M.D., Jia Li, Ph.D., Oleg Averkov, M.D., Ph.D., M. Cecilia Bahit, M.D., Otavio Berwanger, M.D., Ph.D., Andrzej Budaj, M.D., Ph.D., Ziad Hijazi, M.D., Ph.D., Alexander Parkhomenko, M.D., Ph.D., Peter Sinnaeve, M.D., Ph.D., Robert F. Storey, M.D., Holger Thiele, M.D., Dragos Vinereanu, M.D., Ph.D., Christopher B. Granger, M.D., and John H. Alexander, M.D., M.H.S., for the AUGUSTUS Investigators*
C Primary Outcome, According to Intervention Combination

Cumulative Incidence of Event (%)

Days since Start of Intervention

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Vitamin K antagonist and aspirin</th>
<th>Apixaban and aspirin</th>
<th>Vitamin K antagonist and placebo</th>
<th>Apixaban and placebo</th>
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</thead>
<tbody>
<tr>
<td>1123</td>
<td>962</td>
<td>881</td>
<td>838</td>
<td>800</td>
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<tr>
<td>1145</td>
<td>1036</td>
<td>975</td>
<td>937</td>
<td>903</td>
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<td>1126</td>
<td>1007</td>
<td>947</td>
<td>917</td>
<td>883</td>
</tr>
<tr>
<td>1143</td>
<td>1075</td>
<td>1044</td>
<td>1007</td>
<td>975</td>
</tr>
</tbody>
</table>

Event rate per 100 patient-yr:
- Vitamin K antagonist and aspirin, 49.1
- Apixaban and aspirin, 33.6
- Vitamin K antagonist and placebo, 26.7
- Apixaban and placebo, 16.8

Safety and Efficacy of Antithrombotic Strategies in Patients With Atrial Fibrillation Undergoing Percutaneous Coronary Intervention: A Network Meta-analysis of Randomized Controlled Trials

Renato D. Lopes, MD, PhD; Hwanhee Hong, PhD; Ralf E. Harskamp, MD, PhD; Deepak L. Bhatt, MD, MPH; Roxana Mehran, MD; Christopher P. Cannon, MD; Christopher B. Granger, MD; Freek W. A. Verheugt, MD, PhD; Jianghao Li, MS; Jurriën M. ten Berg, MD, PhD; Nikolaus Sarafoff, MD; C. Michael Gibson, MD; John H. Alexander, MD, MHS
Figure 1. Network of 4 Antithrombotic Treatment Regimens

Figure 4. Odds Ratios for TIMI Major Bleeding and MACE
Management of Antithrombotic Therapy in Atrial Fibrillation Patients Undergoing PCI

JACC State-of-the-Art Review

Davide Capodanno, MD, PhD, a Kurt Huber, MD, b Roxana Mehran, MD, c Gregory Y.H. Lip, MD, d,e David P. Faxon, MD, f Christopher B. Granger, MD, g Pascal Vranckx, MD, PhD, h Renato D. Lopes, MD, PhD, g Gilles Montalescot, MD, PhD, i Christopher P. Cannon, MD, f Jurien Ten Berg, MD, j Bernard J. Gersh, MD, k Deepak L. Bhatt, MD, MPH, f Dominick J. Angiolillo, MD, PhD l
Central Illustration: Consensus Recommendations on the Practical Management of Oral Anticoagulation and Antiplatelet Therapy in Patients With Atrial Fibrillation Undergoing Percutaneous Coronary Intervention

- **Default Approach**
  - Prefer Direct Oral Anticoagulant over Vitamin K Antagonist
    - Clopidogrel

- **2018 North American Perspective**
  - High ischemic risk, low bleeding risk
    - Prefer Direct Oral Anticoagulant over Vitamin K Antagonist
      - Clopidogrel or Ticagrelor
  - High bleeding risk, low ischemic risk
    - Clopidogrel
Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH

K. MARTIN*, J. BEYER-WESTENDORF†, B. L. DAVIDSON‡, M. V. HUISMAN§, P. M. SANDSET¶, and S. MOLL*

• BMI \leq 40/\leq 120 \text{ kg}: Standard DOAC dosing for both AF and VTE

• BMI >40/>120 \text{ kg}: do not use DOACs
  o Cite limited clinical, PK data suggesting ↓drug exposure/↓peak/↓half-life
  o If DOAC is used:
    • Suggest drug-specific peak and trough with test calibrated to specific drug (anti-Xa (Xa inhibitors) or ecarin clotting time or dilute thrombin time (dabigatran)
    • Reasonable to continue DOAC if level falls within expected range
    • Replace DOAC with VKA if level falls outside of range
<table>
<thead>
<tr>
<th>Drug</th>
<th>Trial</th>
<th>Weight categories</th>
<th>Number of obese patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>RE-COVER I</td>
<td>≥ 100 kg</td>
<td>502/2539 (20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMI ≥ 35</td>
<td>306/2539 (12)</td>
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<tr>
<td></td>
<td>RE-COVER II</td>
<td>&gt; 100 kg</td>
<td>438/1280 (34.2)</td>
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<tr>
<td></td>
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<td>BMI &gt; 35</td>
<td>302/1280 (23.6)</td>
</tr>
<tr>
<td></td>
<td>RE-LY</td>
<td>≥ 100 kg</td>
<td>3099/18113 (17.1)</td>
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<td></td>
<td>RE-MEDY</td>
<td>≥ 100 kg</td>
<td>299/1430 (20.9)</td>
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<td>RE-SONATE</td>
<td>≥ 100 kg</td>
<td>122/681 (17.9)</td>
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<tr>
<td>Rivaroxaban</td>
<td>EINSTEIN DVT</td>
<td>&gt; 100 kg</td>
<td>245/1731 (14.2)</td>
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<td></td>
<td>EINSTEIN PE</td>
<td>&gt; 100 kg</td>
<td>345/2419 (14.3)</td>
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<td>EINSTEIN EXTENSION</td>
<td>&gt; 100 kg</td>
<td>85/602 (14.1)</td>
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<td></td>
<td>ROCKET-AF</td>
<td>&gt; 90 kg</td>
<td>2035/7131 (28.5)</td>
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<td></td>
<td>BMI &gt; 35</td>
<td>972/7131 (13.6)</td>
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<td>Apixaban</td>
<td>AMPLIFY</td>
<td>≥ 100 kg</td>
<td>522/2691 (19.4)</td>
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<tr>
<td></td>
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<td>BMI &gt; 35</td>
<td>349/2691 (13.0)</td>
</tr>
<tr>
<td></td>
<td>ARISTOTLE</td>
<td>None</td>
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<tr>
<td>Edoxaban</td>
<td>ENGAGE AF TIMI 48</td>
<td>None</td>
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</tr>
<tr>
<td></td>
<td>HOKUSAI VTE &gt;</td>
<td>100 kg</td>
<td>611/4118 (14.8)</td>
</tr>
</tbody>
</table>
Efficacy and Safety of Apixaban Versus Warfarin in Patients With Atrial Fibrillation and Extremes in Body Weight
Insights From the ARISTOTLE Trial
Efficacy and safety of direct oral factor Xa inhibitors compared with warfarin in patients with morbid obesity: a single-centre, retrospective analysis of chart data

Margarita Kushnir, Yun Choi, Ruth Eisenberg, Devika Rao, Seda Tolu, Jackson Gao, Wenzhu Mowrey, Henny H Billett

A Patients with venous thromboembolism (n=366)

- Recurrent venous thromboembolism: 2% (p=0.74)
- Major bleeding: 1% (p=0.77)
- Composite bleeding: 4% (p=0.45)

B Patients with atrial fibrillation (n=429)

- Stroke: 1% (p=0.71)
- Major bleeding: 3% (p=0.063)
- Composite bleeding: 10% (p=0.16)

Lancet Haematol. 2019 Published Online May 24, 2019
http://dx.doi.org/10.1016/S2352-3026(19)30086-9
Case 3: Grandma

**Medical Problems**
- Hypertension
- Dyslipidemia
- Depression
- Myocardial Infarction—2017
- Osteoarthritis (hips, back)
- Urinary incontinence
- Constipation
- Mild cognitive impairment
- **NEW Diagnosis:** HFrEF NYHA Class III, Stage C
**Case 3: Grandma**

**Medications**
- Amlodipine 10 mg PO daily
- HCTZ 12.5 mg PO daily
- Atorvastatin 40 mg PO daily
- Celecoxib 100 mg PO twice daily
- APAP 500 mg PO 1-2x/wk
- Pregabalin 150 mg PO daily
- Docusate 100 mg PO twice daily
- Citalopram 40 mg PO daily
- Clopidogrel 75 mg PO daily
- Aspirin 325 mg PO daily
- Omeprazole 20 mg PO daily
- Atenolol 25 mg PO daily
- Furosemide 20 mg, ½ tab PO daily
- Digoxin 0.25 mg PO daily
- Oxybutynin 5 mg PO three times daily
- Ferrous sulfate 325mg PO daily
What is Deprescribing?

• 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

  o Part of the good prescribing continuum
  o Not about denying effective treatment to eligible patients
  o Should be a positive, patient-centered intervention with shared decision making and close monitoring
To Taper or Not to Taper?

**Taper Needed**
- Beta-blockers
- Clonidine
- Benzodiazepines
- Antidepressants
- Opioids
- Pregabalin/gabapentin
- PPIs

**Generally No Taper Needed**
- ACE-Is, ARBs
- Spironolactone
- Anticholinergics
- NSAIDs
- Insulin, sulfonylureas, metformin
- Cholinesterase inhibitors
- OTCs and supplements
Deprescribing Tools: STOPP and START

STO**P**P: Screening Tool of Older Person’s Prescriptions

- Addresses PIMs
- Most criteria related to drug-drug or drug-disease interactions
- Criteria address
  - Indication
  - Place in therapy
  - Duration of use
  - Dose limit (if any)

ST**A**RT: Screening Tool to Alert doctors to the Right Treatment

- Addresses potential errors of omission or underutilization
- Highlights agents that should be utilized in the context of specific medical conditions

Deprescribing Tools: Beers Criteria

Usefulness
- Evidence-based
- Updated regularly
- Includes evidence rating and evidence tables
- Designed to support good clinical judgment

Limitations
- Evidence-based
  - If no evidence, not included
  - If evidence supports in patients of all ages, drug was not included
- Does not apply to all patients
- Does not replace common sense and clinical judgment
- The criteria are not equally applicable in all countries

# Deprescribing Tools: Medication Appropriateness Index

## Table 2 Medication Appropriateness Index

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
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<tbody>
<tr>
<td>1</td>
<td>Is there an indication for the drug?</td>
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<tr>
<td>2</td>
<td>Is the medication effective for the condition?</td>
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<tr>
<td>3</td>
<td>Is the dosage correct?</td>
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<td>4</td>
<td>Are the directions correct?</td>
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<td>5</td>
<td>Are the directions practical?</td>
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<tr>
<td>6</td>
<td>Are there clinically significant drug–drug interactions?</td>
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<tr>
<td>7</td>
<td>Are there clinically significant drug–disease interactions?</td>
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<td>8</td>
<td>Is there unnecessary duplication with other drugs?</td>
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<td>9</td>
<td>Is the duration of therapy acceptable?</td>
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<tr>
<td>10</td>
<td>Is this drug the least expensive alternative compared to others of equal utility?</td>
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</tbody>
</table>
Deprescribing Tools: MedStopper.com

• Provides guidance for deprescribing with risk/benefit for each drug

• Medications can be arranged by either stopping priority or by condition

• For some medications/indications, just below the faces, there are CALC and NNT links for more information.
  o CALC links to on-line calculators that help you make individual assessments of risks and benefits
  o NNT takes you to the relevant NNT information provided by thennt.com

• Includes suggested tapering approach if applicable
  o Includes possible symptoms to assess during the tapering process

• If the medication is listed in either the Beers or STOPP criteria, click the details button and the specific criteria from these tools will be provided in a popup
**Deprescribing Tools: MedStopper.com**

### MedStopper Plan

Arrange medications by: **Stopping Priority**

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</thead>
<tbody>
<tr>
<td>RED=Highest</td>
<td>pregabalin (Lyrica) / Antiepileptic / pain</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>If used daily for more than 3-4 weeks. Reduce dose by 25% every week (i.e. week 1-75%, week 2-50%, week 3-25%) and this can be extended or decreased (10% dose reductions) if needed. If intolerable withdrawal symptoms occur (usually 1-3 days after a dose change), go back to the previously tolerated dose until symptoms resolve and plan for a more gradual taper with the patient. Dose reduction may need to slow down as one gets to smaller doses (i.e. 25% of the original dose). Overall, the rate of discontinuation needs to be controlled by the person taking the medication.</td>
<td>return of symptoms, pain</td>
<td>None</td>
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<tr>
<td>GREEN=Lowest</td>
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</table>
Deprescribing Tools: Deprescribing.org

- Deprescribing algorithms for clinicians
- Deprescribing educational tools for patients and caregivers
- Deprescribing patient decision aids

- PPIs, benzodiazepines, Z-drugs, antihyperglycemic agents, antipsychotics, antihistamines, NSAIDs, cholinesterase inhibitors/memantine
Deprescribing Tools: Deprescribing.org

Proton Pump Inhibitor (PPI) Deprescribing Algorithm

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Indication still unknown?
- Mild to moderate esophagitis or GERD treated x 4-8 weeks (esophagitis healed, symptoms controlled)
- Peptic Ulcer Disease treated x 2-12 weeks (from NSAID: H. pylori)
- Upper GI symptoms without endoscopy; asymptomatic for 3 consecutive days
- ICU stress ulcer prophylaxis treated beyond ICU admission
- Uncomplicated H. pylori treated x 2 weeks and asymptomatic

Why is patient taking a PPI?
- If unsure, find out if history of endoscopy, if ever hospitalized for bleeding ulcer or if taking because of chronic NSAID use in past, if ever had heartburn or dyspepsia

Recommend Deprescribing

Decrease to lower dose
Stop and use on-demand

Monitor at 4 and 12 weeks
- If verbal: Heartburn, Dyspepsia, Regurgitation, Epigastric pain
- If non-verbal: Loss of appetite, Weight loss, Agitation

Use non-drug approaches
- Avoid meals 2-3 hours before bedtime; elevate head of bed; address if need for weight loss and avoid dietary triggers

Manage occasional symptoms
- Over-the-counter antacid, H2RA, PPI, alginate pm (i.e. Tums®, Rolaid®, Zantac®, Omeprazole®, Gaviscon®)
- H2RA daily (weak recommendation – GRADE; 1/5 patients may have return of symptoms)

If symptoms relapse:
- If symptoms persist x 3 – 7 days and interfere with normal activity:
  1) Test and treat for H. pylori
  2) Consider return to previous dose

Strong Recommendation (from Systematic Review and GRADE approach)
- (evidence suggests no increased risk in return of symptoms compared to continuing higher dose), or
- (daily until symptoms stop) (1/10 patients may have return of symptoms)

Stop PPI

Continue PPI
or consult gastroenterologist if considering deprescribing
Lag Time in Describing

• Lag time > life expectancy: don’t recommend
• Lag time < life expectancy: recommend
• Lag time = life expectancy: pt preference

• Lag time and harms vary
  o Statins vs prostate cancer screening
  o HTN treatment: hypotension immediate, benefit 6-12 months
  o Glycemic treatment: hypoglycemia immediate, benefit years
  o Pain treatment: side effects immediately, benefit immediately
Considerations in Heart Failure

- Despite improvements in mortality, approximately 50% of those diagnosed with HF die within 5 years.

- Consider “Lag time to benefit”
  - The time between an intervention is initiated and when improved health outcomes occur.

- To identify which patients are more likely to be helped vs harmed
  - Focusing on age does not account for comorbidities and baseline health.
  - Compare lag time vs life expectancy.
  - [eprognosis.ucsf.edu](http://eprognosis.ucsf.edu)

References:
- [Br J Gen Pract](http://www.bjgp.co.uk/content/67/648/17.full) 2017; DOI: https://doi.org/10.3399/bjgp17X690533
Think-Pair Share

• What drugs would you like to see deprescribed (or adjusted), why, and how would you accomplish this?