Disclosures

- I have no personal or financial conflicts of interest to disclose
- I will be discussing off-label use of medications

Objectives: Pharmacists

- Describe four evidence-based clinical pearls of depression pharmacotherapy
- Explain five ways older medications may be reformulated into “new” products
- Identify three compelling comorbid conditions that my guide antidepressant selection
- Develop a rational treatment plan for a patient with depression

Objectives: Pharmacy Technicians

- Identify common medications used to treat depression
- Recognize how older medications may be reformulated into “new” products
- Describe medication options for depression

Patient Case

BC is a 60 yo female presenting with:

- ↓ sleep, interest, energy, concentration and weight (20# over 2 months, not intentional)
- ↑ ‘worrying about everything’
- Off work x 1 week, unable to get out of bed
- PMH: hypertension, ‘nerve pain’, and migraines
- SH: no tobacco, ‘occasional’ alcohol, works full time as a retail clerk, financial stressors

Relevant assessment

- BP 130/55 HR 70 Wt 75 kg (down from 84 kg)
- CMP, CBC and thyroid studies WNL

Current medications

- Metoprolol, ibuprofen
- PRN hydrocodone/acetaminophen, tramadol and rizatriptan

Past medications

- Fluoxetine ‘a long time ago’ – ‘helped a lot’
**Patient Case**

- Is this patient depressed?
- If so, what should be our first line treatment for depression in this patient?
- Is there a role for the ‘new’ antidepressants in her treatment?

**Depression Rating Scales**

**HAM-D 17**
- Depressed mood (0-4)
- Insomnia – early, middle, late (0-2 each)
- Work and activities (0-2)
- Irritability (0-4)
- Agitation (0-4)
- Anxiety - psychic (0-4)
- Anxiety - somatic (0-4)
- Somatic symptoms - GI (0-2)
- Somatic symptoms general (0-2)
- Genital - libido (0-2)
- Hypochondriasis (0-4)
- Loss of Weight (0-2)

Based on this patient’s score: 21 (severe)

**QIDS-SR (0-3 each)**
- Insomnia – early, middle, late
- Total sleep hours
- Feeling sad
- Appetite
- Concentration
- Self-worth/guilt
- Thoughts of death/suicide
- Interest
- Energy
- Feeling slowed down
- Feeling restless

Based on this patient’s score: 17 (severe)

**http://www.ids-qids.org**

**Medications By Class**

<table>
<thead>
<tr>
<th>Medications By Class</th>
<th>Therapeutic Uses</th>
<th>Side Effects/Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Selective Serotonin Reuptake Inhibitors (SSRIs)</strong></td>
<td>Depression</td>
<td>Nausea, diarrhea</td>
</tr>
<tr>
<td>Celexa (citalopram)</td>
<td>OCD, GAD, PTSD</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Lexapro (escitalopram)</td>
<td>Social Phobia</td>
<td>Skin rash</td>
</tr>
<tr>
<td>Luvox (fluvoxamine)</td>
<td>Panic Disorder</td>
<td>UTI</td>
</tr>
<tr>
<td>Paxil (paroxetine)</td>
<td>Bulimia</td>
<td>Headache</td>
</tr>
<tr>
<td>Prozac (fluoxetine)</td>
<td>Premenstrual dysphoric disorder</td>
<td>Increased blood pressure</td>
</tr>
<tr>
<td>Zoloft (sertraline)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs) | Depression | Same as SSRIs |
| Effexor/Effexor XR/venlafaxine extended release (venlafaxine) | GAD | Increased heart rate |
| Pristiq (desvenlafaxine) | Social anxiety disorder | Liver toxicity (venlafaxine) |
| Cymbalta (duloxetine) | Panic disorder | |
| S-lineal (milnacipran) | PTSD | |
| Fetzima (levomilnacipran) | | |

**Tricyclic Antidepressants (TCAs)**

<table>
<thead>
<tr>
<th>Medications</th>
<th>Therapeutic Uses</th>
<th>Side Effects/Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anafranil (clomipramine)</td>
<td>Depression</td>
<td>Anticholinergic</td>
</tr>
<tr>
<td>Elavil (amitriptyline)</td>
<td>OCD (clomipramine)</td>
<td>Orthostatic hypotension</td>
</tr>
<tr>
<td>Norpramin (desipramine)</td>
<td>Neuropathic Pain</td>
<td>Arrhythmia</td>
</tr>
<tr>
<td>Pamelor (nortriptyline)</td>
<td>Sleep</td>
<td>Sedation</td>
</tr>
<tr>
<td>Sinequan (doxepin)</td>
<td>Migraine headaches</td>
<td>Sexual dysfunction</td>
</tr>
<tr>
<td>Tofranil (imipramine)</td>
<td>ADHD (desipramine)</td>
<td>Sweating</td>
</tr>
</tbody>
</table>

| Monoamine Oxidase Inhibitors (MAOIs) | Depression | Sedation |
| Nardil (phenelzine) | Panic disorder | Sexual dysfunction |
| Parnate (tranylcypromine) | Other anxiety disorders | |
| Emsam (selegiline) patch | | |

**A Class of Their Own**

<table>
<thead>
<tr>
<th>Medications</th>
<th>Therapeutic Uses</th>
<th>Side Effects/Issues: Less sexual dysfunction than SSRIs and SNRIs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remeron (mirtazapine)</td>
<td>Depression</td>
<td>Sedation, weight gain, increased triglycerides</td>
</tr>
<tr>
<td>Serzone (nefazodone)</td>
<td>Depression, PTSD</td>
<td>Sedation, drug interactions</td>
</tr>
<tr>
<td>Desyrel (trazodone)</td>
<td>Depression, insomnia</td>
<td>Sedation</td>
</tr>
<tr>
<td>Wellbutrin/Zyban (bupropion)</td>
<td>Depression, Smoker cessation, ADHD</td>
<td>Agitation, insomnia, appetite suppression</td>
</tr>
<tr>
<td>Viibryd (vilazodone)</td>
<td>Depression</td>
<td>Similar to SSRIs</td>
</tr>
<tr>
<td>Brintellex (vortioxetine)</td>
<td></td>
<td>Similar to SSRIs</td>
</tr>
</tbody>
</table>

**What Is The Best Traditional Treatment?**

- How do you compare across classes?
- How do you assess efficacy in ‘real world’ environment?
- What do you do if one treatment does not effectively reduce/eliminate symptoms?
- STAR-D show us the way…
STAR-D

- Sequenced Treatment Alternatives for Remission in Depression
  - How do ‘real world’ patients respond/remit?
  - How often can we achieve remission vs response?
  - Is it better to switch medications or augment with another medication?
  - What do patients prefer?
  - Can you use rating scales in practice?
  - Do outcomes differ between primary care and psychiatry specialty clinics?

STAR-D Patient Mix

- Demographics (N=2,876)
  - Primarily Caucasian women aged 31-50
  - Psychiatrist 62% and primary care 38%
  - Severity: Average HAM-D = 22 at baseline
    - Had to be ≥14
  - Recurrent depression 75%
    - Average 6 episodes lifetime; 15 yr history
  - Average duration 2 yrs (25% >2 yrs)
  - Comorbid psychiatric disorders 65%

STAR-D Outcomes

<table>
<thead>
<tr>
<th>Average Dose at Endpoint</th>
<th>Response QIDS-SR</th>
<th>Remission QIDS-SR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1 Citalopram 40 mg</td>
<td>47%</td>
<td>33%</td>
</tr>
<tr>
<td>Level 2 switch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion 282 mg</td>
<td>26%</td>
<td>25%</td>
</tr>
<tr>
<td>Sertraline 135 mg</td>
<td>27%</td>
<td>27%</td>
</tr>
<tr>
<td>Venlafaxine 194 mg</td>
<td>28%</td>
<td>25%</td>
</tr>
<tr>
<td>Level 2 augment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion 268 mg</td>
<td>32%</td>
<td>39%</td>
</tr>
<tr>
<td>Buprione 41 mg</td>
<td>27%</td>
<td>33%</td>
</tr>
<tr>
<td>Level 3 switch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirtazapine 42 mg</td>
<td>13%</td>
<td>8%</td>
</tr>
<tr>
<td>Nortriptyline 96 mg</td>
<td>17%</td>
<td>12%</td>
</tr>
<tr>
<td>Level 3 augment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lithium 360 mg (level 0.6)</td>
<td>16%</td>
<td>13%</td>
</tr>
<tr>
<td>T3 45 mcg</td>
<td>23%</td>
<td>25%</td>
</tr>
<tr>
<td>Level 4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirt./Venl 36 mg/210 mg</td>
<td>24%</td>
<td>16%</td>
</tr>
<tr>
<td>Tranylcypromine 37 mg</td>
<td>12%</td>
<td>14%</td>
</tr>
</tbody>
</table>

Question

Considering STAR-D algorithms, what is the best option for patient BC?
A. Nortriptyline
B. Sertraline
C. Tranylcypromine
D. Venlafaxine
E. New trick

New Tricks

- Combination mechanism
- “Me too” - same mechanism, new chemical
- Active metabolite
- Single isomer
- Extended-release formulation
- Old medication, newly discovered indication

New Tricks – Not So New

- TCAs (active metabolites)
  - Amitriptyline and nortriptyline
  - Imipramine and desipramine
- MAOIs (similar mechanism)
  - Phenelzine
  - Tranylcypromine
- SSRIs (same mechanism)
  - Fluoxetine, sertraline, fluvoxamine, paroxetine, citalopram, escitalopram
Lesser Known Examples

- Fluoxetine
- Serafem
- Prozac Weekly
- Paroxetine
- Pexeva
- Brisdelle
- Venlafaxine
- VERT (venlafaxine extended release tablets)

One Chemical – So Many Options

- Wellbutrin® IR and generic 75 mg, 100 mg
- Wellbutrin® SR 100 mg, 150 mg, 200 mg
  - Generic 100 mg and 150 mg
  - Wax matrix
- Wellbutrin® XL 150 mg, 300 mg
  - Branded generic Budeprion 150 mg only
  - Diffusion controlled coating
- Aplenzin® 174 mg, 348 mg, 522 mg
- Forfivo™ XL 450 mg (brand only)

SSRI Single Isomer

- Citalopram vs. escitalopram
  - Initial claims
    - Fewer side effects
    - 10 mg escitalopram = 40 mg citalopram
    - R isomer inhibits binding of S isomer
  - Final nail
    - QTc prolongation warning

(ES)Citalopram QTc Data

<table>
<thead>
<tr>
<th>Citalopram</th>
<th>Δ QTc msec (99% CI)</th>
<th>Escitalopram</th>
<th>Δ QTc msec (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg</td>
<td>8.5 (6.2, 10.8)</td>
<td>10 mg</td>
<td>4.5 (2.5, 6.4)</td>
</tr>
<tr>
<td>40 mg</td>
<td>12.6 (10.8, 14.3)</td>
<td>20 mg</td>
<td>6.6 (5.5, 7.9)</td>
</tr>
<tr>
<td>60 mg</td>
<td>18.5 (16.0, 21.0)</td>
<td>30 mg</td>
<td>10.7 (8.7, 12.7)</td>
</tr>
<tr>
<td>Mox 400 mg</td>
<td>13.4 (10.9, 15.9)</td>
<td>Mox 400 mg</td>
<td>9.0 (7.3, 10.8)</td>
</tr>
</tbody>
</table>

- Clinically significant QTc prolongation generally considered >500 msec or prolongation of >60 msec
- Actual # of patients with clinically significant prolongation not released

Two New Tricks in One: Levomilnacipran

- Old dog: milnacipran (SNRI)
- New trick: single isomer and extended release
  - Also new indication for MDD
- Limitations
  - Cost
  - Efficacy similar to other available agents

Duloxetine

- Old dog: SNRI
- New trick: equal affinity for both serotonin and norepinephrine across the dosing range
- The caveats
  - Equal affinity ≠ improved efficacy
  - Dual mechanism ≠ improved efficacy
Duloxetine: The Facts

- FDA approved indications:
  - MDD, generalized anxiety, chronic pain, diabetic peripheral neuropathic pain, fibromyalgia
- Recommended dose: 60 mg daily
- Practical pharmacokinetic points:
  - Delayed release capsule
  - CYP 2D6 moderate inhibitor
  - Requires renal dosing

- Should not be used/avoid use in patients with:
  - "evidence of chronic liver disease"
  - "Substantial alcohol use"
  - Severe renal impairment (GFR<30 mL/min)
- Hepatotoxicity risk
- No definitive study demonstrating benefit over alternatives for MDD

Desvenlafaxine

- Old dog: venlafaxine
- New trick: active metabolite
  - The spin: Not prone to genetic variability of 2D6 metabolism or 2D6 inhibition interactions
- Caveat
  - "venlafaxine and o-desvenlafaxine are pharmacologically approximately equiactive and equipotent"

Desvenlafaxine: The Facts

- FDA approved indication: MDD
- Recommended dose: 50 mg daily
- Practical pharmacokinetic points:
  - t1/2: 10 hours
  - Absorption 80% with no impact of food
  - Metabolism – primarily conjugation
    - Minor 3A4

Desvenlafaxine Clinical Trials: MDD

<table>
<thead>
<tr>
<th>Study Arms</th>
<th>Response</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>DeMartina et al</td>
<td>placebo</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>100, 200, 400 mg</td>
<td>51%, 45%, 48%</td>
</tr>
<tr>
<td>Septien-Velez et al</td>
<td>placebo</td>
<td>38%</td>
</tr>
<tr>
<td></td>
<td>200 and 400 mg</td>
<td>60% 56%</td>
</tr>
<tr>
<td>Liebowitz et al</td>
<td>placebo</td>
<td>34%</td>
</tr>
<tr>
<td></td>
<td>100 - 200 mg</td>
<td>43%</td>
</tr>
<tr>
<td>Boyer P et al</td>
<td>placebo</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>50 and 100 mg</td>
<td>65%, 63%</td>
</tr>
</tbody>
</table>
Desvenlafaxine: The Verdict
- FDA approved dose is likely subtherapeutic
- Solves a problem that was not there
- Expensive alternative to venlafaxine
- Place in therapy ??

The Newest New Tricks
- Vilazodone
- Vortioxetine

Vilazodone
- Old dog
  - SSRI activity + 5HT1A partial agonist
  - Similar to SSRI + buspirone or pindolol
- New trick
  - Combine mechanisms into one medication
    - 5HT1A partial agonist activity → ↓ sexual dysfunction
- Caveat
  - Dual mechanism ≠ better efficacy or faster response
  - "...the net result of this action on serotonergic transmission and its role in vilazodone’s antidepressant effect are unknown”

Vilazodone: The Facts
- FDA approved indication: MDD
- Recommended dose: 40 mg daily with need for 2 week titration
- Practical pharmacokinetic points:
  - t₁/₂: 25 hours
  - Absorption increased 2-fold with food
  - Metabolism CYP 3A4 (major), 2D6/2C19 (minor)
  - Dose adjustment required with 3A4 inhibitors and inducers

Vilazodone: Trials
- Four DB, PC efficacy trials; 6-10 weeks each
- Standard MDD inclusion/exclusion criteria
- Montgomery-Asberg Depression Rating Scale (MADRS) change from baseline primary endpoint
- Demographics
  - Primarily caucasian women ~40 yrs of age
  - Average duration current episode ~6 months
  - Average of 3 lifetime episodes of depression
  - MADRS average 30 baseline (just below severe)

Vilazodone: Results
- Response rates 44-59 %
- Remission rates <30% not significantly different from placebo
- Nausea /diarrhea 25-35%
- Sexual dysfunction 1-2%
  - However comparable to active control duloxetine
Vilazodone: The Verdict
- No studies to demonstrate better efficacy or tolerability than SSRI/SNRIs
- High rates of nausea/vomiting
- Outcomes comparable to currently available $4 antidepressant medications
- Drug interactions
- Place in therapy: ??

Vortioxetine
- Old dog
  - SSRI + 5HT1A partial agonist + 5HT3 antagonist
  - Similar to SSRI + buspirone + ondansetron
- New tricks
  - Multiple mechanisms
  - 5HT3 antagonist to minimize nausea/vomiting
  - 5HT1A and 5HT1B partial agonist activity
  - 5HT7 antagonist
  - 5HT1D antagonist
- Caveat
  - Multiple mechanisms ≠ better efficacy or faster response

Vortioxetine: The Facts
- FDA approved indication: MDD
- Recommended dose: 10 mg daily (5-20 mg)
- Practical pharmacokinetic points:
  - t ½: 66 hours
  - Absorption 75% with no impact of food
  - Metabolism CYP 2D6, 3A4 and others
    - Max 10 mg with 2D6 inhibitors or poor metabolizers
    - Increase dose with potent inducers

Vortioxetine: The Studies
- Twelve DB, PC efficacy trials; 6-10 weeks each
- Standard MDD inclusion/exclusion criteria
- MADRS or HAMD change from baseline used for primary endpoint
- Demographics
  - Primarily caucasian women ~40 yrs of age
  - Average duration current episode ~6 months
  - Average of 3 lifetime episodes of depression
  - MADRS average variable

Vortioxetine Results
- Four studies demonstrating no difference from placebo on primary outcome
- Limited comparative response/remission data
- Higher dose of 10 mg appears more effective with higher rates of side effects
- Two studies with no difference in primary outcome for active control (duloxetine)

Vortioxetine: The Verdict
- Unique mechanisms
- No demonstrated benefit over older agents
- Question regarding optimal dose
- High rates of nausea and sexual dysfunction
- Drug interactions
- Place in therapy ??
Atypicals as Adjunct
- Old dog: atypical antipsychotics
- New trick: indication for MDD as adjunct
- Limitations
  - Definition of ‘non-response’ was as little as 6 weeks on antidepressant
  - No head to head with other augmentation options
  - Metabolic syndrome risk

Patient Case: New Tricks

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vilazodone</td>
<td>Less sexual dysfunction?</td>
</tr>
<tr>
<td></td>
<td>$5, must take with food, GI upset limiting</td>
</tr>
<tr>
<td>Vortioxetine</td>
<td>Less GI upset?</td>
</tr>
<tr>
<td></td>
<td>$5, drug interactions</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>May help with pain</td>
</tr>
<tr>
<td></td>
<td>Need more EtOH hx; interacts with metoprol, hydrocodone</td>
</tr>
<tr>
<td>Desvenlafaxine</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>$5, risk of underdosing</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Helps insomnia, anxiety</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome, urinary incontinence, hypotension</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>Metabolic syndrome, akathisia</td>
</tr>
<tr>
<td>Olanzapine/fluoxetine</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>METABOLIC SYNDROME, interactions</td>
</tr>
<tr>
<td>Levomilnacipran</td>
<td>?</td>
</tr>
<tr>
<td></td>
<td>$5</td>
</tr>
</tbody>
</table>

What Else Do We Need To Consider for This Patient?
- Propensity for drug interactions
- Common side effects
- Serious side effects
- Cost

Drug Interactions

The Safe Ones
- Citalopram
- Escitalopram
- Sertraline
- Mirtazapine
- Venlafaxine
- Desvenlafaxine
- Milnacipran

The Risky Ones
- Fluoxetine (2D6>>3A4)
- Fluvoxamine (1A2, 3A4)
- Paroxetine (2D6)
- Duloxetine (2D6)
- Buproprion (2D6)
- Nelfazodone (3A4)
- Vilazodine (3A4 substrate)
- Vortioxetine (2D6 and 3A4)

Question
Which of BC’s current medications potentially interact with fluoxetine?
- A. Hydrocodone/acetaminophen
- B. Tramadol
- C. Metoprolol
- D. All of the above
Common Side Effects

<table>
<thead>
<tr>
<th>Antidepressant Class</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRIs</td>
<td>Anxiety, GI, headache, sexual dysfunction</td>
</tr>
<tr>
<td>SNRIs</td>
<td>SSRI + sweating</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Insomnia; no sexual dysfunction</td>
</tr>
<tr>
<td>Vilazodone</td>
<td>SSRI, GI may be worse; less sexual dysfunction?</td>
</tr>
<tr>
<td>Vortioxetine</td>
<td>Similar to vilazodone</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Sedation, weight gain, hyperlipidemia (?)</td>
</tr>
<tr>
<td>TCAs</td>
<td>SEDATION, ANTICHOLINERGIC, ORTHOSTASIS</td>
</tr>
<tr>
<td>MAO inhibitors</td>
<td>Sedation</td>
</tr>
</tbody>
</table>

Serious Side Effects

<table>
<thead>
<tr>
<th>Antidepressant Class</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRIs</td>
<td>Hyponatremia, bleeding, movement disorders</td>
</tr>
<tr>
<td>SNRIs</td>
<td>SSRI + hypertension, hepatotoxicity</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Seizures (?)</td>
</tr>
<tr>
<td>Vilazodone/</td>
<td>Same as SSRIs</td>
</tr>
<tr>
<td>Vortioxetine</td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Minimal</td>
</tr>
<tr>
<td>TCAs</td>
<td>Cardiac toxicity</td>
</tr>
<tr>
<td>MAO inhibitors</td>
<td>Orthostasis, serotonin toxicity, hypertensive urgency</td>
</tr>
</tbody>
</table>

Cost

<table>
<thead>
<tr>
<th>Generic Available $4 to $40</th>
<th>&gt;$40 per month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clomipramide</td>
<td>Desvenlafaxine</td>
</tr>
<tr>
<td>Desvenlafaxine (IR)</td>
<td>Duloxetine (in transition phase)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Leovilinacipran</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Vilazodone</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Vortioxetine</td>
</tr>
<tr>
<td>Venlafaxine (IR, XR tablets)</td>
<td></td>
</tr>
<tr>
<td>Bupropion (IR, SR, XL)</td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td></td>
</tr>
</tbody>
</table>

Patient Case

<table>
<thead>
<tr>
<th>Compelling Patient Specific Target Symptoms</th>
<th>Treatment considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom</td>
<td></td>
</tr>
<tr>
<td>Low energy</td>
<td>SNRI or bupropion (still need to treat insomnia)</td>
</tr>
<tr>
<td>Insomnia, ↓ appetite, anxiety</td>
<td>Mirtazapine</td>
</tr>
<tr>
<td>Lipids, overweight</td>
<td>AVOID mirtazapine</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>Choose from the ‘safe list’</td>
</tr>
<tr>
<td>Pain, migraines</td>
<td>SNRI</td>
</tr>
<tr>
<td>Financial issues</td>
<td>Choose generic</td>
</tr>
</tbody>
</table>

My Recommendation: Venlafaxine XR + temporary sedative hypnotic and alternatives for pain.

Final Thoughts

- Antidepressants have similar efficacy
- Newest agents do not appear to have efficacy or tolerability benefits over older agents
- Base treatment on
  - Past history of response
  - Drug interactions
  - Side effects
- Remind patients that medications take 8-12 weeks to have optimal effect
  - Devise safety plan and coping strategies for the interim

Questions?