## Program Objectives

- Describe some common perceptions of the term polypharmacy
- Identify essential components of a psychiatric polypharmacy program
- Understand obstacles in the implementation of a successful psychiatric polypharmacy program
- Given a description of a specific patient, determine if he or she meets the criteria for polypharmacy intervention in the Intermountain model

## Disclosure of Interests

- I have no relevant financial interests with respect to this subject

## Polypharmacy: Common Perceptions

- **Third Party**: “we will not pay for all those medications”
- **Physician**: “eye-rolling; pharmacy is at it again”
- **Patient**: “why do I need so many meds?”
- **General Public**: “it’s crazy how many drugs people take”
- **Pharmacy**: “polypharmacy is always bad”
In the News... Public Perception

“In parentheses: One Brutal, Fierce, Enraged, Demented, 2-Week Maniac”

FAMILIES ON THE BRINK
What to do about Mom and Dad? DRIVING SAFELY

http://abcnews.go.com/Health/ElderCare/polypharmacy-seniors-confused-prescription-drugs/story?id=12005243

Definitions of Polypharmacy

- No standard definition - no consensus
- Commonly defined by number of medications (often ≥5)
- Also found in literature:
  - Inappropriate medications
  - Medications to treat other medications’ side effects
  - Excessive dose/duration
  - Diagnosis for medication no longer present

Other Terminology

- “Hyperpharmacotherapy”
- “Overmedication”
- “Moderate polypharmacy”
- “Excessive polypharmacy”

Why Does Polypharmacy Matter?

- Difficult to keep track of medications (especially older adults)
  - Missed doses, overdoses
  - Taking too often or not often enough (multiple drugs with different dosing schedules)
  - Short-term medications not being d/c’d
- Increased chance for drug-drug interactions
  - Examples: fall risk, hypotension, Beers list meds
- CYP interactions
- QTc prolongation
- Increased chance for adverse drug reaction (ADR)
  - 1/3 (33%) of older patients who are taking ≥ 5 medications will experience an ADR in the following year
Focus on ADR: Naranjo Scale or Algorithm

The Naranjo algorithm, Naranjo Scale, or Naranjo Nomogram is a questionnaire designed by Naranjo et al. for determining the likelihood of whether an ADR (adverse drug reaction) is actually due to the drug rather than the result of other factors.

Naranjo Scoring

<table>
<thead>
<tr>
<th>Score</th>
<th>Definite ADR</th>
<th>Probable ADR</th>
<th>Possible ADR</th>
<th>Doubtful ADR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Naranjo Questionnaire

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Are there previous conclusive reports on this reaction?</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2. Did the adverse event appear after the suspected drug was given?</td>
<td>2</td>
<td>-1</td>
<td>0</td>
</tr>
<tr>
<td>3. Did the adverse reaction improve when the drug was d/c or a specific antagonist was given?</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4. Did the adverse reaction appear when the drug was re-administered?</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>5. Are there alternative causes that could have caused the reaction?</td>
<td>-1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>6. Did the reaction reappear when a placebo was given?</td>
<td>-1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>7. Was the drug detected in any body fluid in toxic concentrations?</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10. Was the adverse event confirmed by any objective evidence?</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL SCORE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Keep in Mind: Legitimate Polypharmacy

- Disease state management
  - CHF
  - ACE-I, β-blocker, aldosterone antagonist
  - Diabetes
  - Often requires multiple medications
  - Comorbid disease state treatment
  - Hypertension
  - Cancer
- Risk of non-adherence increases as number of medications increases

Antipsychotic Polypharmacy (APP)

- Generally defined as ≥2 antipsychotic medications in one patient
- Often used to manage refractory s/s of schizophrenia
- Pooled data from 147 studies between 1970s-2009
  - 82.9% were schizophrenic patients (n=1,418,163)
  - APP prevalence of 19.6%
  - Interquartile range (IQR) 12.9%-35%
Psychiatric Population: Polypharmacy Issues\(^5,6\)

- Complexity of medications used for psychiatric illness
- Patient non-adherence
- Patient refusal
- Patient thinks medications “don’t work” so they don’t take them
- Recently overheard by patient at IMH: “I’m not taking my meds; that’s not the problem, YOU’RE the problem!”

Global APP Incidence\(^5\)

- Asia 32% (IQR= 19.2%-53%)
- Europe 23% (IQR= 15%-42.1%)
- Oceania 16.4% (IQR= 9.8%-20%)
- North America 16% (IQR= 7.2%-24.4%)
  - 1980s → 12.7%
  - 2000s → 17.0%
  - Steady increase- not going away

In the News:

- "I can’t balance myself. I can’t walk well. I’m getting very forgetful," Hearne says. "I have prostate cancer. I have a lot of mental problems that’s going on with me. I’m a paranoid schizophrenic. I suffer from manic depression." - 64 year old homeless man, Linwood Hearne

Why Do We Care About APP?\(^7,8\)

- Some states use reduction in APP as a quality-of-care target
- Joint Commission → accreditation! (more to follow)
- More drugs → increased costs
- Difficult to ascertain which drug therapy is contributing to symptom improvements and/or adverse effects
The Joint Commission and Polypharmacy

- Defines polypharmacy as concurrent use of multiple medications in one patient
- **VAGUE!**
- ↑ fall risk
- ↑ hospitalization
- ↑ disorientation
- ↑ medication administration errors
- Associated with ↑ mortality compared to monotherapy

Hospital Based Inpatient Psychiatric Services (HBIPS)

<table>
<thead>
<tr>
<th>Set Measure ID</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBIPS-1</td>
<td>Admission screening for violence risk, substance use, psychological trauma history and patient strengths completed</td>
</tr>
<tr>
<td>HBIPS-2</td>
<td>Hours of physical restraint use</td>
</tr>
<tr>
<td>HBIPS-3</td>
<td>Hours of seclusion use</td>
</tr>
<tr>
<td>HBIPS-4</td>
<td>Patients discharged on multiple antipsychotic medications</td>
</tr>
<tr>
<td>HBIPS-5</td>
<td>Patients discharged on multiple antipsychotic medications with appropriate justification</td>
</tr>
<tr>
<td>HBIPS-6</td>
<td>Post discharge continuing care plan created</td>
</tr>
<tr>
<td>HBIPS-7</td>
<td>Post discharge continuing care plan transmitted to next level of care provider upon discharge</td>
</tr>
</tbody>
</table>

More on HBIPS-4 and HBIPS-5

- Any antipsychotic is included
- If patient is on 2 forms of same medication, it is still counted as 1 medication
- PRN antipsychotics are excluded
- Short-acting IM antipsychotics are excluded
### Joint Commission: Types of Polypharmacy

- **Same-Class**
- **Multiclass**
- **Adjunctive**
- **Augmentation**

### Same-Class Polypharmacy

- The use of more than one medication from the same medication class
- **Example:**
  - risperidone and olanzapine
    - Both atypical antipsychotics
    - Note that some drugs in same class still have variable receptor affinities, side effects, etc
  - paroxetine and fluoxetine
    - Both SSRIs; combo is almost always inappropriate

### Multiclass Polypharmacy

- The use of full therapeutic doses of more than one medication from different medication classes to treat the same symptoms.
- **Example:** mirtazapine + paroxetine
  - Both antidepressants
  - mirtazapine: α2 blockade, 5-HT2A and 5-HT3 blockade
  - paroxetine: SSRI

### Adjunctive Polypharmacy

- The use of one medication to treat the side effects or secondary symptoms of another medication from a different medication class.
- **Example:** fluphenazine + propranolol
- Fluphenazine: antipsychotic
- Propranolol: β-blocker for akathisia related to antipsychotic use
Augmentation\textsuperscript{7,13}

- The use of one medication at a lower than normal dose along with another medication from a \textbf{different medication class} at its full therapeutic dose to treat the same symptoms, \textbf{OR} the addition of a medication that would be used alone to address the same symptoms.

- Example: citalopram + risperidone for resistant depression

Case Example #1

- 17 y/o male
- Mood disorder, agitation
- Medications:
  - Benztropine 1mg PO BID
  - Clonidine 0.1mg PO TID
  - Paliperidone (Invega Sustenna) 156mg/mL IM x1 (monthly)
  - Lamotrigine 50mg PO BID
  - Olanzapine ODT 10mg TID PRN
  - Risperidone 1mg PO BID

Case Example #2

- 28 y/o male
- Mood disorder, depression, anxiety
- Medications:
  - Modafinil 200mg PO QAM
  - Paroxetine 20mg PO QD
  - Trazodone 200 PO QHS
  - Olanzapine (Zyprexa Zydis) 10mg PO Q6H PRN
  - Quetiapine 100mg PO QHS (may repeat x1)
  - Haloperidol 10mg PO TID

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Any other noticeable problems?
### Implementing Polypharmacy Policy

- **Necessities**
  - Clear definition of polypharmacy
  - Physicians/pharmacists/administration in agreement
  - Adequate resources to screen and identify polypharmacy
  - Notify prescribers that polypharmacy requires proper justification
  - Continued monitoring for ADRs
  - Proper documentation of polypharmacy interventions

### Potential Justifications for APP

- Active cross-titration
- Utilizing different routes of administration

### Theoretical Justifications for APP

- Treatment of different types of symptoms
  - I.E. cognitive, negative
- Treatment of comorbid conditions
  - I.E. anxiety, insomnia, depression
- Using drug-drug interactions to augment or speed efficacy of the first antipsychotic
  - Especially if failed clozapine trial
- Using drug-drug interactions to decrease chance of adverse effects

### Reasons Difficult to Justify APP

- Cross-titration stoppage
  - Prescriber hesitant to complete the switch if symptoms improve
- Miscommunications
- Relying on marketing strategies that are unfounded
- Using drugs to treat side effects, but that have no evidence for long-term outcomes
  - Ex: Antipsychotics + benzodiazepines
- Patient or family demand
- Prescriber habits
- Cost
Patient’s chart is flagged if:
- ≥6 psychoactive medications
  - Antipsychotics
  - Antidepressants
  - Anti-anxiety agents
  - Anticonvulsants
  - Stimulants
  - Mood stabilizers
  - Opioids
  - Sedative/hypnotics

Future categories that may need to be added
- “Triptans”
- Muscle relaxants
- Buprenorphine/Naloxone (Suboxone/Subutex)
Implementing Polypharmacy Policy

- Polypharmacy definition unclear
  - Policy may need to be revised/reviewed frequently, especially at first
- Lack of willingness of prescribers to participate
- Lack of resources to screen
  - Pharmacist availability/time constraints
- Lack of physician oversight
- Dosing ceiling
- RPh clinical judgment
- Defined goals:
  - Find the “worst of the worst”/outliers?
  - Find EVERYTHING?

Obstacles

- Polypharmacy definition unclear
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- Lack of willingness of prescribers to participate
- Reimbursement!
- Lack of resources to screen
  - Pharmacist availability/time constraints
- Lack of physician oversight
- Dosing ceiling
- RPh clinical judgment
- Defined goals:
  - Find the “worst of the worst”/outliers?
  - Find EVERYTHING?

Areas Needing More Research

- Antipsychotic combinations
  - More effective than monotherapy?
- Antidepressant/antipsychotic combinations
  - Evidence is lacking
- Clearly defined multiple-drug class research
  - Especially for psychiatric medications
- Clear definition of polypharmacy
  - Based solely on number of drugs or based on outcomes?
  - Who decides?

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Intermountain Hospital Polypharmacy Case Example

- 45 y/o male – dx: schizophrenia

Scheduled medications:
- Clonidine 0.2mg PO QHS
- Diphenhydramine 50mg PO BID
- Docosate 100mg PO BID
- Paliperidone 6mg PO QHS
- Clonazepam 0.5mg PO BID
- Metformin 500mg PO BID
- Risperidone 0.5mg PO QAM
- Risperidone 0.25mg PO QHS

PRN medications:
- Diphenhydramine 50mg/mL inj Q6H PRN
- Haloperidol 10mg PO Q6H PRN
- Hydroxyzine 25mg PO TID PRN
- Trazodone 50-100mg PO QHS PRN

Conclusion

- “Make things as simple as possible. Never simpler”
  — Albert Einstein
- Sometimes multiple medications are necessary
- Sound clinical judgment, guideline-based approach
- “We don’t always know what we don’t know”
  — S.C.
References


References, continued