Psychopharmacology for Collaborative Care Managers

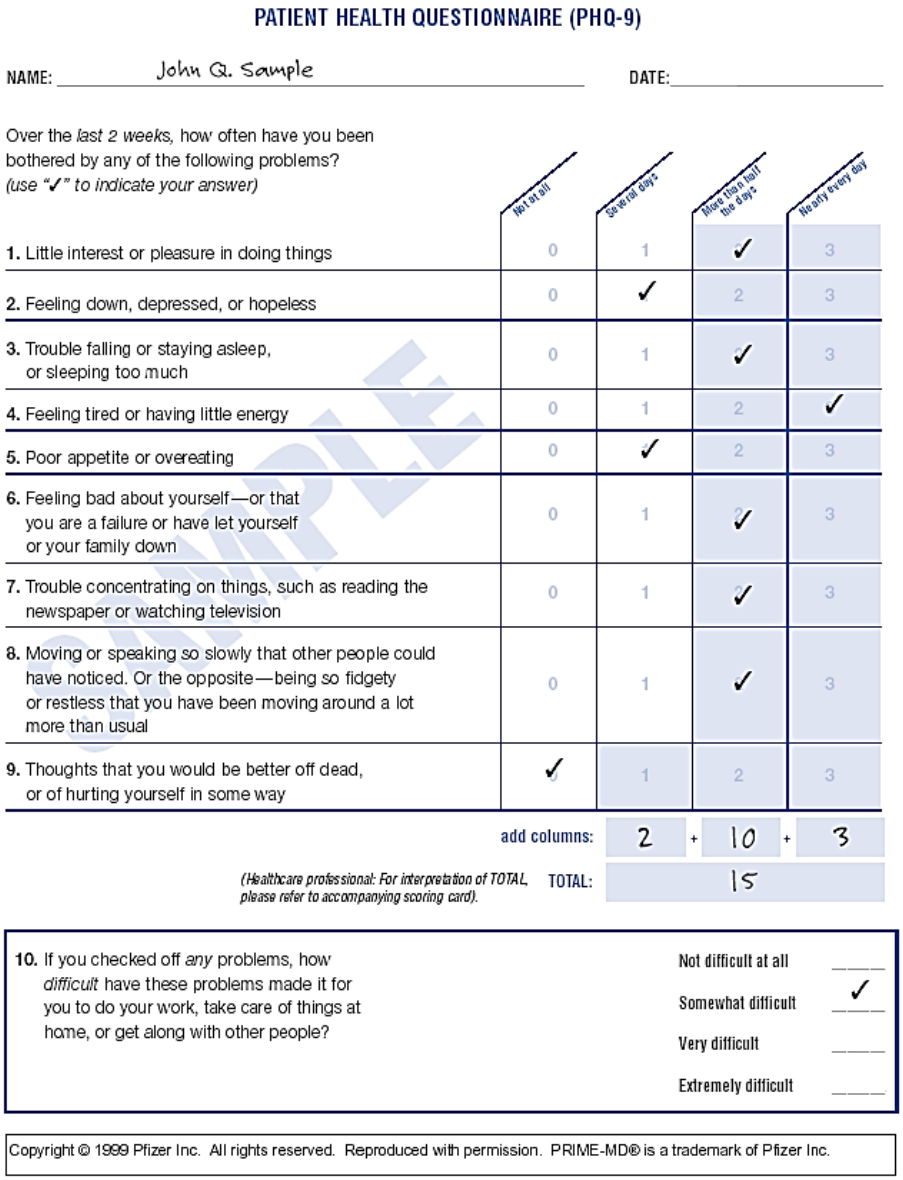
Depression

- Common
  - Lifetime prevalence of 16% (>20% in women)
  - 10-20 percent of primary care patients are depressed.
- Dangerous
  - Depression history = 2 X risk of CAD
  - Increases risk of HTN and stroke by 50%
  - Depression post MI = 6 X risk of death in 18 mos*

» Frasure-Smith N, Lesperance F, Talajic M. Depression and 18-month prognosis after miocardial infarction Circulation 1995; 15;91;999-1005.

Screening , Monitoring Tool - PHQ-9

- Quick, many languages
- First 2 questions must have a positive score
- Score ≥ 10
  - For Major Depression
    - Sensitivity 88%
    - Specificity 88%
- Mild (5),mod (10), mod severe (15) severe depression (20)



PATIENT HEALTH QUESTIONNAIRE (PHQ-9)

NAME: John Q. Sample DATE:

Over the *last 2 weeks*, how often have you been bothered by any of the following problems? *(use "✓" to indicate your answer)*

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	✓	3
2. Feeling down, depressed, or hopeless	0	✓	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	✓	3
4. Feeling tired or having little energy	0	1	2	✓
5. Poor appetite or overeating	0	✓	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	✓	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	✓	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	✓	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	✓	1	2	3
add columns:		2	+ 10	+ 3
(Healthcare professional: For interpretation of TOTAL, please refer to accompanying scoring card). TOTAL:			15	

10. If you checked off *any* problems, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?

- Not difficult at all ____
- Somewhat difficult ✓
- Very difficult ____
- Extremely difficult ____

*Patient Health Questionnaire (PHQ-9). Spitzer et al. Copyright Pfizer Inc. 1999

Could be something else…

- **Bereavement** – feelings tied to loss
- **Thyroid disease** – weight changes, energy changes
- **Cancer** – weight and energy changes, pain
- **Substance induced mood disorder** – tied to use patterns
- **Bipolar disorder** – rapid improvement, mania/hypomania (earlier onset (mean age 24)
- **Attention deficit** – concentration and irritability more than sadness or loss of interest
- **Dementia** – lack of interest or initiative
- **Pain disorders** – related to opiate use
- **Persistent Depressive disorder** – last 2 years or more with no break

Information a clinician gathers as they decide on a medication

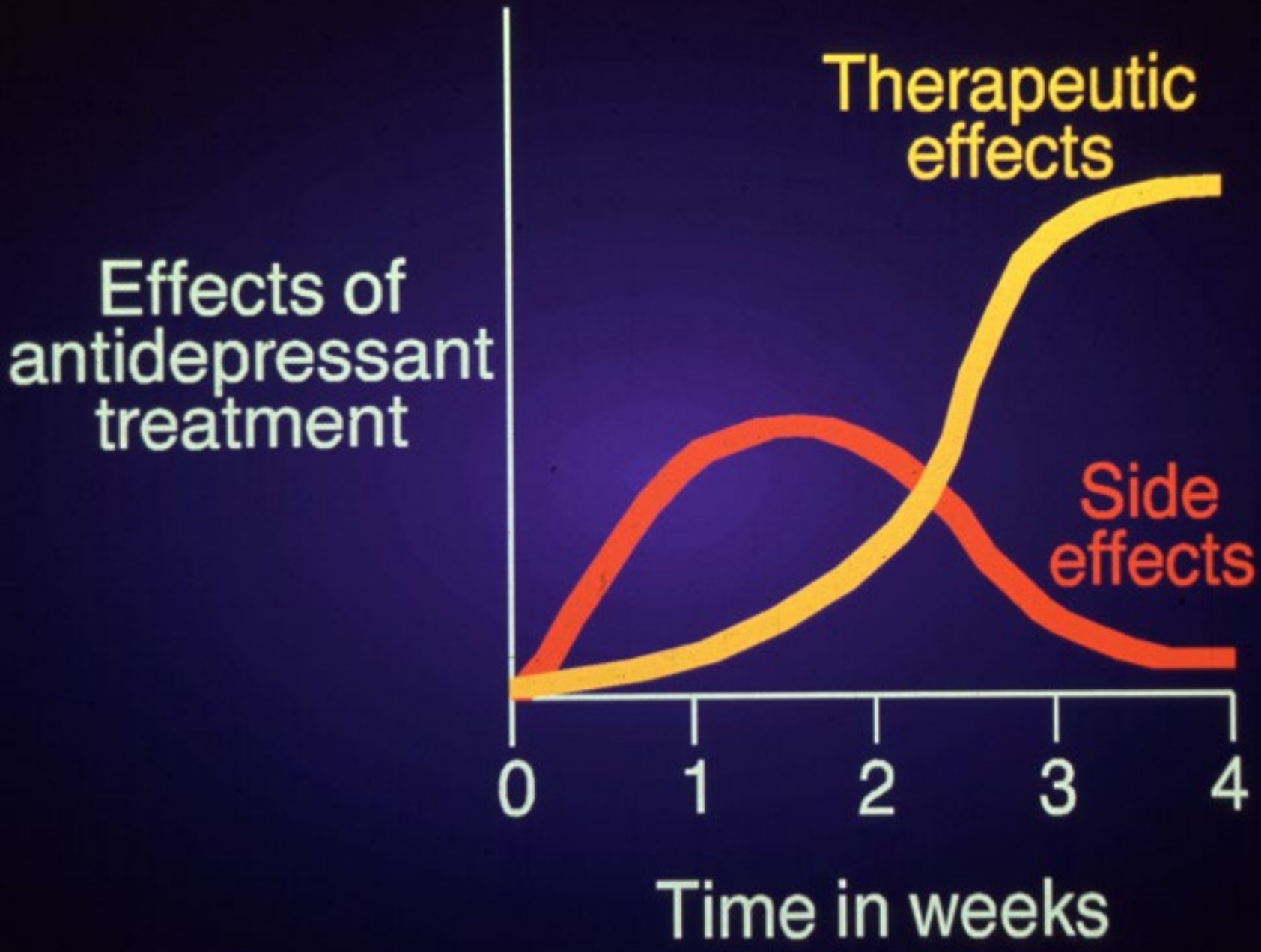
- Medical
  - Hypothyroid, pain, sleep issues, evidence of cognitive decline, fall risk, pregnancy, other medications…
- Psychological/Social
  - Pattern – when did this start? What was going on?
  - Drinking or drug use?
  - Life stressors and timing of mood changes
  - Past history of depression – what happened?
    - Past medication trials – dose, duration, response?
  - Other mental health problems
  - Current life stressors, level of functionin and supports

Comorbid anxiety? GAD7

Over the last 2 weeks, how often have you been bothered by any of the following problems?
Please circle your answers.

GAD-7	**Not at all sure**	**Several days**	**Over half the days**	**Nearly every day**
1. Feeling nervous, anxious, or on edge.	0	1	2	3
2. Not being able to stop or control worrying.	0	1	2	3
3. Worrying too much about different things.	0	1	2	3
4. Trouble relaxing.	0	1	2	3
5. Being so restless that it's hard to sit still.	0	1	2	3
6. Becoming easily annoyed or irritable.	0	1	2	3
7. Feeling afraid as if something awful might happen.	0	1	2	3

- GAD should not be diagnosed when only occurring with a mood disorder or better explained by other anxiety disorder
- Other symptoms of GAD: muscle tension, fatigue, insomnia, poor concentration
- Several types of anxiety - panic, OCD, social anxiety, PTSD


Therapeutic effects
Effects of antidepressant treatment
Side effects
0
1
2
3
4
Time in weeks

How long to wait?

Get to a minimal therapeutic dose

- Good sign if seeing some improvement in 2 weeks
- Leveling off of benefit in 6-8 weeks

Good to have a list of the medications and the dose ranges

- What is the minimal effective dose of each medicine?
- What is the usual maximum dose?

Neurotransmitters: Monoamines

Serotonin: CALM – Reduce strong negative emotions
mood, anxiety, sleep, anger/aggression
sexual functioning, gastrointestinal functioning

Norepinephrine: Can help with focus and pain
mood, anxiety
heart rate, blood pressure, “fight or flight”

Dopamine: enhancing versus blocking
motivation, mood, psychosis, attention, cognition, reward
motor activity, inhibits lactation

Histamine & Melatonin: sleep

Neurotransmitters: Other

GABA: Think of the Valium drugs here as well as gabapentin
major inhibitory role, anxiety
sedation, cognition

Glutamate: This is a work in progress but think ketamine
major excitatory role, cognition, mood
psychosis

Acetylcholine: blocking versus enhancing
cognition and memory
heart rate, bladder, gastrointestinal: “rest & digest”
“anticholinergic” side effects

How to use this information

Explaining it to clients:

Example: “This medication affects the level of a chemical called serotonin in the brain”

Helps to understand what are expected side effects

Establishes classes of medications (e.g. SSRIs or SNRIs)

Easier to remember than learning each individually

Helps understand new medications

Really new or “me too”?

Antidepressant Medications

Old-school Antidepressants

Monoamine Oxidase Inhibitors (MAOIs)

- Require strict dietary restrictions to avoid dangerous side effects, rarely used anymore

Tricyclic antidepressants (TCAs)

- Significant anticholinergic side effects
- Dangerous in overdose (cardiac arrhythmias)
- Still used for migraine headaches, nerve pain, sleep
  - Amitriptyline (Elavil), Nortriptyline (Pamelor), Doxepin (Sinequan)
- Generally not first choice for depression/anxiety
- Often see low dose at night added to another antidepressant but watch for drug interactions

More commonly used Antidepressants

SSRIs – serotonin recycling blocker

SNRIs – impacts serotonin AND norepinephrine

Bupropion (Wellbutrin) – serotonin not involved – impacts norepinephrine and dopamine

Mirtazapine (Remeron)

Trazodone – also serotonin in another way but is so sedating that used mostly for sleep

Others

SSRIs

- **Fluoxetine (Prozac)**
- **Sertraline (Zoloft)**
- **Paroxetine (Paxil)**
- **Citalopram (Celexa) & Escitalopram (Lexapro)**
- **Fluvoxamine (Luvox)**

- FDA approved for major depressive disorder
- This group is often picked when also having anxiety
- Some also approved for:
  - Posttraumatic stress disorder
  - Generalized anxiety disorder
  - Obsessive compulsive disorder
  - Social anxiety disorder

SSRIs: Common Side Effects

- Gastrointestinal upset (nausea, diarrhea), usually transient over the first few days
- Sexual side effects – difficulty with libido, erection, orgasm, reversible upon stopping medication
- "Early activation" – transient period of increased anxiety, restlessness upon initiating treatment
- Discontinuation syndrome – "Brain zaps", electric shock-like sensations in the neck and head
- Insomnia or somnolence
- Weight gain, average about 1% per year

SSRIs & Serotonin Syndrome

- Serotonin Syndrome: uncommon but dangerous consequence of excessive serotonin activity
  - Symptoms: muscle rigidity, fever, agitation
- Causes: overdose of SSRI antidepressants or combination of medications that affect serotonin
- Other pro-serotonin drugs include:
  - Tramadol and other opiates
  - Triptans for migraine headaches
  - Stimulants and drugs of abuse: cocaine, ecstasy (MDMA)
  - Anti-nausea medications, some antibiotics
  - St. John's Wort, some herbal supplements

SSRIs: Differences within class

- Citalopram, escitalopram, and sertraline have the fewest interactions with other medications
  - Good for older patients on lots of medications
- Fluoxetine has the longest half-life
  - Possible better for patients apt to miss doses
  - Also most weight neutral
- Paroxetine may have greater anticholinergic side effects and worse discontinuation syndrome
  - Also more concerns in pregnancy

SNRIs

- **Venlafaxine (Effexor) & Desvenlafaxine (Pristiq)**
- **Duloxetine (Cymbalta)**
- **Levomilnacipran (Fetzima) – rarely used until generic**
- Block reuptake of serotonin and norepinephrine
- Efficacy and side effects generally similar to SSRIs
- Advantage vs. SSRIs: also effective for neuropathic pain (e.g. from diabetes, fibromyalgia)
- Disadvantage vs. SSRIs: greater hypertensive effects

Bupropion (Wellbutrin)

- Mechanism: Inhibits norepinephrine and dopamine reuptake
- Effective for major depression and smoking cessation
- Common side effects: headache, insomnia
- Advantages vs. SSRIs: Less weight gain or sexual dysfunction
- Disadvantage vs. SSRIs: not effective for anxiety disorders
- Avoid in patient with a seizure history

Mirtazapine (Remeron)

- Complex mechanism: blocks some serotonin receptors while increasing serotonin and norepinephrine release
- Effective for major depression
- Common side effects: sedation and weight gain
- Advantage vs. SSRIs: useful if insomnia and weight loss are present, less sexual side effects
- Disadvantage vs. SSRIs: weight gain, not proven effective for comorbid anxiety disorders

SRI plus Serotonin Modulator

- **Vilazodone (Viibryd) – (2011)**
  Vortioxetine (Trintellix) – (2013)

- Serotonin reuptake inhibitor and partial serotonin receptor activator
- Might not be covered by insurance
- Vilazodone may have less sexual side effects
- Vortioxetine may help with cognitive issues in depression
- No clear reason to expect these are better by being new.

Trazodone

- Weak serotonin reuptake inhibitor, blocks and partially activates some serotonin receptors
- Used most often for its primary side effect in low doses: sleep
- Rare side effect: priapism (erection that won't go away)
- Other common side effect: hangover

Other Common Psychotropic Medications

Benzodiazepines

- **Alprazolam (Xanax)**
- **Clonazepam (Klonopin)**
- **Lorazepam (Ativan)**
- **Diazepam (Valium)**

- Mechanism: act on GABA receptors to enhance GABA effects
- Indicated for panic disorder, generalized anxiety disorder
  - Also used to treat alcohol withdrawal
- Best if used short-term (in primary care)
- Not effective for depression or PTSD
- Potential for abuse and dependence
- Caution with driving, not to be mixed with alcohol
- Sudden withdrawal syndrome: anxiety, shakes, insomnia, seizures
- Can worsen cognition in elderly and may increase fall risk

Controlled Substance Prescribing

Benzo use doubles risk of opiate overdose

- MAPS report required prior to prescribing
- Only 30-day supply at a time (+/- refills)
- Consider also:
  - Urine drug screen for other substance use
  - Patient contract
    - Only one doctor at a time
    - No early refills or replacement for lost medications
    - Attend all appointments

Other (non-addictive) anti-anxiety

- **Buspirone (Buspar) – indication is GAD**
  - Serotonin agonist, not effective for depression – but can augment
  - Takes weeks to work, significant GI side effects
- **Hydroxyzine (Atarax, Vistaril)**
  - Anti-histamine (like Benadryl), can be taken PRN, works immediately
  - Avoid in elderly (confusion, falls). Can impact EKG (QTc)
- **Gabapentin (Neurontin), Pregabalin (Lyrica) – also GABA system**
  - Works immediately, safe
  - Good for alcohol withdrawal and related anxiety & neuropathic pain
- **Prazosin (Minipress)**
  - Anti-hypertensive medication, increased dose gradually
  - Evidence primarily for PTSD-related nightmares
  - Effectiveness has been questioned recently

"Z" Drugs -- Hypnotics

- **Zolpidem (Ambien)**
- **Eszopiclone (Lunesta)**
- **Zaleplon (Sonata)**

- Act at same GABA site as benzodiazepines
- Care when combining with other sedating medications (e.g., opiates, benzos)
- Typically want to use for short term if possible
- Higher doses (above max range) can be addictive
- Have been associated with rare disordered behaviors during sleep (e.g., sleep walking)

Other Hypnotics ("Sleep Aids")

CBT for Insomnia recommended 1st line for chronic insomnia

- **Diphenhydramine (Benadryl, other OTCs)**
  - Stops working quickly, anticholinergic side effects
- **Melatonin**
  - Generally safe, not very effective long term
- **Sedating antidepressants: Doxepin, Trazodone, Mirtazapine**
- **Ramelteon (Rozerem): melatonin agonist**
  - Limited effectiveness
- **Belsomra (suvorexant): (2015)**
  - Orexin antagonist

Talking with Patients about Antidepressants

The nuts and bolts

- Antidepressants need to be taken **daily, NOT as needed**
- All antidepressant **take 2-4 weeks to see a benefit**
- Most side effects resolve in a few days, serious side effects are rare
- Antidepressant should be **continued for at least 6 months. Longer if recurrent serious episodes**
- If the first antidepressant doesn't work out, there are many other options – generally 60% rule (change/add)

Conclusion

Antidepressants are effective, generally safe, and preferred by many patients

Keys are:

1. Rule out other causes of depression, including bipolar disorder and medical conditions
2. Provide education to patients about antidepressant treatment, expected response time, and side effects
3. Follow-up with patients to assess treatment response and to ensure changes are made when response is inadequate

Resources Related to Medications

ICSI (Institute for Clinical Systems Improvement), Depression, Adult in primary care depression	https://www.icsi.org/guideline/depression/
APA (American Psychiatric Association) Practice Guidelines	https://psychiatryonline.org/guidelines
American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults	https://onlinelibrary.wiley.com/doi/full/10.1111/jgs.15767
Mayo antidepressant shared decision aid	https://depressiondecisionaid.mayoclinic.org/index
Psychopharmacology and Psychiatry Updates Psychopharmacology Institute (Podcasts)	https://podcasts.apple.com/us/podcast/psychopharmacology-and-psychiatry-updates/id1425185370 (free access to short and preview podcasts)

Questions?