

**SAMHSA-HRSA
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Health Solutions**

**Primary Care Providers Working in Mental Health
Settings:
Improving Health Status in Persons with Mental
Illness**

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**Module 4
Psychopharmacology for Common Illnesses
and Working with Psychiatric Providers**

Learning Objectives:

- Understand the most commonly used psychotropic medications and their potential side effects
- Discuss the problems associated with psychotropic prescribing and the role of the PCP-Psychiatric provider liaison in minimizing risk
- Appreciate the need to work with psychiatric provider colleagues on ownership of prescribing and rules of engagement

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Pre Course Questions

1. Which SGAs lead to the most weight gain?
 1. Olanzapine (Zyprexa) and Quetiapine (Seroquel)
 2. Risperidone (Risperdal)
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 4. Haloperidol (Haldol) and Fluphenazine (Prolixin)
2. Which tests are recommended by the ADA/APA guidelines for SGAs?
 1. Lipid Panel
 2. Fasting Blood Sugar
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 4. All the above
3. What percentage of patients with Schizophrenia smoke?
 1. ~30 - 40%
 2. ~40 - 50%
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 4. ~90%
4. What roles do the psychiatric providers play in the medical treatment of their patients?
 1. Minimize risk by selection of medications
 2. Screen for medical complications of medications
 3. Counsel on lifestyle modification
 4. All of the above

Overview Module 4

- Medication Classes
- Anxiety
- Sleep
- Smoking
- Substance Use
- Pain
- Working with Psychiatric Providers

Classes of Psychotropic Medications

Antipsychotics – 1st and 2nd Generation (SGA)

Antidepressants – TCA, SSRI, SNRI, SDRI

Mood Stabilizers

Anxiolytics



First Generation (FGA) Antipsychotics

Yes, we still use them....Potent D2 receptor blockade

High Potency – decanoate helpful for homeless, few social supports, frequent relapse

- Fluphenazine (Prolixin) has decanoate formulation – IM q 2 weeks
- Haloperidol (Haldol) also decanoate – IM monthly

Low Potency – dopamine + histamine, acetylcholine, muscarinic

- Thioridazine (Mellaril)
- Loxapine (Loxatane)
- Chlorpromazine (Thorazine)
- Thiothixene (Navine)
- Perphenazine (Trilafon)



FGA Side Effects – think Parkinson's

Dyskinesias – movement disorder (nigrostriatal dopamine pathway)

tongue, lips, eye, limbs, fingers

Tardive Dyskinesia – can be permanent

Dystonias – muscle tension

neck (torticollis), arms, legs – any body part

painful – benztropine, diphenhydramine to treat – IM available

Akathisia – extreme restlessness

hard to sit still, pacing, shakiness – can be exhausting, reduce dose

Hyperprolactinemia – D2 blockade (tubuloinfundibular dopamine pathway)

amenorrhea, galactorrhea – lower the dose, switch, work with GYN

DECADE OF THE BRAIN

1990 – 1999

July 17, 1990

Now, Therefore, I, George Bush, President of the United States of America, do hereby proclaim the decade beginning January 1, 1990, as the Decade of the Brain.

Many new medications introduced with novel mechanisms of action during this time

Decade of the Brain from the Trenches



Antidepressants

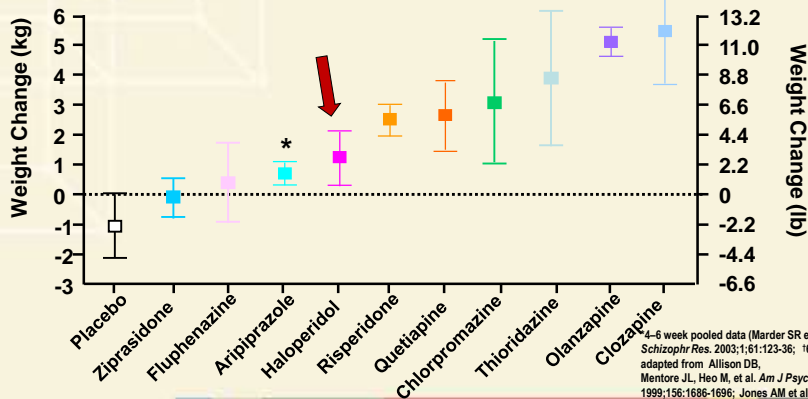
1987 – Prozac (fluoxetine)
 1989 – Celexa (citalopram)
 1989 – Wellbutrin (bupropion)
 1992 – Zoloft (sertraline)
 1992 – Paxil (paroxetine)
 1993 – Luvox (fluvoxamine)
 1993 – Effexor (venlafaxine)

Second Generation Antipsychotics (SGA/"Atypical")

1991 – Clozaril (clozapine)
 1994 – Risperdal (risperidone)
 1994 – Zyprexa (olanzapine)
 1995 – Seroquel (quetiapine)
 2001 – Geodon (zispriazidone)
 2002 – Abilify (aripiprizole)
 x

We started to notice some problems....

Estimated Weight Change at 10 Weeks on "Standard" Dose



SGA Side Effects - “an epidemic within an epidemic”

Medication	Diabetes	EPS	Prolactin	QT Interval	Weight
Aripiprazole	+/-	+	+/-	+/-	+
Asenapine	+	+++	++	+	++
Clozapine	++++	+/-	+/-	+	++++
Illoperidone	++	+	+/-	++	++
Lurasidone	+/-	++	+	+/-	+/-
Olanzapine	++++	+	+	+	++++
Paliperidone	++	+++	+++	+	+++
Quetiapine	++	+/-	+/-	+	+++
Risperidone	++	+++	+++	+	+++
Ziprasidone	+/-	+	+	++	+/-

**ADA/APA Screening Guidelines for Second
 Generation Antipsychotics**

	Baseline	4 wks	8 wks	12 wks	Annually
Review Personal / Family history of illness	X				X
Weight (BMI)	X	X	X	X	X
Waist Circumference	X			X	X
Blood Pressure	X			X	X
Fasting Plasma Glucose	X			X	X
Fasting Lipid Profile	X			X	X

American Association of Clinical Endocrinologists, North American Association for the Study of Obesity:
 Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 2004;
 27:596-601

Newer SGAs

Drug	Dose Range	Side Effects
Lurasidone (Latuda)	40 – 120 mg	Drowsiness, akisthesia, no weight gain/metabolic
Asenapine (Saphris)	20 – 80 mg	Drowsiness, no weight gain/metabolic
Iloperidone (Fanapt)	6 – 12 mg	Dizziness, dry mouth, fatigue

Long-acting Injectable SGAs

Risperdal Consta	every 2 weeks
Invega Sustenna	monthly
Abilfy Maintena	monthly
Zyprexa Relprevv	monthly - PDSS risk: Post-Injection Delirium Sedation Syndrome – 3 hour watch

Clozapine (Clozaril)

- SGA used in treatment resistant patients and can be life saving for those who respond
- However, used as last resort due to life threatening agranulocytosis
- Weekly CBC x 6 months, then q 2 weeks
- Only registered pharmacies may dispense and must have CBC at pharmacy or will not get drug
- Absolute Neutrophil Count (ANC) >2
- “Clozaril clinics” in some sites due to volume and monitoring
- Therapeutic level ~ 200 – 400 ng/ml
- Same APA/ADA screening guidelines apply due to CV risk

CATIE Trial

The NIMH-funded Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Study was a nationwide public health-focused clinical trial that compared the effectiveness of older (first available in the 1950s) and newer (available since the 1990s) antipsychotic medications used to treat schizophrenia. \$42.6 million study was conducted over a five-year period at 57 clinical sites across the country.

Perphenazine:
(FGA)



Olanzapine, risperidone, ziprasidone, quetiapine
(SGA)

Perphenazine (the older medication) equally as effective as the other three newer medications (risperidone, quetiapine, and ziprasidone) and was as well tolerated as the newer drugs. The three newer medications performed similarly to one another. Slight clinical advantage with olanzapine. No substantial advantage of newer medications.

So why did we continue to use SGAs with CATIE trial results?

- **Efficacy
- **Less sedation/more sedation
- **Patient preference
- Low incidence of extra pyramidal symptoms
- Low incidence of tardive dyskinesia
- Cannot tolerate alternatives

Hermes, et al. Prescription of Second Generation Antipsychotics: Responding to Treatment Risk in Real World Practice, Psych Services, 2013 64 (3)

Why Not Just Switch?

If switch could get weight loss, lower FBS, favorable lipid profile, right?

Problems that might occur:

- rebound worsening of psychotic symptoms,
- side effects, such as the addition of side effects of the old and new drugs, or side effects specific to the new drug, or
- differences in efficacy between the drugs and concerns about unequal efficacy
- problems might be specific to the discontinuation of the drug or to the drug to which the patient is switched.

The strategy (sometimes called 'overlap and taper')

- slow tapering of the initial antipsychotic after the new drug had been titrated to the *full dose*
- ensures that the patient is covered with an adequate plasma level of the added drug before the former drug is discontinued
- produces fewer problems during the switch than abrupt discontinuation or gradual discontinuation before starting a new drug.

[Cochrane Database Syst Rev](#), 2010 Dec 8;(12):CD006629.
BMC Medicine 2008, 6:18

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Mood Stabilizers

Medication	Dose	Therapeutic Level	Side Effects	Labs	Cost
Lithium	Varies – start at 300 mg hs	Active 0.8 – 1.2 Maint 0.6 – 0.8 Toxic >1.5 <i>*narrow window</i>	Polyuria, GI, renal, thyroid, wt, diuretics, NSAIDS	12 hr trough TSH Cr	\$4
Valproic Acid	Varies – start at 500 mg	Active 80 – 100 Maint 60 - 80	Hepatic, wt, Platelets, GI Sedation, PCOS	12 hr trough LFTs CBC	\$4
Carbamazapine	Varies – start at 200 mg	none	Sedation, wt WBC, GI, Hepatic	12 hr trough WBC LFTs	\$4
Lamotrigine (depression)	50 – 400	none	Rash, slow titration	none	\$\$
SGAs	varies	none	See previous	See previous	\$\$\$

Texas Medication Algorithm Project

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Treatment of Depression

Unipolar

- Antidepressants
- SGAs augmentation strategy: quetiapine, aripiprazole
- *Evidence based psychotherapy is first line for some – Cognitive Behavioral Therapy (CBT) has good evidence

Bipolar Depression – mood stabilizer first

- lithium
- lamotrigine
- quetiapine
- aripiprazol
- antidepressants with caution – can trigger mania, do not give without a mood stabilizer on board

**Electroconvulsive Therapy (ECT) – can be used for both

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Antidepressant Categories

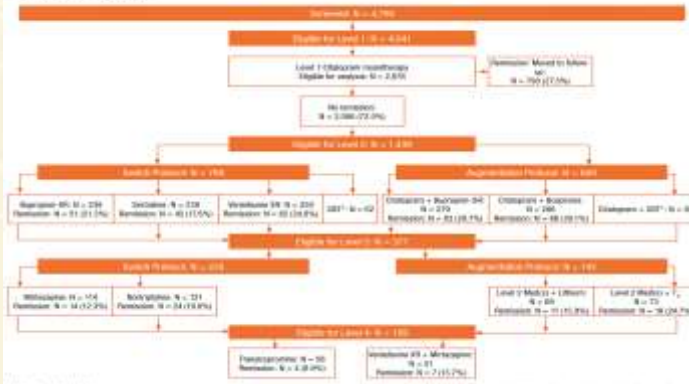
Selective Serotonin Reuptake Inhibitors (SSRI)	<ul style="list-style-type: none"> fluoxetine, paroxetine, citalopram – all \$4 sertraline, escitalopram
Selective Dopamine Reuptake Inhibitors (SDRI)	<ul style="list-style-type: none"> bupropion
Selective Norepinephrine Reuptake Inhibitors (SNRI)	<ul style="list-style-type: none"> venlafaxine duloxetine
Tricyclic Antidepressants (TCA)	<ul style="list-style-type: none"> nortriptyline, imipramine, desipramine amitriptyline
Others	<ul style="list-style-type: none"> remeron, trazodone, vilazadone

NIMH STAR*D, \$35 MILLION, 6

Antidepressant Prescribing

On the Road to Remission

NIMH's STAR*D study treated a complete list of patients started with SSRI monotherapy. For those patients who did not achieve remission (RemD: 01 = 7) or experienced intolerable side effects, multiple treatment options were available within levels 2 through 6. After addressing restrictions, patients were moved to a subsequent follow-up phase of the study leading on long up to 12 months.



Side Effects Antidepressants

Serotonergic (SSRIs)

insomnia
sexual side effects
weight gain
activation
nausea/diarrhea

Dopaminergic - bupropion

activation
insomnia
no sexual SE
no weight gain
seizure risk

Norepinephrine (TCAs)

blood pressure
sedation
weight gain
cardiac in overdose

SNRI

combo SSRI and TCA
nausea
weight gain
blood pressure changes

Approaches to Anxiety

Relaxation Exercises – deep breathing, progressive relaxation
Cognitive Behavioral Therapy

SSRIs, SNRIs (first line med)

Fluoxetine, paroxetine, sertraline, citalopram
Duloxetine, venlafaxine



Others

Benzodiazepines –

Alprazolam (3hr half life)
lorazepam (8 hr half life),
clonazepam (18 hr half life)
diazepam (60 hr half life)

Gabapentin – 300 – 3000 mg (wt gain, loopiness)

Buspirone

SGAs

B blockers

NOT Bupropion - can worsen anxiety

Rational Approach to Benzodiazepines

- Efficacy, rapid onset make them desirable
- Acute stress, fluctuating anxiety, severe panic are indications
- Limit use to acute episode if possible (4 weeks max) – can become difficult to stop this though
- Use in conjunction with other strategies – SSRI, therapy
- Side effects include sedation, tolerance, cognitive impairment, concern with increased risk of dementia, early mortality
- Base choice by half-life:
 - short anxiety attacks, events – alprazolam (3 hours)
 - sleep, intermediate coverage – lorazepam (6-8 hour)
 - longer term coverage – clonazepam (18 hours)

SLEEP

Sleep hygiene (non pharmacologic approach) first!
Naps common due to medication side effects
and interfere with normal sleep patterns

Trazodone 25 – 200 mg

Gabapentin 300 – 900 mg

Mirtazapine 15 mg

SGAs – especially quetiapine

Benzodiazepines

Zolpidem – generic, 5 mg for women



Obstructive Sleep Apnea (OSA)

15% of patients with schizophrenia with OSA

Common with obesity

Excessive daytime sleepiness overlaps with other symptoms of mental illness

Combination of sleep medications, sedating medications, narcotics, benzodiazepines on top of OSA a concern – don't want to make the problem worse

Tips:

**Find a sleep lab willing to work with your patients

**Train case managers in importance of testing so they can help with follow-through

Benson KL, Zarcone VP. Sleep abnormalities in schizophrenia and other psychotic disorders. In: Oldham JM, Riba MB, eds. Review of Psychiatry. American Psychiatric Press; 1994:677-705

Chronic Pain

SNRIs – Venlafaxine, duloxetine – some additional benefit with chronic pain due to norepinephrine activity

Gabapentin – up to 3,000 mg – watch dizziness, weight gain, renal clearance

Narcotics are CNS depressants so interfere with antidepressant action. Many chronic pain patients are depressed so do not get antidepressant benefit

Polypharmacy

- 40% of patients with schizophrenia took 2 antipsychotics
 - Add on quetiapine for sleep common
- Common: 1 or 2 antipsychotics, med for side effects, antidepressant, anxiolytic
- **Reconciliation with other meds important and difficult to accomplish. Use your Care/Case managers, EMR
- Work as a team with your psychiatric providers to avoid duplication
- Find non-pharmacologic interventions when possible



Day in the life of a psychiatric provider

- 49 yo female, Anxiety, citalopram 40 mg (the easy one – not SMI)
- 53 year old female, Bipolar I, lamotrigine 400 mg, Abilify 15 mg, chlorpromazine 300 mg, fluvoxamine 100 mg
- 33 year old male, Schizoaffective DO, Invega Sustenna, sertraline 100 mg, trazodone 100 mg, trileptal 300 bid
- 28 year old male, Schizoaffective DO, Invega Sustenna 234 mg, Invega 6 mg, Trazodone 100 mg, Depakote 1000 mg
- 41 year old female, Schizophrenia, olanzapine 10 mg, topomax 100 mg bid, trazodone 100 mg
- 53 year old male, Schizophrenia, Invega Sustenna, Bupropion SR 300 mg, trazodone 150 mg, citalopram 40 mg

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Non Pharmacologic Approaches: Evidence Based Therapies

Cognitive Behavioral Therapy (CBT) for residual psychotic symptoms and anxiety disorders

Dialectical Behavioral Therapy (DBT) for personality disorders, chronically suicidal patients, teaches Distress Tolerance Skills

Motivational Interviewing – for health behavior change including smoking, weight loss, alcohol use, exercise

Behavioral Activation – great for patients that are “stuck”

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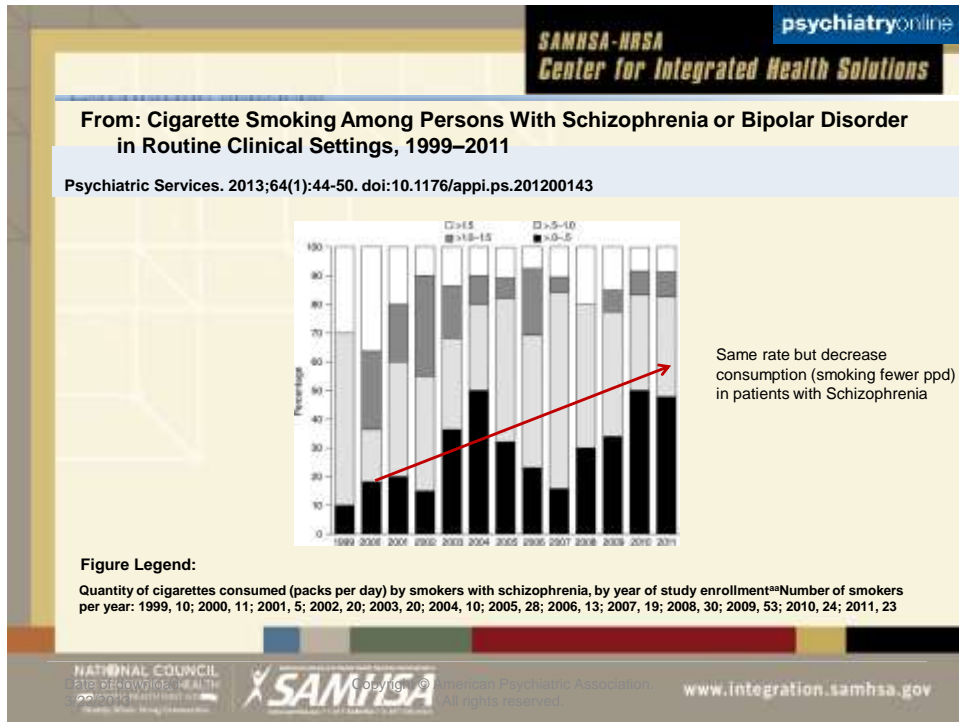
SMOKING



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Smoking and Drug Metabolism

- Increases metabolism at CP450 A12 so lowers drug level of olanzapine, clozapine
- 7-12 cigs to cause induction
- Need to watch if stop smoking or go to non smoking inpatient treatment setting

We give medications that block Dopamine and smoking increases dopamine so patients feel it makes them feel less “dull”. Depressed patients may find it helps their mood. Also – remember smoking is an appetite suppressant

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Tobacco Cessation – Use your Team – *including the psychiatric providers*

2 mg per day
Watch for suicidal ideation



300 mg/day-
Watch for activation



21 mg/day start for most
Watch for smoking while using, may need breakthrough gum/lozenges





Psychosocial Supports
(Case Manager, Peers)



Kreyenbuhl, et al. The Schizophrenia Patient Outcomes Research Team (PORT): Updated treatment recommendations. Schiz Bull 36: 94-103, 2010

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Alcohol Treatment

“Double Trouble”, Peer Run Groups, AA


- Naltrexone - 50 – 100 mg per day
(watch hepatic functions)
- Vivitrol – injectable version of Naltrexone
- Campral - 333 mg, 2 tid
(renal impairment)
- Antabuse - 250 mg per day







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Remember Motivational Interviewing!

“People are generally better persuaded by the reasons that they themselves discovered than by those which have come into the mind of others.”

17th Century French Polymath Blaise Pascal – in *Pensées*

Working with Psychiatric Providers

Co-Management

- Each provider has their own caseload
- PCP manages all medical problems
- Psychiatrist manages all mental health problems
- Work together to re-enforce treatment plans

Manage with Primary Care Consult

- Psychiatrist works with a care manager
- Manages a caseload of patients for BOTH mental health and basic medical health concerns using protocols from PCP
- PCP available for consultation and stepped care as needed

Comprehensive Management

- Typically dually trained psychiatrist – Psych/FP, Psych/IM, Child Psych/Peds
- Provider manages both medical and mental health problems
- Limited number of providers have this expertise

All psychiatrists are responsible for “not making people sicker”.

Psychiatric Providers' Responsibilities

- **Minimize**: Effects of SGAs and other psychotropic medications
- **Screen**: For Illness (APA/ADA Guidelines, etc.), others
- **Counsel**: Lifestyle Modification – smoking, weight loss
- **Treat**: Some chronic medical conditions with adequate training/consultation if desired

Engage Psychiatric Providers

- Shared patients, shared illnesses – they can counsel, switch meds, minimize side effects, treat – work in partnership with PCP
- Patients see them as their “doctor” and may want their approval first before starting medications from PCP
- Complications of psych meds and medical comorbidities require discussion among colleagues

TIPs

- *Staffing complicated patients together is encouraged
- *Go to medical staff meetings – be part of their team
- *Educate – help restore their skills in treating chronic medical problems – help them be more well-rounded medical providers

Working with Psychiatric Providers

- Some places have no nurses, no MAs and psych feel stressed about trying to do this all themselves with scales and blood pressure cuffs
- Can be insecure about medical skills
- Uncomfortable treating other medical problems “out of my scope of practice”, “not safe”. Liability concerns.
- Check in with each other before changing each others meds, agree on changes
- May see this as intrusive meddling instead of much needed support? These are “their” pts
- ***We’re on the same team so lot of potential for successful partnerships!***



Examples – Working with Psychiatric Providers

Psych A is community psychiatrist that has been working for the past 12 years with patients in an urban setting. She feels constrained by the 15 minute med check environment and wishes that she has more time to talk with her patient's and develop a therapeutic alliance more often. She feels that checking vital signs, weighing the patient and talking about lifestyle changes is impossible without more staff and time for patient interaction. Her patients have a number of complex medical problems. She does not have time to call and discuss patients since she does not have a nurse or medical assistant. She has a 16 week back log for new patients.

***** How might a partnership with this psychiatrist improve patient care?***

Examples - continued

Psych B did a residency in internal medicine and then psychiatry. He has worked for the past 15 yrs only as a psychiatrist and never recertified for internal med. He feels comfortable refilling medications for blood pressure and diabetes in his patients that don't have a PCP however, recently, he is getting concerned about the new medications and new tests coming out for treatment of HTN and DM. He feels he has no other choice since his patients will only come to see him and no other doctor.

***How could you help this psychiatrist provide better care?*

Examples - continued

Psych 3 is a CRNP working in a community behavioral health center. She sees patients that are also managed in a federally qualified with center in the area. She admits that she is frustrated that the doctors at the FQHC seem to be giving her patients clonazepam for anxiety. She refers to the docs at the FQHC as "knuckle heads" that don't know drug addicts shouldn't be prescribed these kind of medications.

***What approach could be used to find a solution to this problem?*

Example - continued

Psych 4: has managed a CTT/ACT team for 5 years. She lost 4 patients last year to heart attack and cancer. She became frustrated by the lack of PCP's in her area that would see her patients or take the time to manage their medical problems. She has been working with two family practice doctors to develop a working relationship. She has exchanged secure email, and cell phone numbers with these providers and they talk about patient care regularly to coordinate medications and test results.

Working together for successful partnership



*Partners in Health - Primary Care/County Mental Health Collaboration Toolkit, Integrated Behavioral Health Project (IBHP), October 2009

Interactive Exercise: Reflections and Discussion

What do you see as the boundaries of care with your psychiatric colleagues?

What might be a best approach to discussing care concerns, such as a patient with cardiovascular disease on olanzapine, with psychiatric provider?

Who could you talk to if there is disagreement among the treating providers?

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Resources

- Marder SR et al. *Schizophr Res*. 2003;1;61:123-36
- Allison DB, Mentore JL, Heo M, et al. *Am J Psychiatry*. 1999;156:1686-1696;
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- Hermes, et al. Prescription of Second Generation Antipsychotics: Responding to Treatment Risk in Real World Practice, Psych Services, 2013
- Benson KL, Zarcone VP. Sleep abnormalities in schizophrenia and other psychotic disorders. In: Oldham JM, Riba MB, eds. Review of Psychiatry. American Psychiatric Press; 1994:677-705
- Kreyenbuhl, et al. The Schizophrenia Patient Outcomes Research Team (PORT): Updated treatment recommendations. *Schiz Bulletin* 36: 94-103, 2010

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End of Module 4

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