Antipsychotics for the HIV Primary Care Provider

Samuel Jackson, MD (he/him)
Assistant Professor
UW Department of Psychiatry and Behavioral Sciences

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Disclosures

I have no conflicts of interest or relationships to disclose

Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

Data Considerations

Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities

Poll Question

- How many of you are managing your patients' antipsychotic medications?

Where do HIV PCPs fit in with antipsychotic management?

- Consideration of drug-drug interactions with ART
- Management of SGA cardiometabolic risk factors
- Augmentation of antidepressants
- Management of behavioral and psychological symptoms in dementia
- Co-management of severe mental illness

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HIV & Severe Mental Illness

- Severe mental illness
  - Psychotic disorders (schizophrenia, schizoaffective disorder)
  - Bipolar disorder
  - Major depression with psychotic symptoms
  - Treatment-resistant depression
  - Other mental illness with severe functional impairment
- Adults with severe mental illness are 4 to 10 times more likely to acquire HIV than the general population
  - A study of New Jersey Medicaid recipients found that 5.7% of PWH also suffered from schizophrenia

Evans TS, Berkman N, Brown C, et al. Disparities Within Serious Mental Illness [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2016 May. (Technical Briefs, No. 25.) Background.
Remien, R. H., Stirratt, M. J .,Nguyen, N., Robbins, R. N., Pala, A. N., & Mellins, C. A. (2019). Mental health and HIV/AIDS: the need for an integrated response. *Aids*, *33*(9), 1411-1420.

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HIV & Severe Mental Illness

- Individuals with severe mental illness are more likely than not to be prescribed antipsychotic medications
- Many commonly used antipsychotics are CYP 3A4 substrates and are affected by boosted ART regimens
- Individuals with untreated HIV are 7x more likely to develop extrapyramidal symptoms when exposed to antipsychotics* than those without HIV
  - * FGAs > risperidone = paliperidone >>> other SGAs

Hriso, E., Kuhn, T., Masdeu, J. C., & Grundman, M. (1991). Extrapyramidal symptoms due to dopamine-blocking agents in patients with AIDS encephalopathy. The American journal of psychiatry, 148(11), 1558-1561.
Rao, C. (1997). Incidence of extrapyramidal syndromes in AIDS patients and a comparison group of medically ill inpatients. *Neurosciences*, *9*, 579-583.
Diduch, M. N., Campbell, R. H., Borovicka, M., Cunningham, E. A., & Thomas, C. J. (2018). Treating psychosis in patients with HIV/AIDS. *Current Psychiatry*, *17*(5), 35-42.

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Antipsychotics of Concern

- Haloperidol
  - Efavirenz decreases plasma concentration
  - Increased risk of QT prolongation with boosted regimens
    - Especially ATV/c, ATV/r and LPV/r
    - QT prolongation by route: Haloperidol IV > IM >> PO
  - Increased risk of EPS in non-suppressed individuals

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Antipsychotics of Concern

- Predominately 3A4 Substrates
  - Cariprazine
  - Lurasidone
  - Lumateperone
  - Quetiapine
- Mixed 3A4, 2D6 Substrate
  - Aripiprazole
  - Brexpiprazole

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	FDA Approved Indication					Side Effect Profile	
	Schizophrenia	Bipolar Mania	Bipolar Maintenance	Bipolar Depression	Adjunctive Therapy MDD	QT Prolongation	Weight Gain
Aripiprazole	Yes	Yes	Yes	Yes	Yes	Low Risk	Low Risk
Cariprazine	Yes	Yes	No	Yes	Yes	Minimal Risk	Low Risk
Lumateperone	Yes	No	No	Yes	No	Minimal Risk	Low Risk
Lurasidone	Yes	No	No	Yes	No	Minimal Risk	Low Risk
Quetiapine	Yes	Yes	Yes	Yes	Yes	Low Risk	High Risk

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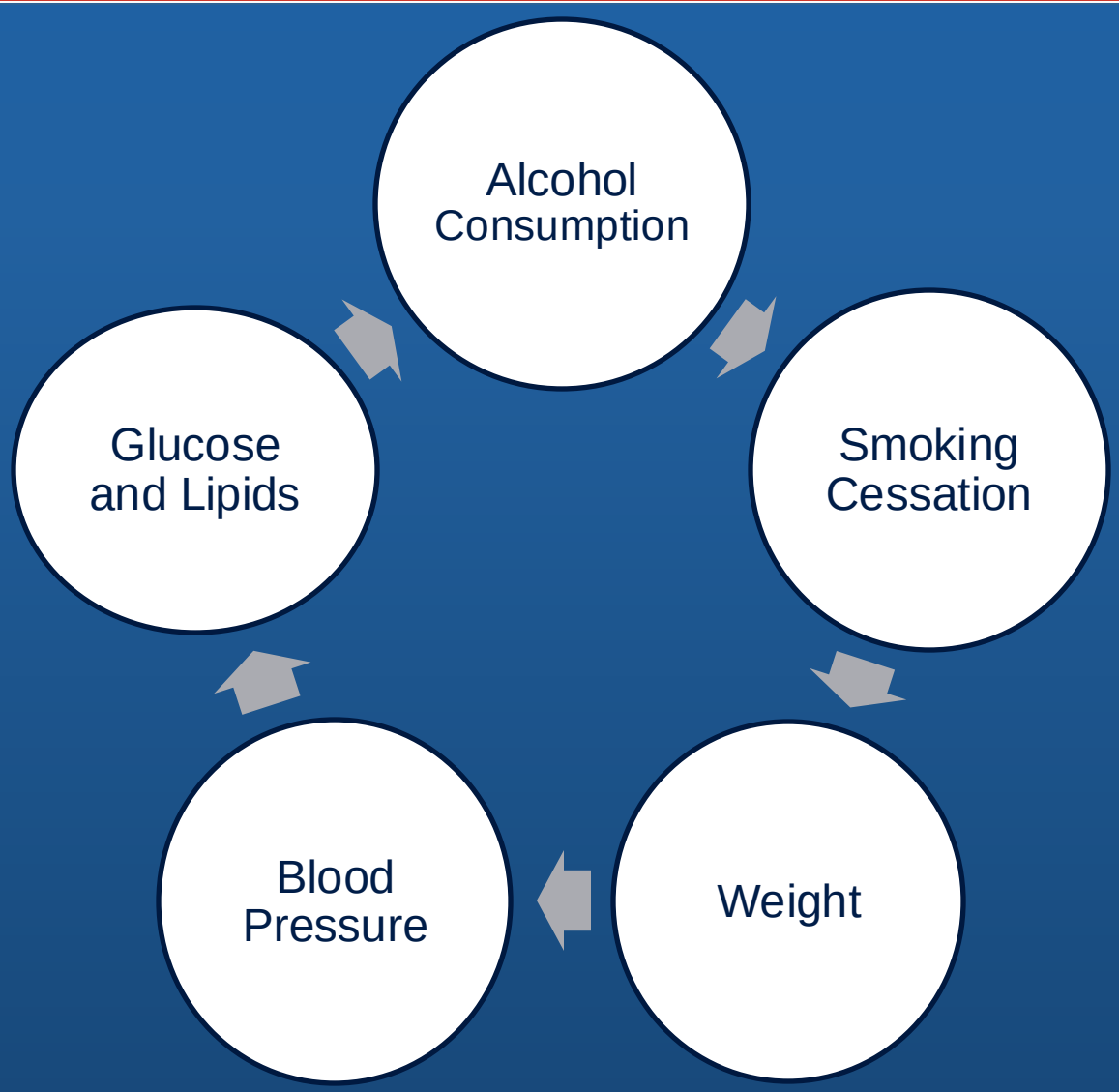
Preventative Care for Individuals on Antipsychotics



Monitoring Parameters of Antipsychotics

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Annually
Weight	X	X	X	X	X	
Waist Circumference	X	X		X	X	
Blood Pressure, Heart Rate	X	X	X	X	X	
ECG	X					X
Fasting Glucose or HbA1c	X			X		X
Fasting Lipid Profile	X			X		X
Serum Prolactin†	X					X
CBC‡	X			X		X
Abnormal Involuntary Movement Scale	X			X		X

†: Indicated in FGA, Risperidone, Paliperidone
‡: Monitor for neutropenia/agranulocytosis

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Antipsychotic-Induced Weight Gain

Antipsychotic	Estimated weight change at 10 weeks (kg)
Aripiprazole	0.99
Asenapine	1.6
Chlorpromazine	2.58
Clozapine	4.45
Haloperidol	1.08
Iloperidone	3.0
Lurasidone	0.9
Olanzapine	4.15
Quetiapine	1.8
Risperidone	2.1
Ziprasidone	0.4

Roerig, J. L., Steffen, K. J., & Mitchell, J. E. (2011). Atypical antipsychotic-induced weight gain: insights into mechanisms of action. CNS drugs, 25, 1035-1059.

Management of Antipsychotic Weight Gain

- Non-pharmacologic
  - Cognitive-behavioral interventions, nutritional counseling and combined nutritional and exercise interventions are all effective in weight loss and preventing weight gain
  - Average 2.5kg weight loss in one meta-analysis
- Antipsychotic Switching
  - Changing to a “weight neutral” antipsychotic can be effective in weight loss
    - Aripiprazole has the best evidence
    - Lurasidone, Cariprazine, Lumateperone all have more favorable weight profiles
    - Ziprasidone is consistently shown to have the lowest weight gain potential

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Management of Antipsychotic Weight Gain

- Augmentation Strategies
  - Metformin has the best evidence for the prevention and treatment of antipsychotic-induced weight gain
    - 3.3kg average weight loss
  - Naltrexone *may* be effective in the prevention and treatment of antipsychotic-induced weight gain
    - Evidence is variable
    - Olanzapine + Samidorphin (combination product) has been shown to cause significantly less weight gain than Olanzapine alone
  - Aripiprazole added to olanzapine has been shown to induce weight loss
  - Topiramate may be considered; however, side effects limit usefulness
  - GLP-1 agonists are promising, but data is sparse thus far

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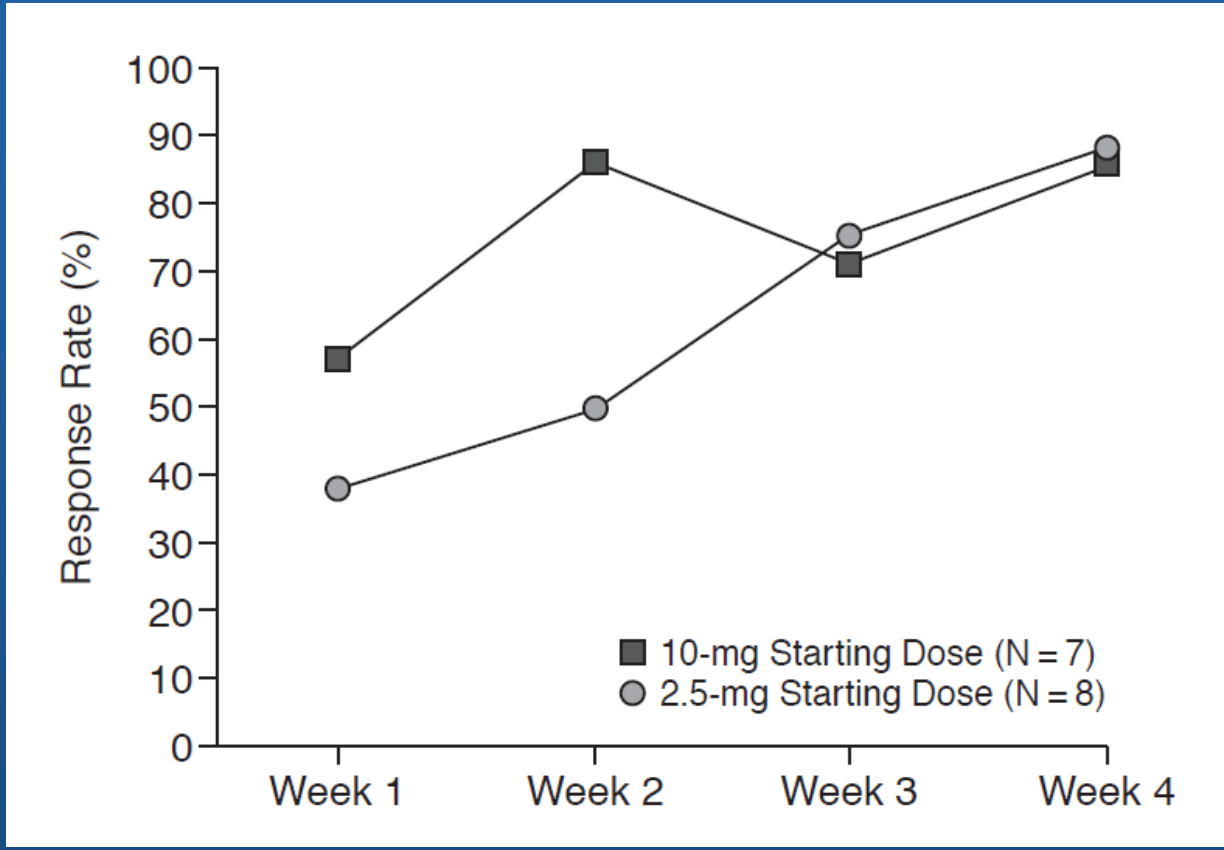
Antidepressant Augmentation

- Certain antipsychotics added to an antidepressant agent can improve residual symptoms of depression, especially in cases of severe depressive episodes
  - Note: This is augmentation of non-psychotic depression; treatment of psychotic depression is different
- Aripiprazole, Quetiapine XR, Olanzapine + Fluoxetine, and Cariprazine have the best evidence for augmentation of antidepressant effect

The Case for Aripiprazole Augmentation



- Standard dose Aripiprazole (10mg) has faster symptom resolution
- Greater side effect burden in the 10mg arm
  - Specifically Akathisia
- Low dose Aripiprazole (2.5mg), while slower, may be better

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Behavioral and psychological symptoms of dementia and Antipsychotics

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

See full prescribing information for complete boxed warning.

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. RISPERDAL® is not approved for use in patients with dementia-related psychosis. (5.1)

- Numerous studies examining the efficacy of antipsychotics in the treatment of BPSD have demonstrated an increased risk of cerebrovascular events, including stroke and death due to any cause
- 80% of people living with dementia will have BPSD
- 20% to 30% of persons with dementia are prescribed antipsychotic medications

Kirkham, J., Sherman, C., Velkers, C., Maxwell, C., Gill, S., Rochon, P., & Seitz, D. (2017). Antipsychotic use in dementia: is there a problem and are there solutions?. The Canadian Journal of Psychiatry, 62(3), 170-181.

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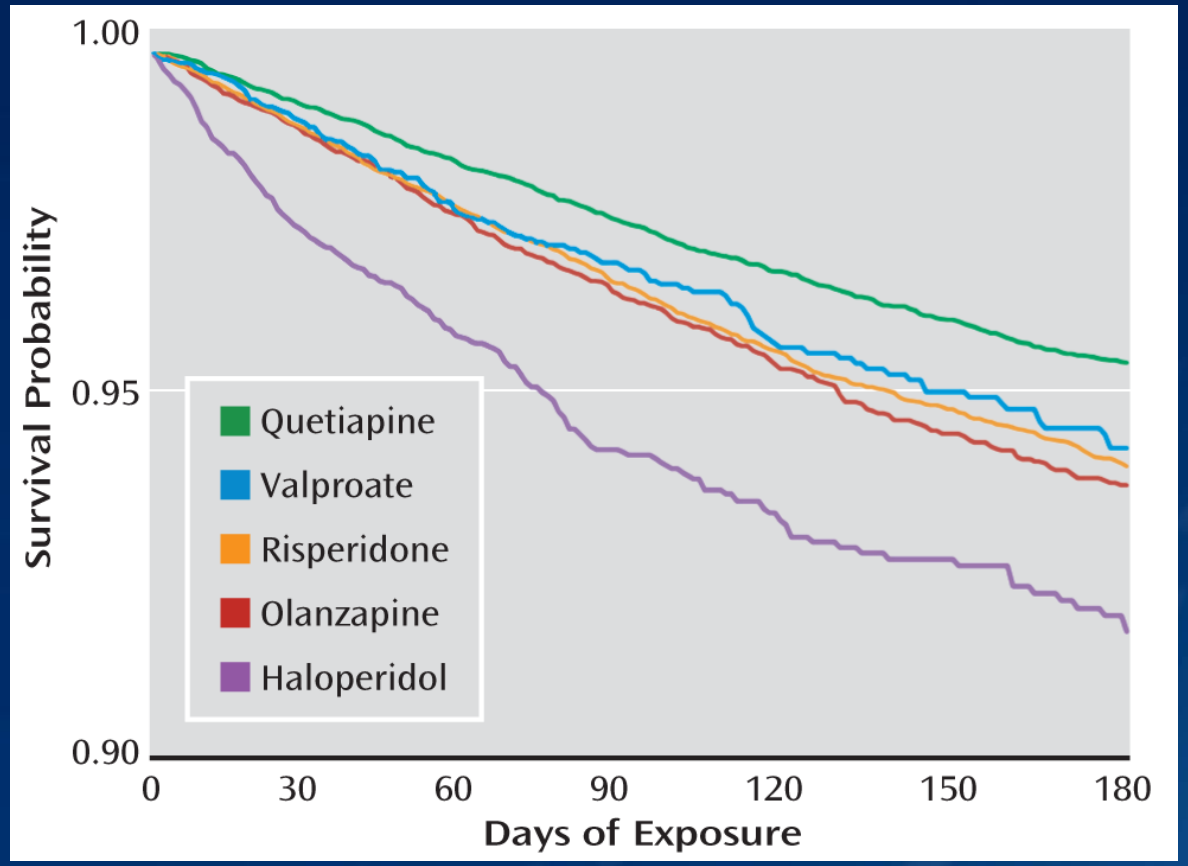
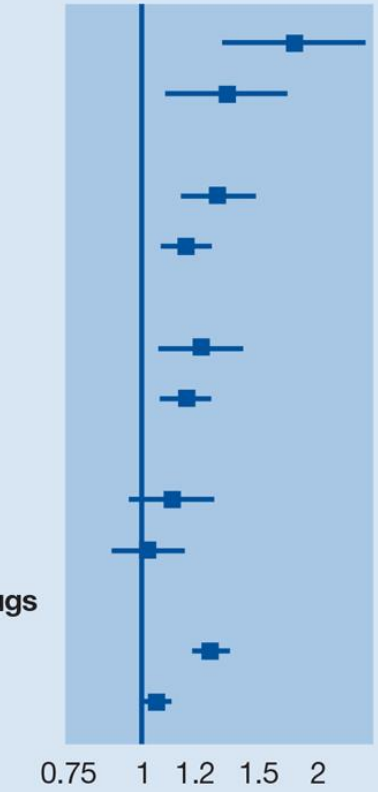


Figure

Hazard ratios for death from causes other than cancer by dose of various antipsychotics, with low-dose group of each drug as reference

Effect	Adjusted hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)
Haloperidol		
High *v* low dose		1.84 (1.38 to 2.43)
Medium *v* low dose		1.40 (1.10 to 1/77)
Risperidone		
High *v* low dose		1.35 (1.17 to 1.57)
Medium *v* low dose		1.19 (1.08 to 1.31)
Olanzapine		
High *v* low dose		1.26 (1.07 to 1.49)
Medium *v* low dose		1.19 (1.08 to 1.31)
Quetiapine		
High *v* low dose		1.12 (0.95 to 1.33)
Medium *v* low dose		1.02 (0.89 to 1.18)
All antipsychotic drugs		
High *v* low dose		1.31 (1.22 to 1.39)
Medium *v* low dose		1.24 (1.16 to 1.32)



Source: Reference 14

CI: confidence interval

Kales, H. C., Kim, H. M., Zivin, K., Valenstein, M., Seyfried, L. S., Chiang, C., ... & Blow, F. C. (2012). Risk of mortality among individual antipsychotics in patients with dementia. American Journal of Psychiatry, 169(1), 71-79.

Burke, A. D., & Burke, W. J. (2018). Antipsychotics FOR patients WITH dementia: The road less traveled: Second-generation agents have an important but limited role in treating behavioral and psychological symptoms. Current Psychiatry, 17(10), 26-36.

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Guidelines for Treating BPSD with Antipsychotics

- Indications to use antipsychotics for patients with dementia include:
  - Severe agitation and aggression associated with risk of harm
  - Delusions and hallucinations
  - Comorbid preexisting mental health conditions (eg, bipolar disorder, schizophrenia, treatment-resistant depression, etc.)
- Symptoms that do not usually respond to an antipsychotic include wandering, social withdrawal, shouting, pacing, touching, cognitive defects, and incontinence
- First generation antipsychotics should not be used
- When beginning treatment with an antipsychotic, the starting dose should be as low as possible
- Clearly document the targeted behaviors
- Review every 3 months and attempt to taper if symptoms resolve

Reus et al (2016). The American Psychiatric Association practice guideline on the use of antipsychotics to treat agitation or psychosis in patients with dementia. American Journal of Psychiatry, 173(5), 543-546.

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