Mental Health and Addiction Care

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Epidemiology

- 1 in 7 North Americans meet criteria for a substance use disorder in their lifetime
  - Alcohol – 13%
  - Drugs – 3%
- 20% of visits to primary care physicians are related to alcohol, tobacco, and other drug problems.
- Psychiatric disorders and substance use disorders have overlapping etiologies resulting in reciprocal causality
- Lifetime prevalence of substance use co-morbidity:
  - Major depressive & dysthymic disorders – 32% - 54%
  - Anxiety disorders – 36%
  - Bipolar disorder – 56.1%
  - Adult ADHD – 15 - 45%
- Annual Cost to Canadian Society
  - $40,000,000,000.00

Reiger DA, et al. *JAMA* 1990;264:2511-2518
Kessler RC, et al. *Arch Gen Psychiatry* 1994;51:8-19
Brook DW, et al. *Arch Gen Psychiatry* 2002;59:1039-1044
Kushner MG, et al. *Am J Psychiatry* 1999;156:723-732
Bradley KA. *Alcohol Health Res World* 1994;18:97-104
Hasin D, et al. *Arch Gen*
Farone SV, et al. Am J Addict 2007;16:24-32
Davis LL, et al. Compr Psychiatry 2005;46:81-89

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  - **Other:** none

Most Common Substances

- Caffeine
- Alcohol - >90% drink, 13% lifetime abuse or dependence
- Nicotine – 18% of Canadians current daily smokers
- Drugs – 3% lifetime abuse or dependence
  - Cannabis
  - Opioids – prescription opioids #1 abused drug in Canada
  - Sedative-Hypnotics – benzodiazepines and barbiturates
  - Stimulants – cocaine, amphetamines, designer drugs
  - Hallucinogens – LSD, psilocybin
  - NMDA Antagonists – PCP, Ketamine
  - Inhalants – gas, nitrous oxide, amyl nitrate, paint

Learning Objectives

- Learn the principles of good concurrent mental health and addiction care.
- Apply them to the more common mood and anxiety disorders.
- Appreciate that Borderline Personality Disorder management is not an oxymoron.
- Understand the challenges in prescribing methylphenidate or benzodiazepines to this population.
- Explore case examples.

DSM-5 Criteria for Substance Use Disorder

- **12 month period of maladaptive substance use leading to:**

SUD	CRITERIA
+	Use in Physically Hazardous Situations
+	Failure to Fulfill Major Role Obligations
+	Use Despite Social/Interpersonal Problems
+	Tolerance
+	Withdrawal
+	Craving
+	Larger amounts or longer than intended
+	Unable to cut down/control
+	Great deal of time spent
+	Activities given up
+	Continued use despite consequences

- 0-1 = No diagnosis 2-3 = Mild 4-6 = Moderate 7+= Severe
- In early remission, in sustained remission, on maintenance therapy, in a controlled environment

"Dependence" & Change Measures

- Term to be used to describe physiologic dependence only rather than addiction
- Tolerance/withdrawal – neither necessary nor sufficient to define addiction
- Within person change to be determined by:
  - # of criteria met before/after
  - % days used before /after
  - Averages daily amounts used before/after
  - Biological measures, pt report, informant report

Management of Concurrent Psychiatric and Substance Use Disorders

- Psychoeducation:
  - Psychosis: Link positive & negative symptoms to use
  - Depression: Link symptoms of sleep disturbance, low mood, amotivation to use
  - Anxiety: Discuss rebound and protracted withdrawal
- Access/utilize cognitive behavioral interventions
- Avoid benzodiazepines/habit-forming medications if possible
- Increase follow-up care/structure
- Involve family
- Follow urine drug screens
- Facilitate involvement in self-help &/or other specific addiction treatments especially if action oriented

Whooley MA, Simon GE. NEJM 2000;343:1942-50. Brady KT, Sinha R. Am J Psychiatry 2005;162:1483-1493
Brown RA et al. J Consult Clin Psychol 1997;65:715-726 Nunes EV, Levin FR. JAMA 2004;291:1887-96.
Posternak MA, Mueller TI. Am J Addict 2001;10:48-68 Moos RH & BS. Alcohol Clin Exp res 2005;29:1858-1868

Issues & Key Components for Inclusion

- Social Mores vs Neurophysiology
- Key Components:
  - Clinical need
  - Distinction from other disorders
  - Harm or impairment related to behaviour
  - Potential for treatment
- Problem Gambling moved from Impulse Control to Substance-Related and Addictive Disorders, renamed Gambling Disorder or "Disordered Gambling", legal criterion eliminated and craving added

Signs of a Primary Psychiatric Disorder

- Psychiatric symptoms predate substance use
- Limited quantity of substance use
- Prominent family history of psychiatric disorders
- Persistent psychiatric symptoms with abstinence
- Full Psychiatric disorder criteria met with typical presenting features (e.g. auditory hallucinations, melancholia)
- Female
- History of good response to psychiatric treatments or substance use treatment failures

Brady KT, Malcolm RJ. Textbook of Substance Abuse Treatment, 3rd Ed, 2004:529-537

Management of Concurrent Psychiatric and Substance Use Disorders

- Best outcomes occur when both disorders are treated simultaneously by the primary treating physician
- Treat psychiatric symptoms to full remission
- Tailor pharmacotherapy to target symptoms (sleep, anxiety, cravings, physical complaints)
- Inquire about substance use and utilize brief interventions at each visit
- Consider agents for sleep during withdrawal (e.g.: trazodone, zopiclone)
- Avoid confrontation! Be encouraging and sympathetic
- Accept relapse to substance use, but work towards abstinence (Aim to help them shift one stage of change with each interaction)

Kranzler HR, Van kirk J. Alcohol Clin Exp Res 2001;25:1335-1341
Chick J et al. Br J Psychiatry 1992;161:84-89. Crum RM et al. Am J Psychiatry 2004;161:1197-1203
Le Fauve CE et al. Alcohol Clin Exp Res 2004;28:302-312
Reiff-Hekking S et al. J Gen Intern Med 2005;20:7-13 Paykel ES et al. Psychol Med 1995;25:1171-1180

Consequences of Co-Morbidity

- Decreased treatment adherence
- Decreased response & remission rates
- Increased risk of relapse to both disorders
- Increased suicide risk
- Increased risky drug use practices (IVDU)
- Worse overall social function
- Increased health care utilization
- Problematic diagnosis
- Exclusion from treatment

Brady KT, Sinha R. Am J Psychiatry 2005;162:1483-1493
Davis LL., et al. *Comprehensive Psychiatry* 2005;46:81-89
Sullivan LE, et al. [illegible]
Fisher B, et al. Can J Psychiatry 2006;51:624-634

Goals of Treatment:

- Full Remission of Psychiatric Disorder (if present)
- Progressive Reduction of Substance Use Aiming for Abstinence (Behaviour Change!)
- Functional Improvement
- Retention in Treatment
  - Engagement & Persuasion
  - Active Intervention
  - Relapse Prevention

The Nature Of Things "Wasted"

- https://www.youtube.com/watch?v=fezqA2uUebY
- http://www.cbc.ca/natureofthings/episodes/wasted

Choice of Treatment Setting:

- Initial reviews → treatment setting unrelated to outcome
- ASAM patient placement criteria
- Patients with greatest substance use &/or co-morbidity severity benefit most inpatient/residential treatment
- Stimulant dependent patients have better outcomes with initial residential treatment
- Prior suicide attempts or current suicidal ideation should suggest inpatient/residential treatment rather than outpatient treatment at least initially

Ilgen MA et al. Alcohol Clin Exp Res 2005;29:1664-1671
Moos RH et al. Addiction 2000;95:833-846
McKay JR et al. Am J Drug Alcohol Abuse 2002;28:307-338
Timko C, Moos RH. Adm Policy Ment Health 2002;30:35-54

Neurobiological Overlap Between Substance Use and Depressive/Anxiety Disorders

- Decreased prefrontal cortex and increased amygdala activity
  - Present in panic disorder, depression, and with abstinence from substance dependence
- Negative affect states & emotional stress
  - Predispose to substance craving
  - Increase subjective reinforcing effects of substance use
- Common dysfunction of limbic-cortical network
- Decreased dopamine receptor availability with dependence during initial abstinence may predispose to dysphoria

Brady KT, Sinha R. *Am J Psychiatry* 2005;162:1483-1493
Tremblay LK, et al. *Arch Gen Psychiatry* 2005;62:1228-1236
Drevets WC. *Ann NY Acad Sci* 2003;985(29-44)
Goldapple K, et al. *Arch Gen Psychiatry* 2004;61:34-41
Seminowicz DA, et al. *Neuroimage* 2004;22:409-418

Rational Pharmacotherapy for Addiction?

Few evidence based pharmacotherapy options! (* = clinical indication)

- ***Naltrexone:** opioid antagonism blocking high
- *Acamprosate: GABA, glutamate modulation
- ***Disulfiram:** inhibits aldehyde dehydrogenase
- **Modafanil:** 2 positive RCTs for cocaine dependence
- D2 Antagonists, SSRIs & other antidepressants: primarily negative trials
- *Bupropion: partially blocks dopamine uptake (methamphetamine, nicotine)
- ***Varenicline** (nicotine)
- Anticonvulsants: withdrawal, GABA modulation of DA activity (topiramate: alcohol, cocaine)
- Baclofen (cocaine, smoking, alcohol)
- ***Methadone, *Buprenorphine** (opioids)

Tihonen J et al. Am J Psychiatry 2007;164:160-2.
Vocci FJ, Appel NM. Addiction 2007;102:96-106
Barr AM et al. J Psychiatry Neurosci 2006;31:301-313
Elkashef A et al. Addiction 2007;102:107-113.
Ling W et al. Curr Psychiatr Reports 2006;8:345-354

Does Concurrent Substance Abuse/Dependence Alter Treatment Outcome of Depression?

- Current recommendations emphasize that concurrent substance abuse/dependence NOT be a barrier to depression treatment
- Ideally, a period of abstinence (2 weeks minimum) should be sought to aid diagnosis and for best treatment outcome
- Efficacy of antidepressants for depressive symptoms similar for depressed outpatients with or without alcohol dependence (0.38 and 0.43, respectively), but worse in those with drug dependence
- Substance use minimally changed with depression treatment, emphasizing importance of concomitant treatment

Nunes EV, Levin FR. *JAMA* 2004;291:1887-1896
Torrens M, et al. *Drug Alcohol Depend* 2005;81:1-7
Walsh BT, et al. JAMA 2002;287:1840-1847

Bipolar Disorder - Management

- DDx: Stimulant induced mania vs. Bipolar I disorder – manic
  - Clues:
    - FH
    - Lack of insight
    - Timing of use
    - Persistence
    - Prior Rx
- Treatment:
  - Hospitalization / detoxification
  - Lithium vs. DVP; Atypical Antipsychotic
  - Timing of substance treatment

Interventions for Substance Use

- Identifying AND reducing substance use are the targets
- Limited research in effective psychosocial interventions to reduce cannabis use in people with early psychosis
- MI has some limited support in reducing cannabis use
- CBT and psycho-education are equivalent
- Addiction services
  - 32% of Canadian Early Psychosis Programs surveyed have formal addiction services (individual and group MI, CBT, and psychoeducation for patients/families)
  - 82% of Canadian Early Psychosis Programs surveyed have informal addictions services (individual and group psycho-education, individual MI and information resources)

Aydin C, *et al.* Poster presented at CPA 2012. In press.

Psychosis - Management

- Differential Diagnosis Clues:
  - Hallucinations / Thought disorder
  - Orientation
  - FH
  - Timing of use
  - Persistence of symptoms
- Treatment:
  - Hospitalization / detoxification
  - Initiation of 2nd generation antipsychotic, consider LAI
  - Time intervention to improvement and base on stage of change
  - Compliance
  - Psychoeducation / monitoring
  - Nicotine - ↓ EPS, ↓ negative sx, ↑ med dose, ↑ positive sx

Can Cannabis Use Cause Schizophrenia?

- Psychosis in context of clear sensorium well described:
  - Abrupt onset; hypomania and agitation
  - Less incoherence of speech, affective flattening, and auditory hallucinations
  - Clears with abstinence
- Cannabis use aggravates the severity of positive symptoms in schizophrenics and worsens the prognosis
- Onset of schizophrenia 6.9 years earlier in regular users
- Role of endocannabinoids (anandamide)?
  - Elevated with arousal and exercise
  - Not altered with treatment of psychosis

Linszman Dit et al. Arch Gen Psychiatry 1994
Negrete JC et al. Psychological Med 1986
Zammit et al. BMJ 2002;325:1199.
Degenhardt L & Hall W. Can J Psychiatry 2006;51:556-565.
Potvin S et al. J Psychopharm 2008;22:262-9
Johns A. Br J Psychiatry 2000
Macleod et al. Lancet 2004;363:1579-88,
Arsenault L et al. BMJ 2002;325:1212-3.
Moore THM et al. Lancet 2007;370:319-28.
Can J Psychiatry 2005 Clinical Practice Guidelines

Substance Use in FEP

- Substance use in first-episode psychosis (FEP) prevalence rates ranging from 37% - 74%
  - Cannabis is the most commonly used substance with 86% of patients reported having experimented with cannabis
- Cannabis use negatively impacts outcomes
  - reduced compliance to psychiatric medications
  - nine times increase in exhibition of aggression among males
  - decreased global functioning
  - increased risk of relapse
  - increased severity and chronicity of symptoms

Aydin C, *et al.* Poster presented at CPA 2012. In press.

Can Cannabis Use Cause Schizophrenia?

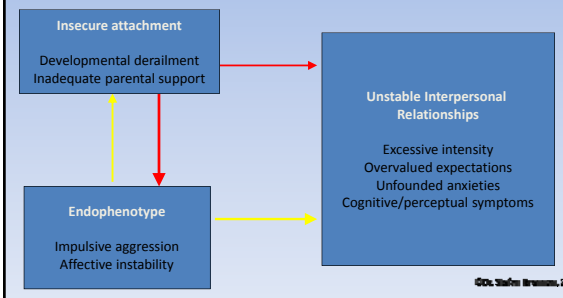
- Con: Later use predicts psychosis > earlier use
- Con: Decreased D2 receptor availability with regular use
- Evidence suggesting cannabis use leads to psychotic illness persisting with abstinence confounded, but users should be advised of increased risk.
- Cannabis use is likely a marker, rather than a cause, of future psychosocial problems / mental illness
- Increased risk in those predisposed/vulnerable

Linszman Dit et al. Arch Gen Psychiatry 1994
Negrete JC et al. Psychological Med 1986
Zammit et al. BMJ 2002;325:1199.
Degenhardt L & Hall W. Can J Psychiatry 2006;51:556-565.
Can J Psychiatry 2005 Clinical Practice Guidelines
Johns A. Br J Psychiatry 2000
Macleod et al. Lancet 2004;363:1579-88,
Arsenault L et al. BMJ 2002;325:1212-3.

Tobacco/Nicotine

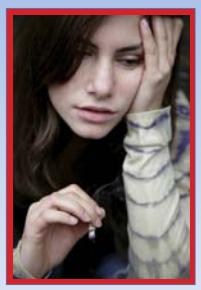
- Smoking is the primary preventable cause of premature death and disability (Canada and world)
- Majority of substance dependent patients die of tobacco related illnesses
- Mental health and SUDs primary consumers – 35-65% prevalence rates
- Acts on nicotinic acetylcholine receptors widely distributed throughout the brain
- Induces CYP450 1A2, metabolized by CYP450 2A6
- Half-life of 2 hours therefore resolution of accumulation in 6-8 hours

Pathogenesis of Borderline Personality Disorder ("Emotional Intensity/Regulation Disorder")



Smoking and Schizophrenia

- Among the mentally ill, smoking prevalence is highest in patients with schizophrenia (~70%-90%)
- Schizophrenic patients smoke at nearly 3 times the rate of the general population
- Smokers with schizophrenia experience increased:
  - Psychiatric symptoms
  - Number of hospitalizations
  - Medication doses
- Cigarette smoking in patients with schizophrenia in some studies has been linked to improvement in specific symptoms and cognitive measures.



Williams et al. Addict Behav. 2004;29:1067-1083.
Dalack et al. Am J Psychiatry. 1998;155:1490-1501; http://www.istockphoto.com/file_closeup/who/character_traits/weakness/2700932_temporary_solution.php?id=2700932. Accessed October 11, 2007.

Four Categories for Borderline Symptoms

- **Poorly regulated emotions**
  - Mood swings and unstable emotions
  - Anxiety
  - Inappropriately intense anger
  - Difficulty controlling anger
  - Chronic feelings of emptiness
- **Impulsivity**
  - Reckless behavior
  - Suicidal behavior and self harm
  - Munchausen's Syndrome and by Proxy
  - Suicide

Schizophrenia And Tobacco

- Mortality: 50% of regular users.
- Leading cause of preventable mortality and morbidity.
- Increased cancer risk in schizophrenia, increased vulnerability for subsequent alcohol use.
- Smoking increases the metabolism of antipsychotic medications by inducing hepatic cytochrome P450 enzymes (especially 1A2); clozapine levels increased by 57.4% upon smoking cessation in one study (Meyer, 2001).
- However, nicotine has been shown to temporarily normalize auditory evoked potential deficits in some schizophrenics (via the alpha 7 subunit of the nicotinic acetylcholine receptor), possibly accounting for the high rate of nicotine dependence (Adler et al, 1998).

Four Categories for Borderline Symptoms

- **Impaired perception or reasoning**
  - Paranoid thinking
  - Dissociative episodes
  - Depersonalization
  - Unstable self image or sense of self
- **Markedly disturbed relationships**
  - Intense and unstable interpersonal relationships
  - Black and white thinking
  - Frantic efforts to avoid real or imagined abandonment

Addictions & Personality Disorders

- Cluster A (Paranoid, Schizoid, Schizotypal)
  - Characterized by social awkwardness and withdrawal
  - Often co-occur with addictions
- Cluster B (Borderline, Narcissistic, Histrionic, Antisocial)
  - Characterized by dramatic, emotional, erratic behaviour
  - Behavioural patterns overlap with addiction
- Cluster C (Obsessive-Compulsive, Avoidant, Dependent)
  - Characterized as anxious and fearful
  - May co-occur with addiction

Personality Disorders And Addictive Disorders III

- Dialectical behaviour therapy (an accepted treatment for chronically suicidal patients with BPD) has been shown to be effective for substance-dependent patients with BPD. In one study where DBT was compared to TAU ("treatment as usual") the DBT group showed greater reduction in drug use, longer retention in treatment, and greater social global gains (Linehan et al, 1999).

Personality Disorders And Addictive Disorders I

- Personality disorders and substance use disorders have a high comorbidity. A study in which 200 patients referred for treatment of personality disorders were assessed for substance use disorders found a lifetime prevalence of 50%; 34.5% for alcohol, 24.5% for cannabis, 9.5% for cocaine, and 8% for polysubstance abuse (Skodol et al, 1999).
- 70% of cocaine dependent individuals were comorbid for at least one Axis II diagnosis (majority with a Cluster B diagnosis) and 44% of alcohol dependent individuals were comorbid for an Axis II diagnosis in one European study (Verheul et al, 1995).

Treatments For Borderline Personality Disorder Are Now Proven To Be Effective And Available In Many Places

- DBT : Dialectical Behavior Therapy (Marsha Linehan, WA) www.behavioraltech.org
- CBT: Cognitive Therapy (Aaron Beck, PA) www.academyofct.org
- SFT: Schema-Focused Therapy (Jeffrey Young, NY) www.schematherapy.com
- Mentalization (Andrew Bateman and Peter Fonagey, UK) www.menninger.edu
- TFP: Transference-focused Psychotherapy (Otto Kernberg, NY) www.borderlinedisorders.com
- STEPPS: Systems Training for Emotional Predictability and Problem Solving (Nancy Blum et al, IO) www.uihealthcare.com/topics/medicaldepartments/psychiatry/stepps/index.html

Personality Disorders And Addictive Disorders II

- The most common personality disorders comorbid with substance abuse are borderline and antisocial personality disorders (Widiger & Trull, 1993); avoidant and dependent personality disorders are also common.
- A diagnosis of antisocial personality disorder is a poor prognostic indicator in the treatment of alcoholism or opiate addiction.
- Substance abusers with borderline personality disorder (BPD) are more disturbed than other substance abusers; the prevalence of current substance use disorders in patients receiving treatment for BPD ranged from 25% (Miller et al, 1994) to 67% (Dulit et al, 1990).

Benzo Basics

- BZs are one of our oldest classes of pharmacotherapeutic agents
- First discovered by Sternbach in 1955
- Reportedly the most frequently prescribed psychotropic medication
- In a recent study of a Canadian general population cohort (12 year follow-up), at each interview the frequency of BZ/sedative-hypnotic use was 2% to 3%

Benzodiazepines – Mechanisms of Action

- Large family of compounds; act as agonists on specific receptors on cell membranes
- Two subtypes of BZ receptors (BZ-1 and BZ-2) are part of the GABA-A receptor
- GABA is a major inhibitor inhibitory neurotransmitter in the brain; stimulating BZ receptors increases the affinity of GABA receptors for GABA, increasing the amount of time the chloride channel stays open
- Benzodiazepines potentiate GABA's inhibitory control over nerve impulse conduction

Physiologic Dependence

- Dose and duration of exposure to BZ determines the development of physiological dependence; continued exposure of a receptor to its agonist results in a reduction in the number of those receptors
- Almost never seen in patients treated for less than 2 weeks
- Occurs in about 50% of patients treated daily for more than 4 months

Benzodiazepines – Mechanisms of Action

- Reinforcing effects of BZ may be mediated via an opioid mechanism as well as GABA receptors
- This may explain the high level of co-occurrence of BZ and opioid dependence
- BZ are the only major class of drug with abuse potential that decrease dopamine levels in the mesolimbic system

Physiologic Dependence

- Short- and long-acting BZs produce comparable severity of withdrawal
- Dependence is reduced with intermittent versus continuous exposure to BZs
- Tolerance to sedative effects usually develops among patients prescribed a stable dose of BZs; however, memory impairment can persist after several years of daily administration

Benzodiazepine Indications

- Anxiety Disorders
- Sleep Disorders
- Seizure Disorders
- Movement Disorders
- Muscle Spasticity
- Anaesthesiology
- Agitation (Psychotic, Mood, Cognitive Disorders)
- Withdrawal (Alcohol & Sedative-Hypnotics, Agitation from Stimulants)

Loss of Control....

- Most patients treated chronically with BZs do not develop compulsive substance use
- A small subset (likely those who have abused other substances) develop compulsive drug-seeking behaviour with loss of control; often there is a positive family history of drug or alcohol dependence
- BZs as the primary substance of abuse in patients admitted for addiction treatment make up < 1% of admissions; most report abuse of alcohol or opioids as well
- Comorbidity: co-occurring mood, anxiety and Cluster C personality disorder in up to 50% of these admissions

What concerns do you have regarding long-term use of benzodiazepines?

- Sedation
- Potential for cognitive impairment / ataxia (especially in the elderly); BZs may have negative effects on cognitive performance and functioning in the community
- Increased risk of falls
- Increased frequency of motor vehicle accidents
- Dependence / withdrawal issues
- Benzodiazepines are generally recommended only for short-term use
- Some patients may require long-term adjunctive treatment

Canadian Psychiatric Association Guidelines. *Can J Psychiatry* 2006.

Targeting High-Risk Patients

- Reduction of physiological dependence
  - use of adequate doses over only a few weeks
  - drug holidays
- Differentiate physiological dependence (common) versus iatrogenic addiction (rare)

Responsible Prescribing

- APA guidelines and NICE guidelines for Panic Disorder and GAD recommend SSRIs and not BZs as the principle choice of medication, along with CBT and self-help approaches
- BZs associated with poorer long-term outcomes, and are not recommended beyond 2 to 4 weeks in GAD

Some General Advice

- BZs with a rapid entry into the CNS and a more potent effect on CNS receptors will have a greater psychoactive effect and therefore a greater risk for dependence
- Higher Risk

  diazepam, lorazepam, alprazolam, triazolam
- Lower Risk

  oxazepam, chlordiazepoxide, clonazepam

Responsible Prescribing

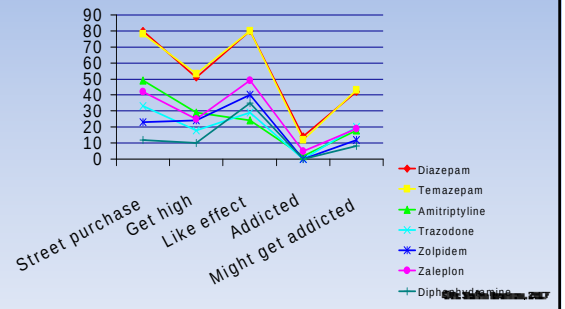
- In the short-term, prescription of high-potency BZs may be helpful to reduce anticipatory anxiety and the severity of panic attacks; non-BZ anti-anxiety medication and CBT often take weeks before there is any beneficial effect
- With comorbid anxiety and depression, SSRIs and SNRIs are first-line medications; in GAD antidepressants should be started earlier as earlier treatment leads to better prognosis. BZs as an adjunct may lead to better speed of response and overall response

What About Benzodiazepines?

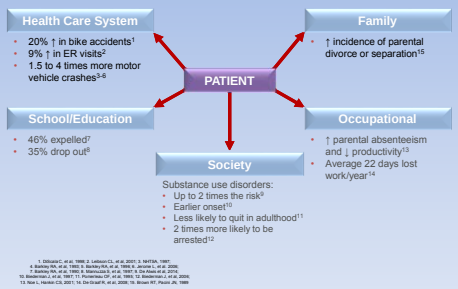
- Safe: Overdoses rarely fatal
- Low addiction potential: BZDs are primary substance of abuse in less than 1% of all admissions
- Look it up: BZD use debated in The Canadian Journal of Psychiatry, Vol 55, No 11, November 2010

el-Guebaly N et al. *Can J Psychiatry* 2010;55(11):709-714.
Substance Abuse and Mental Health Services Administration (SAMHSA).
Treatment Episode Data Set (TEDS): 1995-2005; national admissions to substance abuse treatment services; 2007.

Relative Abuse Liability of Hypnotic Drugs



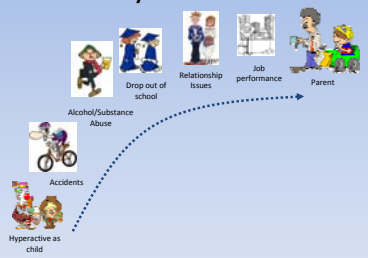
Impact of Untreated and Undertreated ADHD



Attention-Deficit/Hyperactivity Disorder And Addictive Disorders

- 23% (averaged number) of adults and adolescents with a substance use disorder had a comorbid diagnosis of ADHD (Wilens et al, 1994).
- Diagnosis can be difficult, as problems with attention are common during substance intoxication and withdrawal. Symptoms of ADHD are best assessed during a period of abstinence, with questioning about clear childhood symptoms of ADHD (Gallanter, 1999).
- Stimulants are the first-line treatment for ADHD, but in a dual diagnosis population the abuse potential is problematic, particularly with short-acting agents.

Lifecycle of ADHD



Attention-Deficit/Hyperactivity Disorder And Addictive Disorders

- Other options include TCAs and bupropion (treat ADHD, comorbid depression), atomoxetine (Strattera, norepinephrine reuptake inhibitor), guanfacine (Intuniv).
- Behavioural therapies can help with increasing focus and attention. Psychotherapy can be used as part of a psychoeducational approach.

ADHD and Substance Abuse

- Legal products
  - Tobacco[1]:
    - 1.7 times higher risk of smoking
    - Start smoking at early age
  - Coffee and colas[2]
  - Alcohol[1]
- Drugs[3]
  - More frequent cannabis use
  - Cocaine, stimulants
  - Hallucinogens

Treatment with psychostimulants does not increase risk of drug dependence. In fact, treating ADHD could reduce risk of substance abuse.[4]

Misuse and Abuse Liability of ADHD and Medications

- Among individuals with ADHD, what percentage misuse their medication?
  a. 5%
  b. 10%
  c. 20%
  d. 30%

Faraone and Upadhyaya, 2007

Definitions

Therapeutic Use: Clinical indication(s)

Misuse: used other than as prescribed

Diversion: Process of redirection to someone else for whom it was not prescribed

Abuse: used for the purpose of intoxication

***Dependence: the pleasurable effects of a drug and its propensity to produce dependent behavior (psychological and/or physical)**

*** Physical dependence involves increasing tolerance, intense craving, and withdrawal reaction when drug use is stopped.**

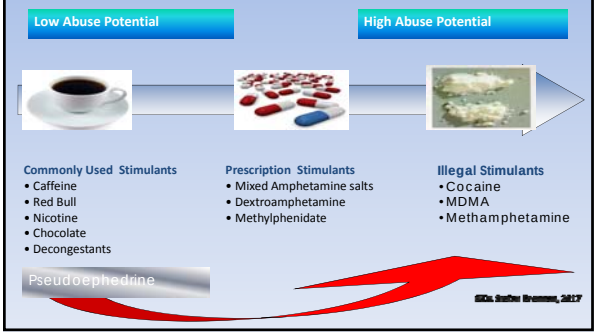
Wilens et al., J Am Acad Child Adolesc Psychiatry 2008; 47(1):21-31.
APA - Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Text Revision (DSM-IV TR), 2000.

Stimulant Abuse and Diversion in Canada

- *Canadian Medical Association Journal*, Oct 2001[1]
- 13,549 randomly selected students in Atlantic Canada in grades 7, 9, 10 and 12 were surveyed in 1998.
  - ~ 15% who were prescribed stimulants have given away some of their pills
  - ~ 7 % had sold some of their pills
- Students with ADHD asked to trade, give, or sell their prescriptions[2]
  - 16-29%

[1]Poulin. CMAJ 2001
[2] Wilens et al JACAP 2008

Stimulant Class



Evolution of Amphetamine Abuse / Misuse

- From 1969 – 1971 the US Government:
  - Markedly reduced the production of Amphetamines by 80%
  - Alerted physicians to possibility of dependence
  - FDA reschedules Amphetamines to Schedule II
  - **The pendulum has swung back to the point that potentially important clinical uses are being avoided by physicians**

* The Substance Abuse – Handbook, Ruiz, 2007

Stimulants

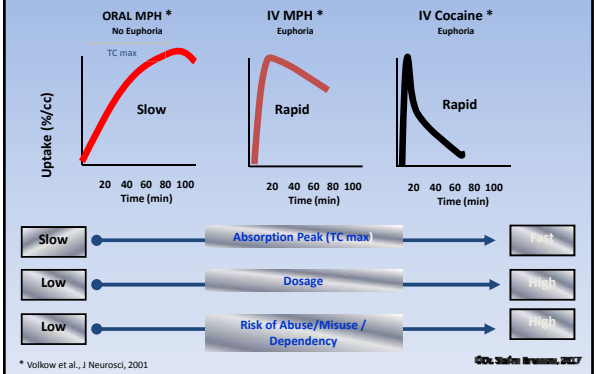
- Cocaine – catecholamine re-uptake inhibitor
  - Crack = cocaine HCl + Na bicarbonate → able to be smoked
  - Free base → IV
  - Cocaine powder → insufflated
- Amphetamines – promote catecholamine release from the vesicle at VMAT2 receptor
  - Methamphetamine → smoked
  - Prescription amphetamines → oral, snorted
- Designer amphetamines (MDMA, MDA, etc)
  - Mix of hallucinogen (serotonin release promoter) and amphetamine
- Direct effect on DA pathway = highest dependence liability

Methamphetamine Use

- Canadian Addiction Survey (2004) – 15 & over:
  - 6.4% used at least once in lifetime
  - Less than 1% reported use in last year
- Peak use during late adolescence/early adulthood (15-30 yrs)
- West >> East
- 1 in 10 who use become dependent
- Use more common in street involved youth, gay men and homeless populations
  - 71% of a convenience sample of street involved youth in Vancouver had used
  - 37% of homeless youth in Toronto used at least once a month
- Few dependent users present for treatment

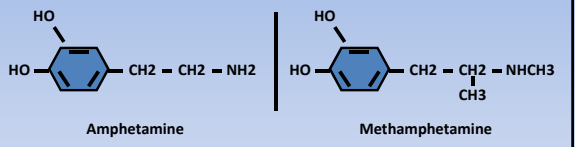
CCSA 2006

Route of Administration is Everything



* Volkow et al., J Neurosci, 2001

How are Prescription Amphetamines Different from Illegal Amphetamines?



Although illegal and prescription amphetamines come from the same class of drugs, they have completely different chemical structures and therefore do not have the same effects on the brain

Westfall & Westfall, 2006

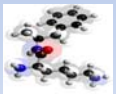
Do all Oral Medications Share the Same Risk?

High-Tech Delivery Systems

Immediate Release Formulations

Low — Risk of Abuse / Dependence — High

Microtrol Delivery System



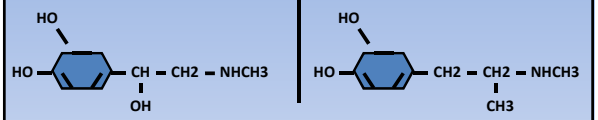
Pro-Drug Technology

Releasing Mechanism lowers the Potential for Psychostimulant Abuse

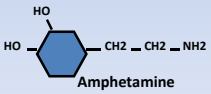
Short acting formulations can be crushed, snorted or injected having rapid effects on the brain that produce a 'high'

Wilens, Gignac et al., J Am Acad Child Adolesc Psychiatry 2006; 45(4):408-414.
Wilens et al., J Am Acad Child Adolesc Psychiatry 2008; 47(1):21-31.

Similar Structures – Very Different Effects



- Methamphetamine has a methyl group substituted on the terminal amine portion of the amphetamine molecule.
- This substitution may be responsible for methamphetamine entering the brain rapidly and producing more CNS effects.

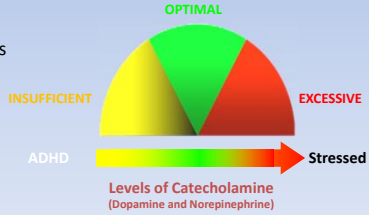


Westfall & Westfall, 2006

Why are Extended-Release Formulations Recommended for Adults with ADHD?

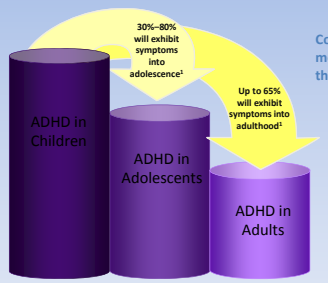
- No stigma of taking medication during the day
- Better adherence[1,2]
- Some research shows better effectiveness[2] and higher rates of remission[1]

Prefrontal cortex requires proper "tuning" of catecholamine levels for optimal function[3]



Hosenbocus S and Chahal R. *Can Acad Child Adolesc Psychiatry.* 2009;18(4):331-39; Ramos-Quiroga JA, et al. *CNS Drugs.* 201
Stahl's essential psychopharmacology (3rd ed). 2008.

ADHD Persists from Childhood to Adulthood



Co-morbidities (sleep, mood and anxiety) fill in the gaps

*According to results from the National Comorbidity Survey Replication in 3199 respondents aged 18 to 44 years.
Dulcan M, et al. *J Am Acad Child Adolesc Psychiatry*. 1997;36(10, suppl):85S-121S; Kessler RC, et al. *Am J Psychiatry*. 2006;163:716-23.

Prevention of Substance Abuse in Youth With ADHD

- Reasons for Discrepant Results
- Risk reduction was greater in studies that followed children into adolescence than into adulthood
  - Older studies used medications that were not routinely used as children transitioned into adulthood
  - Lack of medication coverage in adulthood may have made it difficult to resist using substances
- Children with severe ADHD were more likely to be treated
  - Studies that did not factor in baseline severity were more likely to find no protective effect

Diagnosing ADHD in Adults Is Complex

DSM-IV has child bias for ADHD to begin with
- Symptoms seen in other disorders or in normals

Patients often undiagnosed
- 1. Co-morbidity is caught, (Depression) but ADHD is missed
- 2. ADHD correctly diagnosed but primary co-morbidity is missed (bipolar/anxiety)
- 3. Both are missed and written off to substance abuse/personality disorder

Prejudice of the ADHD diagnosis
- Negative: Physician more than patient
- Positive: patient may be more willing to admit ADHD than mood/anxiety disorder
- Coping strategies can "cover up" the true extent of the impairment more than other illnesses

Prevention of Substance Abuse in Youth With ADHD

- General Conclusions on Pharmacotherapy for ADHD and SUD Risk
- Pharmacotherapy for ADHD
  - Reduces the risk of SUD
  - Does not immunize patients against SUD
- Controlling ADHD and the biological effects of ADHD in the brain can control the incremental effect of substance use

ADHD And Substance Use Disorder

- ADHD and SUD Comorbidity
- Self medication?
- Shared risk factors?
- Potential effect of stimulants?
  - Brain alteration in children with ADHD via reward system
  - Symptom diversion

A Good Reference….

- "Pharmacological and clinical dilemmas of prescribing in co-morbid adult attention-deficit/hyperactivity disorder and addiction"

Perez de los Cobos, Sinol, Perez and Trujols

Br J Clin Pharmacol, 77:2, 337-356 (December 2012)

Case 1 - The Good ADHD Patient

- 40 year-old police officer
- Major Depressive Disorder, Generalized Anxiety Disorder, Post-Traumatic Stress Disorder
- Symptoms improved with Cipralex 20mg QD, Sublinox 10mg QHS, counselling with Dr. Carverhill, RTW planning
- Nephew diagnosed with ADHD/being treated, identifies strongly with his symptoms, wife says "you're just like him"
- Reviews ADHD symptoms checklist in waiting room, endorses inattention, impulsiveness, legs bounce/"vibrating with energy"

Case 2 - The Good ADHD Patient

- Completes Adult ADHD Self-Report Scale (ASRS), scores most symptoms "often" or "very often"
- Completes Conners' Continuous Performance Test II (CPT II), scores 70% Clinical versus 30% Non-Clinical profile; high inattention and impulsivity scores, poor vigilance (reaction times slower and less consistent as test progressed)
- Scores normalize with trial of methylphenidate
- Started on trial of Concerta 36 mg QD, reports significant symptom improvement at home and work, dose titrated up to 72mg QD
- Continues to struggle with PTSD symptoms, but is more functional in work and home settings, though has recently separated from his wife

Adult Self-Report Scale v1.1 (ASRS)- Symptom Checklist

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months.	Never	Rarely	Sometimes	Often	Very Often
1. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					X
2. How often do you have difficulty getting things in order when you have to do a task that requires organization?				X	
3. How often do you have problems remembering appointments or obligations?				X	
4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					X
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?				X	
6. How often do you feel overly active and compelled to do things, like you were driven by a motor?				X	
7. How often do you make careless mistakes when you have to work on a boring or difficult project?					X
8. How often do you have difficulty keeping your attention when you are doing boring or repetitive work?					X
9. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?				X	

Adler L, et al, 2003.

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4. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?		X			X
5. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?	X			X	
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7. How often do you make careless mistakes when you have to work on a boring or difficult project?			X		X
8. How often do you have difficulty keeping your attention when you are doing boring or repetitive work?			X		X
9. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?		X		X	

Adler L, et al, 2003.

Adult Self-Report Scale v1.1 (ASRS)- Symptom Checklist (con't)

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months.	Never	Rarely	Sometimes	Often	Very Often
10. How often do you misplace or have difficulty finding things at home or at work?					X
11. How often are you distracted by activity or noise around you?				X	
12. How often do you leave your seat in meetings or other situations in which you are expected to remain seated?			X		
13 How often do you feel restless or fidgety?				X	
14. How often do you have difficulty unwinding and relaxing when you have time to yourself?			X		
15. How often do you find yourself talking too much when you are in social situations?			X		
16. When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish them themselves?		X			
17. How often do you have difficulty waiting your turn in situations when turn taking is required?				X	
18. How often do you interrupt others when they are busy?			X		

Adler L, et al, 2003.

Adult Self-Report Scale v1.1 (ASRS)- Symptom Checklist (con't)

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X in the box that best describes how you have felt and conducted yourself over the past 6 months.	Never	Rarely	Sometimes	Often	Very Often
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17. How often do you have difficulty waiting your turn in situations when turn taking is required?	X			X	
18. How often do you interrupt others when they are busy?		X	X		

Adler L, et al, 2003.

Case 2 – The Westside Clinic ADHD Patient

- 26 year-old female patient, followed by family physician and psychiatry at Westside Community Clinic, Methadone Assisted Recovery Services (MARS)
- Has 2 daughters (10 and 4) from previous relationships, relationship conflicts and unstable living situation has limited access to her children
- Diagnoses include Borderline Personality Disorder, Post-Traumatic Stress Disorder, Mood Disorder, ADHD, Substance Use Disorder (Opioids – prescribed Methadone, Stimulants, THC, Alcohol)

Case 2 – The Westside Clinic ADHD Patient

- Challenges remain engaging patient in treatment, frequently misses appointments with psychiatry and limited success in starting trauma-focused therapy
- Current treatment includes Methadone, Sertraline QHS, Clonazepam BID, Concerta, previous trials of medications including Aripiprazole and Quetiapine; plan is for limited amounts of medications prescribed at shorter intervals to lessen concerns regarding inappropriate use

Case 2 – The Westside Clinic ADHD Patient

- Limited benefit seen with previous admission to Calder Centre, regular discussions about rehabilitation centre/addictions treatment options
- Ongoing stressors include substance use issues, family of origin issues/ongoing stressors in relationships with family members, previous sexual assault, skills deficits in coping with life stressors

Resources

- Canadian ADHD Resource Alliance (CADDRA)
  www.caddra.ca
- Learning Disabilities Association of Saskatchewan (LDAS)
  www.ldas.org

•ADHD: Not Just For Kids, March 2017

http://www.cbc.ca/natureofthings/episodes/adhd-not-just-for-kids

Case 2 – The Westside Clinic ADHD Patient

- Patient did have a recent period of stability, attending follow-up appointments with family physician, who manages medications
- Has had investigations regarding dyspareunia (small fibroid on ultrasound), recent work-up for Hepatitis C

Marijuana and Legalization

- Currently a very controversial topic in Canada
- New government created provincial-federal task force to lead consultations on the subject
- Recent poll (February 2016) found a majority of Canadians supporting or somewhat supporting the legalization of marijuana (Globe and Mail/Nanos Research)
- On 420 (2016), Health Minister Jane Philpott formally announced the Liberal government's plans to introduce legislation to legalize and regulate marijuana in spring 2017

CAMH – Ten Basic Principles To Guide Regulation Of Legal Cannabis Use

- 1) Establish a government monopoly on sales. Control board entities with a social responsibility mandate provide an effective means of controlling consumption and reducing harm.
- 2) Set a minimum age for cannabis purchase and consumption. Sales or supply of cannabis products to underage individuals should be penalized
- 3) Limit availability. Place caps on retail density and limits on hours of sale
- 4) Curb demand through pricing. Pricing policy should curb demand for cannabis while minimizing the opportunity for continuation of lucrative black markets. It should also encourage use of lower-harm products over higher-harm products
- 5) Curtail higher-risk products and formulations. This would include higher-potency formulations and products designed to appeal to youth

http://www.camh.ca/en/hospital/about_camh/influencing_public_policy/documents/camhcannabispolicyframework.pdf

Marijuana and Mental Health

- Continues to be an active topic of debate in the literature, particularly youth/adolescents' use of THC
- Recent studies have attempted to look at associations between chronic adolescent marijuana use and later physical/mental health problems

https://www.apa.org/pubs/journals/releases/adb-adb0000103.pdf

- New analysis suggests marijuana use may be associated with an increased risk for developing alcohol and drug disorders, but not mood or anxiety disorders

http://archpsyc.jamanetwork.com/article.aspx?articleid=2491944

- Recent Lancet editorial addresses limitations in the literature; the referral to cannabis as though it were one type of drug is unhelpful and misleading, and that we need to be careful in the assumptions that we make about how far scientific knowledge has advanced in exploring the links between cannabis and mental health (particularly psychosis)

http://www.thelancet.com/pdfs/journals/lanpsy/PIIS2215-0366(16)00086-9.pdf

CAMH – Ten Basic Principles To Guide Regulation Of Legal Cannabis Use

- 6) Prohibit marketing, advertising, and sponsorship. Products should be sold in plain packaging with warnings about risks of use
- 7) Clearly display product information. In particular, products should be tested and labelled for THC and CBD (cannabidiol) content
- 8) Develop a comprehensive framework to address and prevent cannabis-impaired driving. Such a framework should include prevention, education, and enforcement
- 9) Enhance access to treatment and expand treatment options. Include a spectrum of options from brief interventions for at-risk users to more intensive interventions
- 10) Invest in education and prevention. Both general (e.g. to promote lower-risk cannabis use guidelines) and targeted (e.g. to raise awareness of the risks to specific groups, such as adolescents or people with a personal or family history of mental illness) initiatives are needed

Marijuana and Legalization

- Federal marijuana task force report: December 2016
- Recommended that sales be limited to those 18 and older, with a personal possession limit of 30 grams. Provinces to have significant flexibility regarding how cannabis products are regulated and marketed
- Liberal government announced legislation in April 13, 2017 (Bill C-45, the Cannabis Act) that will legalize marijuana in Canada by July 2018
- https://www.canada.ca/en/services/policing/justice/legalization-regulation-marijuana.html

Not All Agree….

- Dr. Harold Kalant (U of T professor emeritus of pharmacology and toxicology) has critiqued the CAMH policy framework, questioning whether the prohibition of marijuana has actually failed, whether it imposes serious harms on Canadians that would be removed by legalization, and whether legalization would eliminate the illicit market in the drug

Case 3 – Westside Clinic Success Story!

- 57 year-old male patient, followed by family physician and psychiatry at Westside Community Clinic, attends groups at McKerracher Centre
- Previous hospitalization for treatment of concurrent disorders (mood disorder and alcohol use disorder), past symptoms have included significant sleep disruption
- Over 1200 days sobriety as of most recent follow-up appointment in April, 2017

Case 3 – Westside Clinic Success Story!

- Diagnoses include Bipolar II Disorder, Alcohol Use Disorder (in Sustained Remission)
- Has attended AA/12 Step meetings previously, though no longer finds them as helpful; actively maintains sobriety and attends groups at McKerracher Centre once/twice per week

Case 4 – Problems In The Community

- Patient only seen intermittently as part of concurrent disorders follow-up, is able to maintain abstinence for greater than one year, has a trial of methadone, psychiatrist maintains medication at a dose of Olanzapine 5mg QHS
- Patient becomes noncompliant with medications, substance use resumes, admitted in January 2012 with prominent delusions, had called police stating that his father had unregistered firearms in the home
- Hospitalized for one month, medications switched to Seroquel XR 600mg Qsupper, Flupenthixol Decanoate 60mg IM Q2weeks

Case 3 – Westside Clinic Success Story!

- Completed Peer Support Training Program through Mental Health and Addiction Services; has begun to provide peer support services on a weekly basis
- Maintained on stable doses of medication, Quetiapine XR and Bupropion XL to manage mood symptoms and sleep issues
- Attends regular follow-up appointments with family physician and psychiatry through Westside Community Clinic, as well as local hard rock/metal concerts

Case 4 – Assuming Care

- Writer assumes primary care with patient as previous psychiatrist moves away; by May 2012 is unhappy with current treatment, sleeping up to 12 hours per day, is smoking more tobacco, and has discontinued Seroquel XR despite dosage being decreased
- Working with CMHN, Invega Sustenna initiated at 150mg then continued on 100mg IM q4weeks

Case 4 – Substances Complicate The Diagnosis

- 36 year-old male, initially seen in consultation in 2009 for his primary treating psychiatrist when he was an inpatient to address concurrent disorder concerns, has had previous hospitalizations
- Symptoms include prominent mood and anxiety symptoms, delusions including beliefs that his family wishes to harm his sons and that gangs wish to harm him
- Diagnosis becomes that of Schizoaffective Disorder (Bipolar Subtype), in the context of significant Substance Use Disorder (preferred substances included crack cocaine, methamphetamine, opioids, and cannabis) and Antisocial Personality Traits (weapons charge, drug charges, history of violent behaviour)

Case 4 – Moving On With Life

- Reports continuing sedation with medication, and dosage is decreased to 75mg Q4weeks
- Period of stability, is more involved in the care of his two sons, driving record is clean, discussions about registering for Life Skills Program through CMHA
- In February 2014, reports he experiences no ongoing psychotic symptoms (collateral history from father confirms this), no substance use (provides random UDS), but experiencing ongoing sedation and periods of low mood/depression
- Started on Abilify (Aripiprazole), by summer 2014 dose has been titrated up to 10mg QD and Invega Sustenna decreased to 50mg IM Q4weeks at patient's request

Case 4 – Maintenance?

- By late 2014/early 2015, collateral history from father and CMHN is of increasing irritability and frustration, increasing paranoia and delusions
- Patient reports that he takes Abilify "most days", though concerns raised about noncompliance; despite his reservations about medication dosage Invega Sustenna is increased to 100mg IM Q4weeks (previous stable dose)
- As of summer 2015, continues to take prescribed medications and denies substance use; ongoing discussions about medication dosage and possibility of applying to Saskatoon Housing Coalition to consider independent living for him
- Becomes noncompliant with medications in fall 2015, relapses to crystal methamphetamine use, suffers from psychotic symptoms and is charged with assaulting his father; has now restarted medication and seeking addictions treatment
- Legal charges resolved, currently abstaining from substances, but continues to rebuild relationships with family

Questions?