Best Practices: Concurrent Disorders

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Concurrent Disorder Lead

VCH Acute and Tertiary

BOOST COLLABERATION

LEARNING SESSION -2

15th March 2018 at 12pm

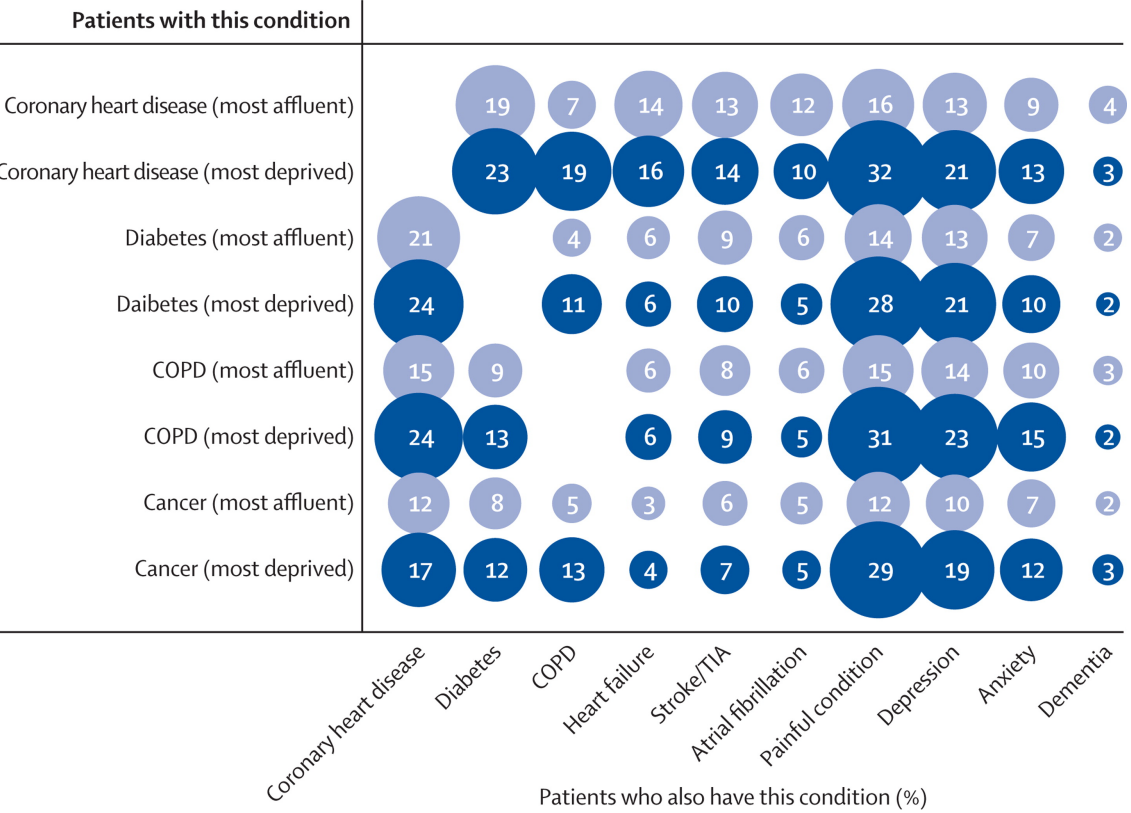
Declaration of interest

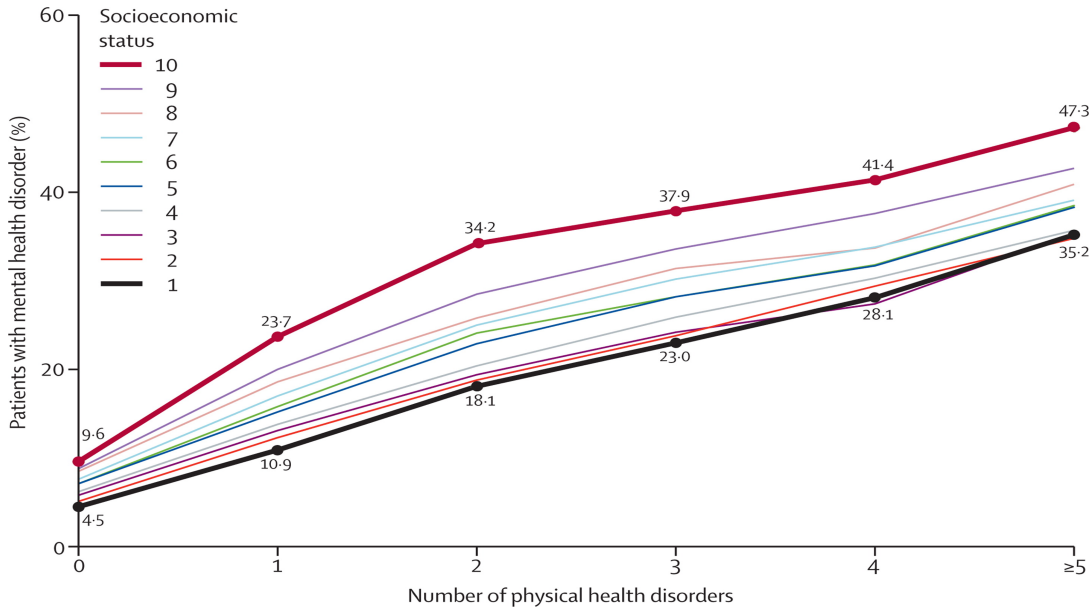
- None

Overview

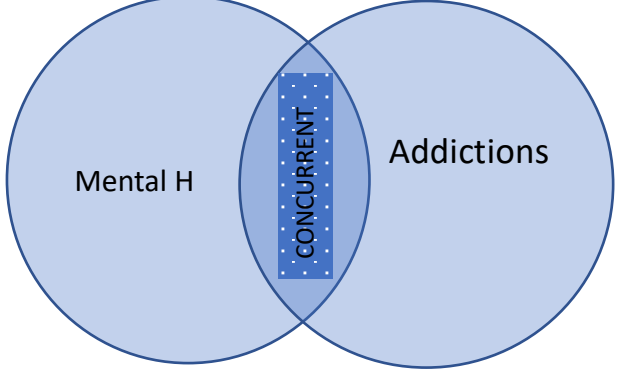
1. Background
2. Models of care for addiction & concurrent disorder.
3. Practical Tips
4. Case- Examples (Anxiety & AUD)
5. Depression, PTSD, ADHD, HIV, Benzodizepine
6. Best practice guidelines links & References

MULTI-MORBIDITY





Barnett et al, 2012, Volume 380, Issue 9836 *The Lancet*



1. Addiction or Withdrawal facility (60 to 80%, 1 in 3 have severe depression)

Polysubstance user (Opioids & **Cocaine**) - Depression, anxiety

2. Psychiatrist - private clinic/Outpatient or Academic setting

(25 – 50% of Mental health population have drug or alcohol problems)

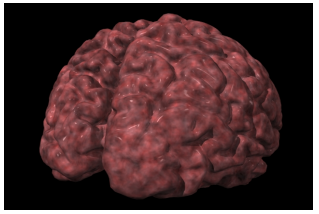
3. Psychiatric in-patient or Consults service (More than 50%):

Schizophrenia with Crystal Meth or Crystal meth with unspecified Psychosis.

Alcohol withdrawals with PTSD, Borderline personality, Eating disorder, Self harming behaviors.

Alcohol, Cocaine & Bipolar

Definitions



Mental Illness/Psychiatric Disorder

a. WHO, 2016: Characterized by some combination of abnormal **thoughts, emotions, behaviour** and relationships with others.

b. DSM – 5 (APA, 2013): Behavioral or psychological syndrome or pattern that occurs in an individual

the consequences of which are clinically significant distress or disability.

Reflects an underlying **Psychobiological dysfunction**

Addictions (ASAM)

- **Addiction** is a primary,

Chronic disease of

Brain reward

Motivation

Memory and

Related circuitry.

Dysfunction in these circuits leads to characteristic ***biological, psychological, social and spiritual*** manifestations.

This is reflected in an **individual pathologically pursuing reward and/or relief by substance use and other behaviors**.

Concurrent Disorders: “Mental illness and a Co- morbid substance abuse problem”

Extent of the problem

CONCURRENT DISORDERS

Specialist Settings

Drug and Alcohol services

Mental Health	Drug services 75%	Alcohol 85%
Affective and Anxiety Disorders	68%	81%
Severe Depression	**27%**	**34%**
Mild Depression	40%	47%
Severe anxiety	**19%**	**32%**
Personality Disorder	*37%*	*53%*
Bipolar	1%	5%
Schizophrenia	3%	3%
Non Specific Psychosis	5%	11%

Community Mental Health Teams

44%	Any drug	Dependent use
Alcohol	50%	25% (10%Severe)
Any Drug	30%	17% (4%-Poly)
Cannabis	25%	13%
Crack Cocaine Amphet	6% 3.2%	4%
Sedatives	7%	2%
Heroin	4%	2%

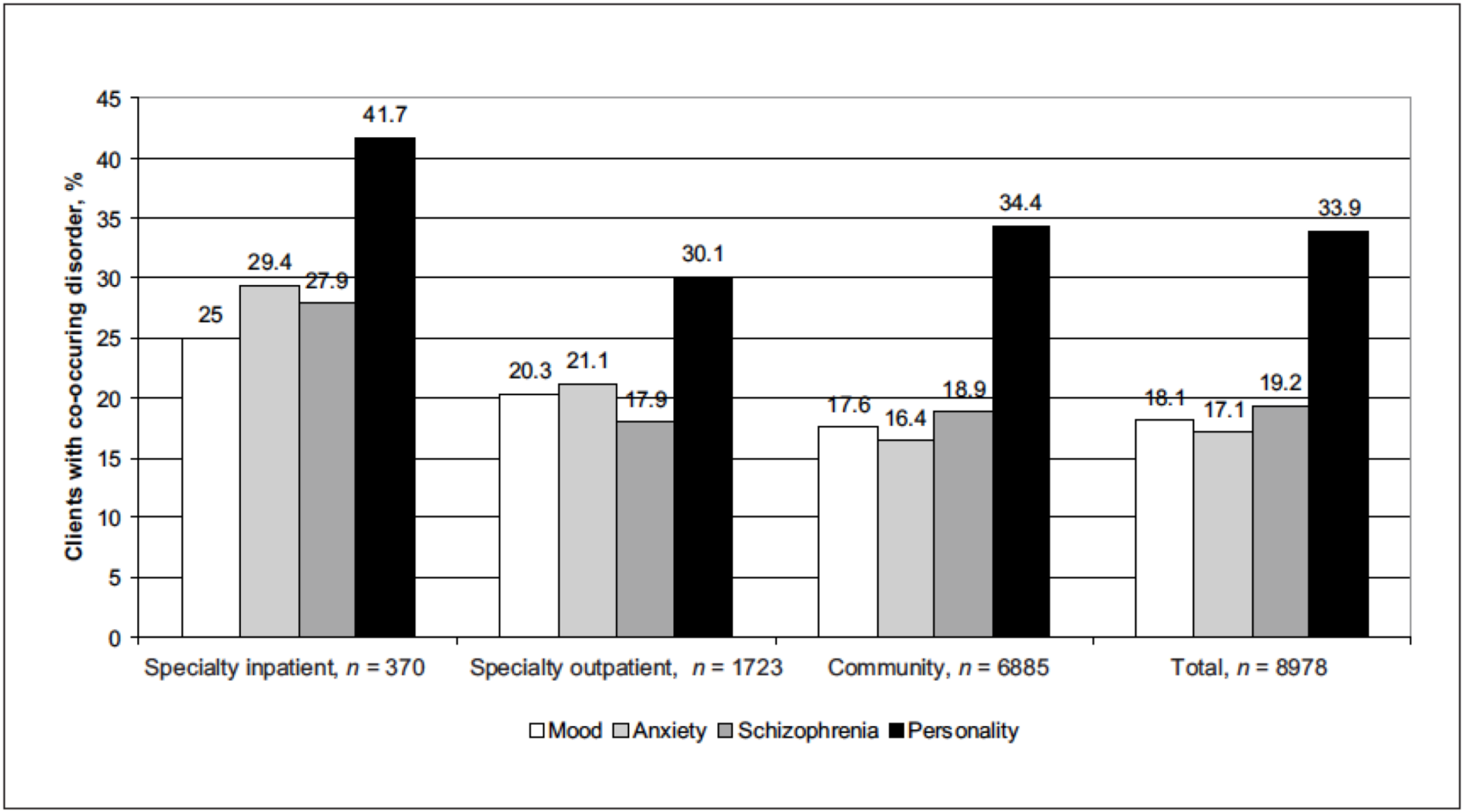
Weaver et al, 2003: BJP 183, 304-313

Prevalence

- USA: 17.5% of adults with a mental illness had a co-occurring substance use disorder *(National Survey on Drug Use and Health, 2012)*
- **Canadian: 40-60% of adults with a severe and persistent mental illness experiencing a substance use disorder in their lifetime *(Health Canada, 2002)***
- UK- National House hold survey *(Farrel et al, 2001)*

  Psychiatric disorders: 30%(Alcohol dependency), 45% (Drug dependency),12% Non drug population.

Figure 1 Prevalence of co-occurring substance use disorder within diagnostic groupings by level of care



Rush et al, Can J Psychiatry 2008

Reasons for increase?

- Rapid increase in the number of people in the community with concurrent disorders over the last 20-30 years (Ryglewicz & Pepper, 1996)

a. **Increase** availability of Drugs 1960s onwards.

b. **Alcoholism** was not seen as a problem &

c. **Drug addiction** was seen as confined to a small segment of society and viewed largely in a criminal context.

a. **Major Mental Health**: De-institutionalization (60's to 80's) –

(E.g. River-view was closed)

Why do Substance Use & Mental Health Co-occur

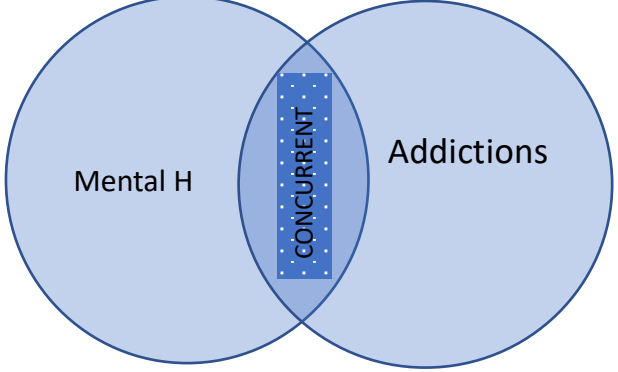
- ***Self-Medication:*** *Means to alleviate mental health symptoms* (1 in 4 have mental health issues & 2/3 never seek treatment, ***WHO,2017***)
- ***Causal effects:*** *Substance abuse increase vulnerability to mental illness*
- ***Double Trouble:*** *Overlap of Common or Correlated Causes or Risk factor:*

a. **Genetic & Neuroendocrine factors**

b. **Psychological:** Trauma, Feeling of alienation (e.g., loss of hope and feeling that there is nothing else to loose)

c. **Social & Stigma:** Family dysfunction, unstable living situation (e.g., poverty, unemployment)

Untreated



Morbidity:
Health (Physical, mental)
& Substance use

Mortality: Suicide (Alcohol disorder 7%
vs Mood 6%)

UNTREATED

Cost Of Health Care

Untreated Co-morbid groups cost substantially more:

Effects of Comorbid dysthymia on substance use service.

SUD + Dysthymia = 4.7 times SUD*Westermeyer et al (1998)*

SOCIAL:
- CRIME
- HOMELESSNESS AND HOUSING INSTABILITY

DISABILITY:
43% Mental health

PERSONAL:
- INCREASE INTERPERSONAL CONFLICT
- FINANCIAL

Andrews, Sanderson & Beard, 1998
Drake et al., 2001

Barriers & Challenges…..

1. **Service delivery:** Agencies, planners and policy makers have been stuck in the ***single-problem*** **mode of thinking** because of the long established barriers between the treatment systems for mental health and substance abuse.

2. **Historical: 'Two Silos'** Separate training and development in the two fields, which became entrenched in separate funding, administrative and policy structures.

3. **Provider :** *Perceived* complexity, uncertainty, and level of difficulty associated with a more integrated approach.

Pillar to post: Falls into the trap of emphasizing the primacy of one diagnosis over another in the acute situation, potentially perpetuating the passing of complex patients from 'pillar to post'.

4. Stigma: "Double Trouble"

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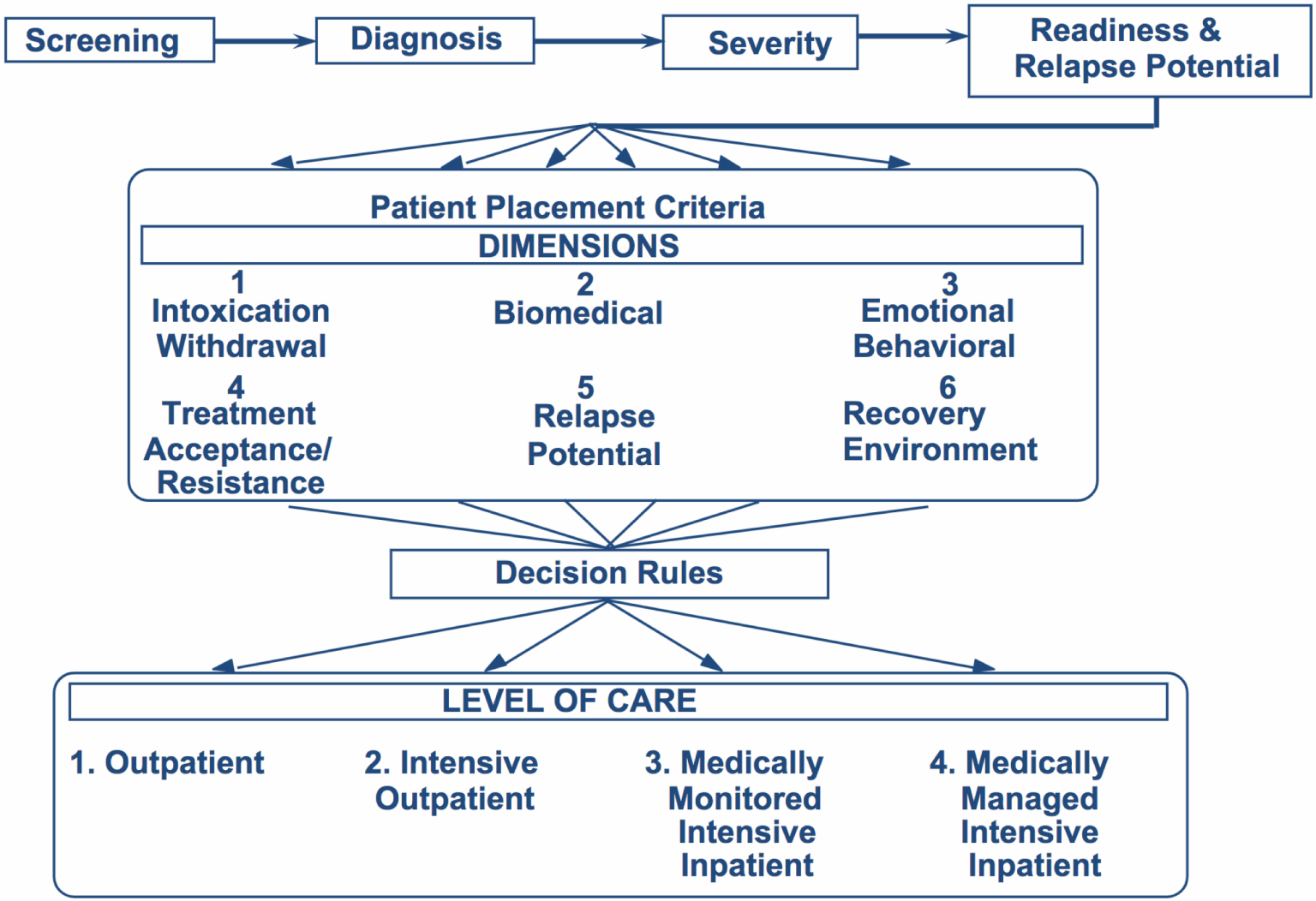
Issues

- Prescribing practices in complex cases
- Effectiveness of Medications & Poly-pharmacy
- Drug interaction in Poly-pharmacy & Substance Use Disorder
- Risk of Accidental OD
- Assumptions: Treatment of the primary disorder may resolve the secondary disorder, which is not considered to require specific treatment.
- Possible toxic interaction between the prescribed medication and the substances that are Misused

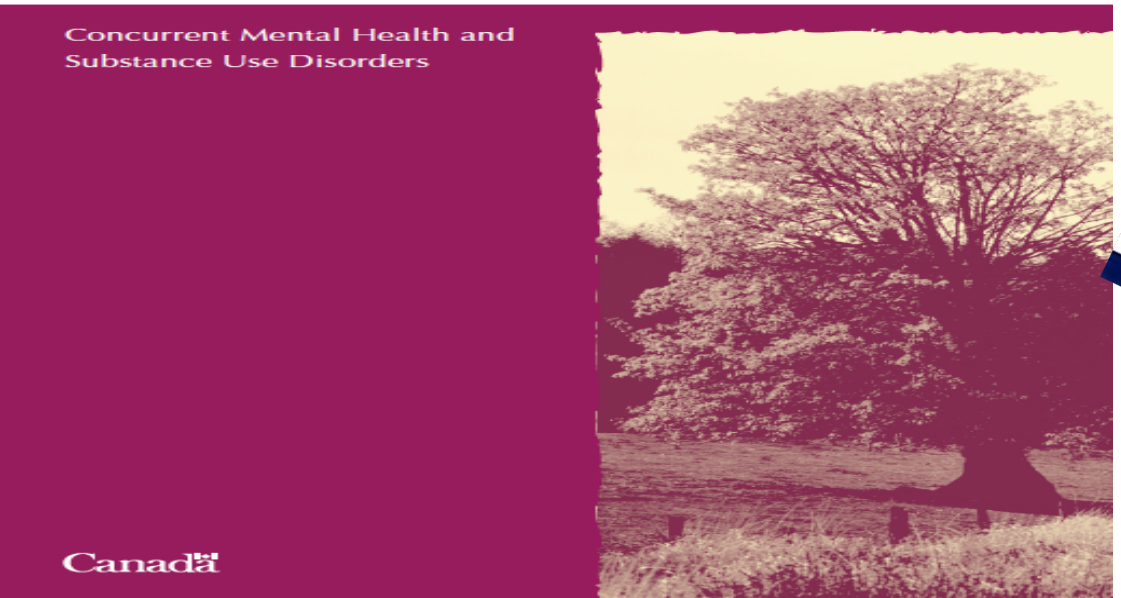
Models of Care for Concurrent Disorders

ASAM Patient Placement Criteria



Concurrent Disorders: Evidence Based Updates

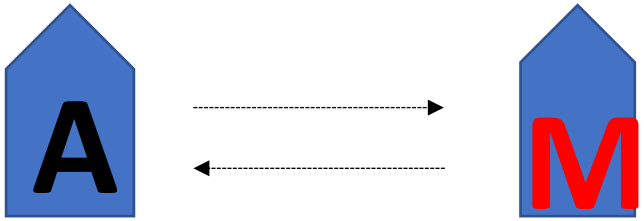
National Institute for Health and Clinical Excellence



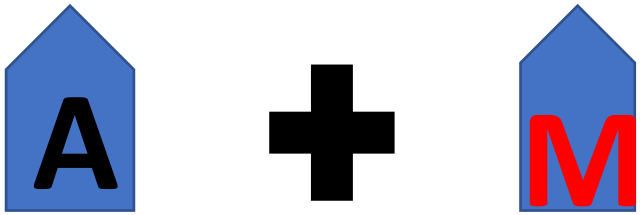
MODELS OF CARE:

ADDICTION (A) + MENTAL HEALTH (M)

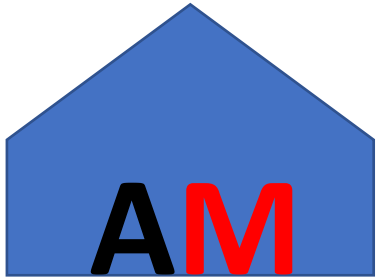
1. SEQUENTIAL:



2. PARELLEL:



3. INTEGRATED:

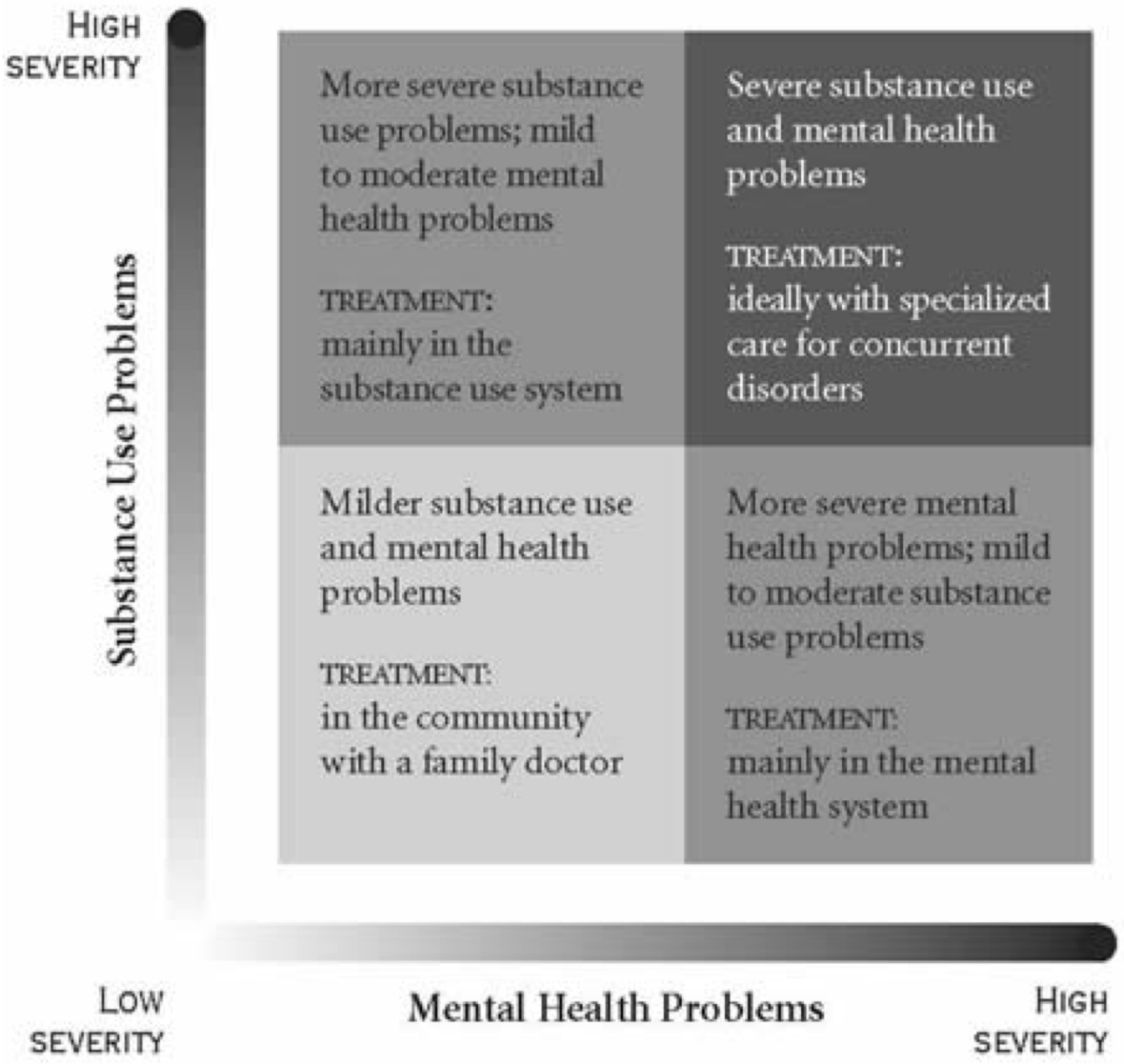


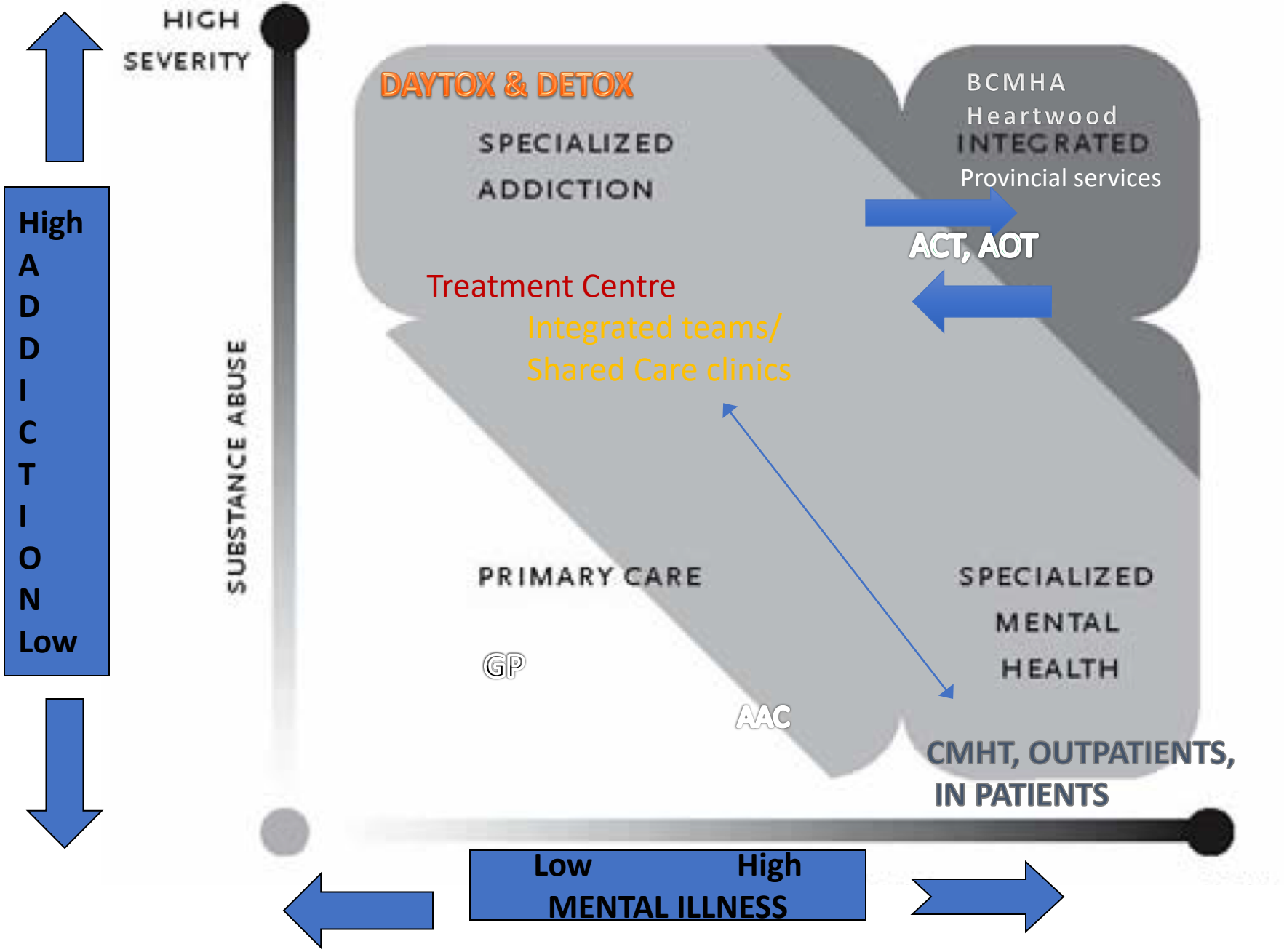
A – ADDICTIONS

M – MENTAL HEALTH

Parallel Treatment

Thanks for the slide Enrico
(Dual Diagnosis Psychiatrist Melbourne)


HIGH SEVERITY
Substance Use Problems
More severe substance use problems; mild to moderate mental health problems
TREATMENT: mainly in the substance use system
Severe substance use and mental health problems
TREATMENT: ideally with specialized care for concurrent disorders
Milder substance use and mental health problems
TREATMENT: in the community with a family doctor
More severe mental health problems; mild to moderate substance use problems
TREATMENT: mainly in the mental health system
LOW SEVERITY
Mental Health Problems
HIGH SEVERITY


HIGH SEVERITY
High ADDICTION Low
SUBSTANCE ABUSE
DAYTOX & DETOX
SPECIALIZED ADDICTION
BCMHA Heartwood INTEGRATED Provincial services
ACT, AOT
Treatment Centre
Integrated teams/ Shared Care clinics
PRIMARY CARE
GP
AAC
SPECIALIZED MENTAL HEALTH
CMHT, OUTPATIENTS, IN PATIENTS
Low High
MENTAL ILLNESS

Integrated Model/Approach

Concurrent Disorder

CASE MANAGEMENT

Assertive Care to Retain Patent

CLOSE MONITORING

UDS, Medication Supervision

SUBSTANCE USE TREATMENT

PHARMACOTHERAPHY

INTEGRATED APPROACH

HOUSING

Supported Independent

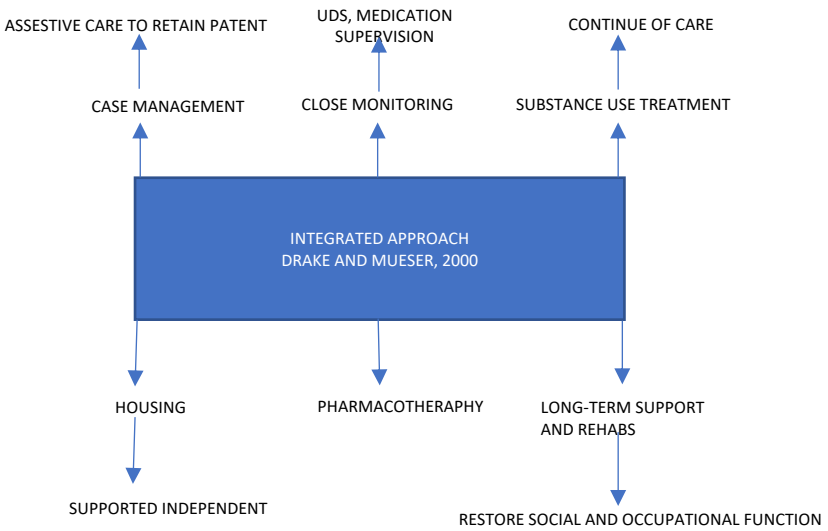
CONTINUE OF CARE

LONG-TERM SUPPORT AND REHABS

Restore Social And Occupational Function

Drake And Mueser, 2000

INTEGRATED CARE



R RESPONSIVE AND FLEXIBLE

E ENGAGING

A ACCESS

C CONTINUOUS CARE

T TRAINING

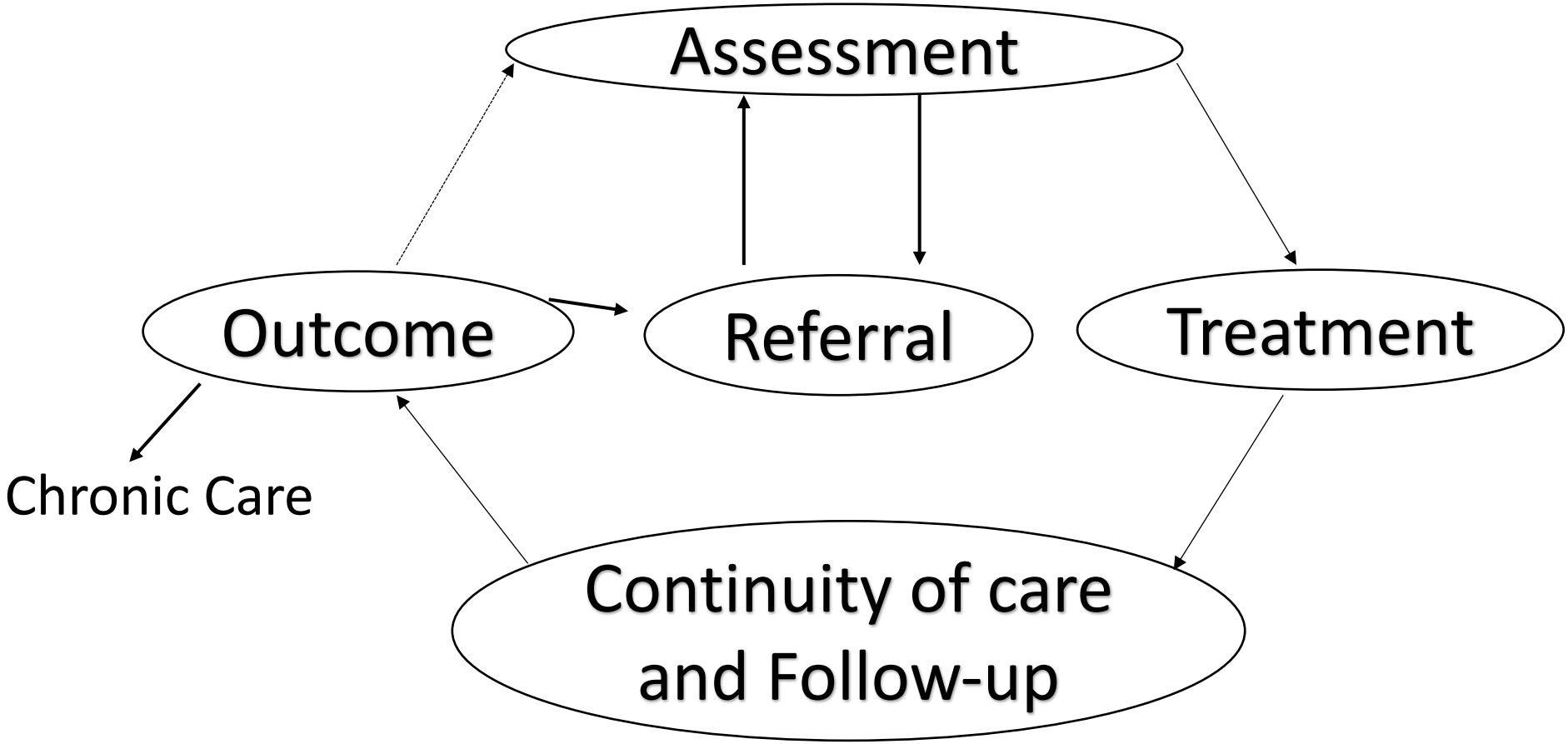
Summary: Models of Care

- **Access** to relevant services (crisis, support, housing, after-care, therapeutic and legal services)
- Responsive and **flexible approaches** (assessment, engagement, retention, managing chaos and crisis, individual responses)
- **Continuous care** and management (monitoring, liaison, involvement of carers, risk assessment and management)
- **Adequately trained staff** (access to mental health trained staff)

Practical Tips

Concurrent Disorders

TYPICAL PATIENT JOURNEY



12 Steps to Assessing a Complex Client

1. Engage the Client
2. Identify and Contact Collaterals (Family, Friends, Other Providers) To Gather Additional Information
3. Screen for and Detect Co-Occurring Disorders
4. Determine Quadrant and Locus of Responsibility
5. Determine Level of Care
6. Determine Diagnosis
7. Determine Disability and Functional Impairment
8. Identify Strengths and Supports
9. Identify Cultural and Linguistic Needs and Supports
10. Identify Problem Domains
11. Determine Stage of Change
12. Plan Treatment/ MDT approach (Physician, Detox Coordinator, SW, Community)

(TIP) Series, No. 42 (2005, SAMHSA/CSAT)

Assessment

1. Mental Health

Axis 1

Axis 2

2. SUD

Dependency

Intoxication

SUD induced Psychiatric

Screening tools

1. Is there a co-occuring disorder 2. Symptom onset
3.Persistence of symptoms with 1months abstinence
4. In Excess of what is expected of withdrawal

3. Functional assessment

Relationship

Housing, work, Leisure

Crime

Stage of Change

4. Risk Assessment

DSH, Suicide

Aggression

Self Neglect, **Accidental OD**

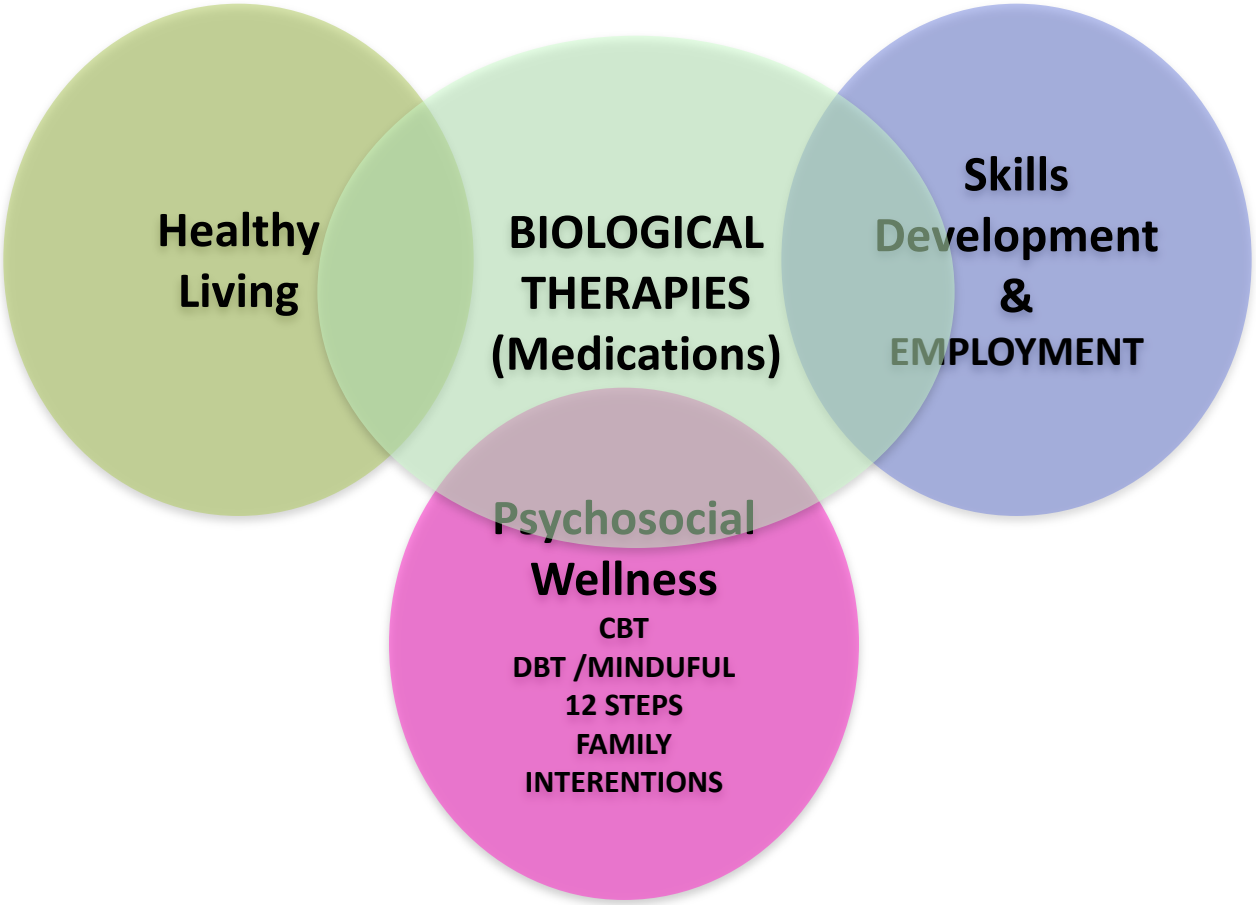
Blood Bourne Virus

RATING SCALES:

a. **Intake** - **Objective** – Brief Psychotic Rating scale **(BPRS) or HoNOS** (Health of Nations Outcome Scales)
Subjective - PHQ-9, GAD-7, RISK RATING SCALES

b. **Follow up** (4 weeks) – Repeat PHQ-9, GAD-7, ADHD Self-Report Scale (ASRS-v1.1)
Post traumatic Stress Disorder – PCL (C)
MMSE/MoCA

Domains of Care



Psychotropic drug interactions

Potential for Drug-Drug Interaction	Antidepressants	Atypical Antipsychotics
Minimal or low potential	• Citalopram • Desvenlafaxine • Escitalopram • Mirtazapine • Venlafaxine	• Paliperidone
Moderate potential	• Agomelatine (1A2 substrate[a]) • Bupropion (2D6 inhibitor) • Duloxetine (2D6 inhibitor; • 1A2 substrate[a]) • Levomilnacipran (3A4 substrate) • Sertraline (2D6 inhibitor) • Vilazodone (3A4 substrate) • Vortioxetine (2D6 substrate)	• Aripiprazole (2D6, 3A4 substrate) • Olanzapine (1A2 substrate[b]) • Risperidone (2D6, 3A4 substrate)
Higher potential	• Fluoxetine (2D6, 2C19 inhibitor) • Fluvoxamine (1A2, 2C19, 3A4 inhibitor) • Moclobemide (MAO inhibitor precautions[c]) • Paroxetine (2D6 inhibitor) • Selegiline (MAO inhibitor precautions[c])	• Clozapine (3A4, 1A2 substrate) • Lurasidone (3A4 substrate) • Quetiapine (3A4 substrate)

Can J Psychiatry. 2016 Sep; 61(9): 540–560

Maudsley, 2011	Cannabis	Heroin/methadone	Cocaine Amphetamines	Alcohol
General considerations	Usually smoked in cigarettes (induces CYP1A2 Can be sedative Dose related to tachycardia	Can produce sedation/ respiratory depression	sedative in higher doses) Arrhythmias possible Cerebra/cardiac ischaemia with cocaine Hyperthermia/dehydration with Ecstasy	Sedative Liver damage possible
Antidepressants	Tachycardia has been reported (monitor pulse and take care with TCA's)	Avoid very sedative antidepressants Some SSRI's can increase methadone plasma levels (Citalopram is SSRI of choice)	Avoid TCA's (arrhythmias) Various antidepressants have been used in 'crack' withdrawal and may lower the 'high' experienced with stimulantsor	Avoid very sedative anti depressants Avoid anti that are toxic in OD Impaired psychomotor skills (*not* SSRI's)
Benzodiazepines	Monitor level of sedation	Over sedation (and respiratory depression possible) Concomitant use can led to accidental overdose Possible pharmacokinetic interaction (increased methadone levels)	Over sedation (if high doses of cocaine have been taken) Widely used after cocaine intoxication	Over sedation (and respiratory depression) possible Future misuse possible Widely used in alcohol detoxification
Atypicals	Risk of additive sedation Cannabis can reduce serum levels of Olanzapine via induction of CYP1A2	Risk of additive sedation Case report of methadone withdrawal being precipitated by risperidone	Risperidone may reduce the euphoric effects of cocaine, but does not reduce cocaine use	Increased risk of hypotension with olanzapine (and possibly other ß-blockers)
Older Antipsychotics	Antipsychotics reduce the psychotropic effects of almost all drugs by blocking dopamine receptors (dopamine is the neurotransmitter responsible for 'reward') Patients prescribed antipsychotics may increase their consumption of illicit substances to compensate Patients who have taken ecstasy may be more prone to EPSE's Cardiotoxic or very sedative antipsychotics are best avoided, at least initially.			

Case Examples

Depression and Substance Use

Depression and Opioid Use Disorder

- 50% Opioids addicts meet the criteria for major depression (- Chronic pain conditions)
- Often other substances such as alcohol and cocaine contribute to their depressed mood.
- Perform equally well as non-depressed[1]
- MMT: Higher dose, Enrollment and Stabilization[2] vs Suboxone
- Direct effect of opioid agonism on the reward pathway as well as secondary consequences on their chaotic lifestyle
- Depression will persist 10-20%[1]

1 Ngo et al., 2011; Nunes et al., 2004; 2 Tenore, 2008;

Depression and AUD

- A comprehensive assessment is essential to determine how

  alcohol and depression are linked
- Antidepressants improves mood in those with a significant depressive disorder
- Consider using an antidepressant with mixed serotonergic/noradrenergic pharmacology
- Use of alcohol relapse prevention such as naltrexone or acamprosate

The stepped-care model

Focus of the intervention	Nature of the intervention
STEP 4: Severe and complex[1] depression; risk to life; severe self-neglect	Medication, high-intensity psychological interventions, electroconvulsive therapy, crisis service, combined treatments, multiprofessional and inpatient care
STEP 3: Persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions; moderate and severe depression	Medication, high-intensity psychological interventions, combined treatments, collaborative care[2], and referral for further assessment and interventions
STEP 2: Persistent subthreshold depressive symptoms; mild to moderate depression	Low-intensity psychosocial interventions, psychological interventions, medication and referral for further assessment and interventions
STEP 1: All known and suspected presentations of depression	Assessment, support, psycho-education, active monitoring and referral for further assessment and interventions

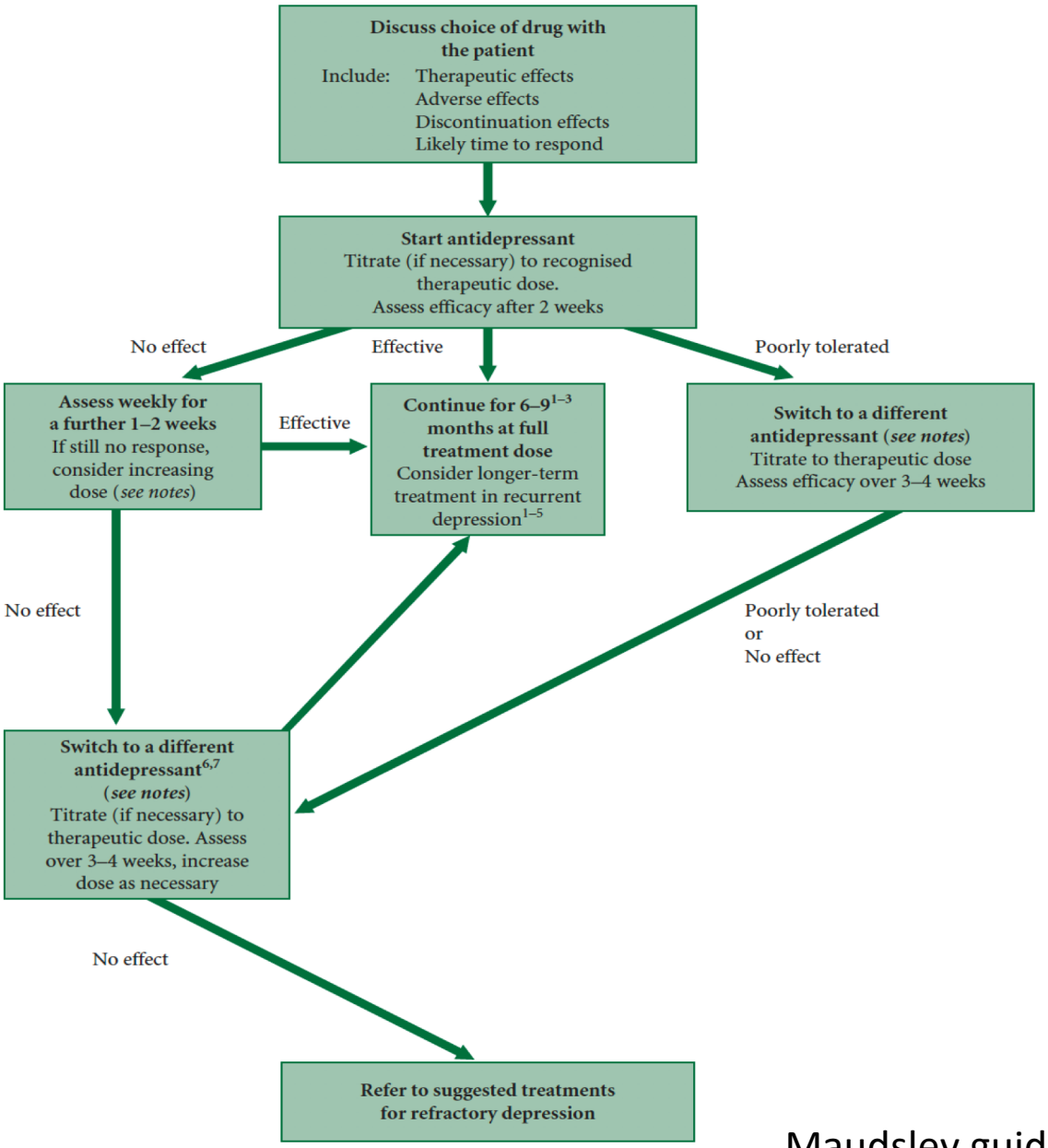
NICE,2009

Pharmacotherapy

	SSRI	Others& Mixed Pharmacology(TC)	Substance Outcome
Depressed Alcoholic	Fluoxetine Sertraline OR= 1.85[1]	Imipramine Desipramine OR=4.5[1] **Mirtazepine** improved mood, anxiety and Cravings	***SSRI OR=0.93[1]*** Others OR=1.99
Depressed Opioid user	Escitalopram Sertraline	Imipramine Doxepine OR 3.65	

1. Torrens et al, 2005; 2. Brook et al., 2008; 3. Petrakis et al., 2012; 4. Malec et al. 1996

Drug treatment of depression



Maudsley guidelines, 2012

ANXIETY AND SUBSTANCE USE

Anxiety as a feature of Substance Misuse (Maudsley guidelines, 2012)

Substance	Use	Intoxication	Withdrawal	Long-term effects
Alcohol	To overcome anxiety (Social)		Pronounced anxiety	Panic disorder and GAD can emerge from misuse
Stimulants (Cocaine, Amf)	To overcome social anxiety	Anxiety with tachycardia, pupillary dilatation, psychomotor agitation	Yes	Panic disorder, Phobias and GAD can emerge from misuse
Nicotine			Pronounced anxiety	
Caffeine		Anxiety	Anxiety	
Opioids		Rarely used for anxiety relief		
Cannabis			Can present like a panic attack but with paranoid thoughts; more likely in inexperienced smokers	

Anxiety and AUD

- Twice as likely to relapse post detox with persistent anxiety (Kushner et al., 2005)
- Benzodiazepine abuse: Severely dependent alcoholic with ASPD, poly-substance user
- Buspirone, Paroxetine
- Acamprosate and baclofen have shown some benefit in reducing anxiety
- PTSD: Naltrexone and/or Disulfiram (reduced drinking); Desipramine superior over Paroxetine
- PTSD: Sertraline not superior to Placebo, worsened the drinking outcomes in severely dependent (Brady et al., 2005)

CANADIAN CLINICAL PRACTICE GUIDELINES, FOR ANXIETY 2014

Table 15 Recommendations for pharmacotherapy for panic disorder

First-line	Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, paroxetine CR, sertraline, venlafaxine XR
Second-line	Alprazolam, clomipramine, clonazepam, diazepam, imipramine, lorazepam, mirtazapine, reboxetine
Third-line	Bupropion SR, divalproex, duloxetine, gabapentin, levetiracetam, milnacipran, moclobemide, olanzapine, phenelzine, quetiapine, risperidone, tranylcypromine
Adjunctive therapy	**Second-line**: alprazolam ODT, clonazepam **Third-line**: aripiprazole, divalproex, olanzapine, pindolol, risperidone
Not recommended	Buspirone, propranolol, tiagabine, trazodone

Table 24 Recommendations for pharmacotherapy for GAD

First-line	Agomelatine, duloxetine, escitalopram, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR
Second-line	Alprazolam*, bromazepam*, bupropion XL*, buspirone, diazepam*, hydroxyzine, imipramine, lorazepam*, quetiapine XR*, vortioxetine
Third-line	Citalopram, divalproex chrono, fluoxetine, mirtazapine, trazodone
Adjunctive therapy	**Second-line:** pregabalin **Third-line:** aripiprazole, olanzapine, quetiapine, quetiapine XR, risperidone **Not recommended:** ziprasidone

Table 30 Recommendations for pharmacotherapy for core symptoms of PTSD

First-line	Fluoxetine, paroxetine, sertraline, venlafaxine XR
Second-line	Fluvoxamine, mirtazapine, phenelzine
Third-line	Amitriptyline, aripiprazole, bupropion SR, buspirone, carbamazepine, desipramine, duloxetine, escitalopram, imipramine, lamotrigine, memantine, moclobemide, quetiapine, reboxetine, risperidone, tianeptine, topiramate, trazodone
Adjunctive therapy	**Second-line:** eszopiclone, olanzapine, risperidone **Third-line**: aripiprazole, clonidine, gabapentin, levetiracetam, pregabalin, quetiapine, reboxetine, tiagabine **Not recommended**: bupropion SR, guanfacine, topiramate, zolpidem
Not recommended	Alprazolam, citalopram, clonazepam, desipramine, divalproex, olanzapine, tiagabine

32 year old female with a history of chronic anxiety, Alcohol history on paxil, Alprazolam, Gabapentin, Zopiclone.

Is this withdrawal anxiety either from alcohol or benzos or both, anxiety predisposed to substance use vs. using substances to get relief from anxiety?

1. ***Prescribed Paxil 60mg (Evidence-based treatment as first line)***
2. ***Alprazolam 0.5mg twice day (2nd line for GAD and Panic Disorder but not recommended for PTSD)***
3. ***Gabapentin 600mg tid and (3rd line for Panic Disorder, pregabaline – 1st line for GAD)***
4. ***Zopiclone 15mg (may be treated as diazepam dependency 7.5mg zopiclone = 5mg diazepam)***

Canadian Practice Guidelines, 2014

Revisiting Case

First step: Good assessment and formulate a plan (Use ASAM/Four quadrant criteria)

Detox from alcohol and benzodiazepine and stabilize:

Decide inpatient vs. outpatient

1. *Excessive drinking: Benzodiazepine detoxification using 10mg – 20mg qid over 7 days*
2. *Suspected use other illicit sedative-Hypnotics: Benzodiazepines*

a. Mild dependency – Reassurance and regular monitoring. In the community, dose can be reduced by 5mg diazepam (or 5 percent) every 1-2 weeks.

b. Moderate to severe dependency with comorbid alcohol (with or without seizure history) – Inpatient/ detox setting: using tapering Diazepam regime vs. Sodium Valproate 250mg – 500mg bid or Carbamazepine 100-200mg tid.

Revisiting Case

Post detox:

1. Continue on Gabapentin and titrate the dose to help with anxiety, relapse prevention for alcohol. Monitor carefully for misuse. Consider Naltrexone 50mg and/or Campral 666mg tid.
2. Optimize on antidepressant therapy for anxiety
3. CBT for anxiety
4. Psychosocial relapse-prevention programs: Case management or SMART recovery or AA
5. Regular review and follow up

CBT strategies

Comorbid Anxiety and Depression:

- Problem Definition
- Functional analysis of the symptoms
- Identifying Cognitive Distortions and Schema
- Arousal Management
- Exposure to Phobic Stimuli

PTSD: Seeking Safety (CBT)

- Increase client knowledge of both disorders
- Enhance life structure
- Increase coping skills in management of Painful Affect
- Enhance self care & Interpersonal relationship

Pharmacotherapy

	SSRI	Others& Mixed Pharmacology(TC)	Substance Outcome
Alcohol + Anxiety Alcohol +SA	Paroxetine> Placebo[2]	***Buspirone***[4]	Slight improvement
Alcohol+ PTSD	**Sertraline, not effective**	Desipramine[3] +Naltrexone	***S= Worsened*** D+N= Reduced substance use and symptoms

1. Torrens et al, 2005; 2. Brook et al., 2008; 3. Petrakis et al., 2012; 4. Malec et al. 1996

ADHD

CO-MORBIDITY

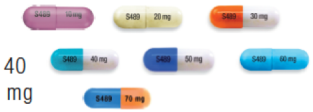
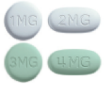
SUD and ADHD

- 15% to 25% of adults with drug- and alcohol use disorders have ADHD
- ADHD and SUDs may have a polygenic mechanism or represent variable expressivity of a shared risk factor
- Neuro imaging studies: fronto-subcortical systems and deficits in anterior cingulate activation in the pathophysiology of ADHD, findings that have also been observed in studies of SUDs

**Charach et al, 2011: Childhood attention deficit/hyperactivity disorder and future substance use disorders: comparative meta-analyses. J Am Acad Child Adolesc Psychiatry. 2011;50:9-21.*

^Levin et al, 1998: Prevalence of adult attentiondeficit/ hyperactivity disorder among cocaine abusers seeking treatment. Drug Alcohol Depend. 1998;52:15-25.

Quick Guide to ADHD Medication in CANADA - April 2017

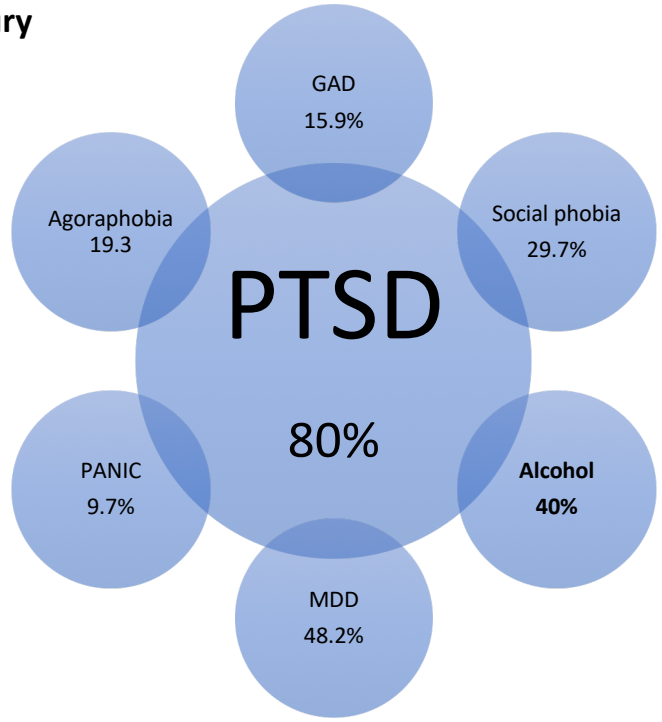
Medications available and illustrations of Tabs	Liberation mode (% immediate / delayed)	Particularities	Duration of action [1]	Starting Dose [2]	Dose titration as per product monograph
Amphetamine-based psychostimulants					
Dexedrine® Tablets 5 mg **Dexedrine®** spansules 10, 15 mg 	(100/0) (50/50)	Pill can be crushed [3] Spansule	~ 4 h ~ 6 - 8 h	Tablets = 2.5 to 5 mg BID Spansules = q.d. 10 mg am	↑ 2.5 - 5 mg at weekly intervals; max. dose/day: (q.d. or b.i.d.) All ages = 40 mg
Adderall XR® Capsules 5, 10, 15, 20, 25, 30 mg 	(50/50)	Sprinkable Granules	~ 12 h	5 - 10 mg q.d. a.m.	↑ 5 mg at weekly intervals max. dose/day: Children = 30 mg Adolescents and Adults = 20 - 30 mg
Vyvanse® Capsules 10, 20, 30, 40 50, 60, 70* mg 	Prodrug	Capsule content can be diluted in water, orange juice and yogurt	~ 13 - 14 h	20 - 30 mg q.d. a.m.	↑ by clinical discretion at weekly intervals max. dose/day: All ages = 60 mg
Methylphenidate-based Psychostimulants					
Methylphenidate short acting Tablets 5 mg (generic) 10, 20 mg (**Ritalin®**) 	(100/0)	Pill can be crushed [3]	~ 3 - 4 h	5 mg b.i.d. to t.i.d. Adult: consider q.i.d.	↑ 5 mg at weekly intervals max. dose/day: All ages = 60 mg
Biphentin® Capsules 10, 15, 20, 30, 40, 50, 60, 80 mg 	(40/60)	Sprinkable Granules	~ 10 - 12 h	10 - 20 mg q.d. a.m.	↑ 5 - 10 mg at weekly intervals max. dose/day: Children and Adolescents = 60 mg Adults = 80 mg
Concerta® Extended Release Tabs 18, 27, 36, 54 mg 	(22/78)	Pill needs to swallowed whole to keep delivery mechanism intact	~ 12 h	18 mg q.d. a.m.	↑ 9 - 18 mg at weekly intervals max. dose/day: Children = 54 mg Adolescents = 54 mg / Adults = 72 mg
Non psychostimulant - Selective Norepinephrine Reuptake Inhibitor					
Strattera[MD] (Atomoxetine) Capsules 10, 18, 25, 40, 60, 80, 100 mg 	Not applicable	Capsule needs to swallowed whole to reduce GI side effects	Up to 24 h	Children and Adolescents : 0.5 mg/kg/day Adults = 40 mg q.d. for 7-14 days	Maintain dose for a minimum of 7 - 14 days before adjusting: Children = 0.8 then 1.2 mg/kg/day 70 kg or Adults = 60 then 80 mg/day max. dose/day : 1.4 mg/kg/day or 100 mg
Non psychostimulant - Selective Alpha-2A Adrenergic Receptor Agonist					
Intuniv XR® (Guanfacine XR) Extended Release Tabs 1, 2, 3, 4 mg 	Not applicable	Pills need to be swallowed whole to keep delivery mechanism intact	Up to 24 h	1 mg q.d. (morning or evening)	Maintain dose for a minimum of 7 days before adjusting by no more than 1 mg increment weekly Max. dose/day: Monotherapy: 6-12 years = 4 mg, 13-17 years = 7 mg As adjunctive therapy to psychostimulants 6-17 years = 4 mg

PTSD

Comorbidity

Concurrent/co-morbidity

Brain Injury



Keller et al, 1995 Arch Gen Psychiatry, 52:1048

+ 68% Chronic Pain relating to MVA

Somatoform Pain

Other Concurrent physical Issues

Psychological and Social

RELAPSE PREVENTION

Concurrent and Substance use

Relapse Prevention: Pharmacotherapy

	Naltroxone (Revia)	Disulfiram (Antabuse)	Acamprosate (Campral)	Combination & Others
Depressed Alcoholic	S 200mg + N 100mg vs P+NP= 50% vs 25% 14wks[1]	Safe[2]	Modest effect[3]	
Depressed Opioid	Improved Mood[4]			
Alcohol+ PTSD	Improved Drink outcome	Reduction in NA = Dampening around Improved drink Outcomes		D+N
Alcohol+Anxiety			Positive Outcome	Baclofen

1. Pettinati et al 2010; 2. Petrakis et al 2005, 2007;3. Lejoyeux & Lebert,2011;4. Mysels et al,2011

Relapse Prevention - Alcohol

http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/problem_drinking_3_appendix_a.pdf

BCGuidelines.ca

Appendix A: Prescription Medication Table for Alcohol Dependence [a]

Generic Name Brand/Trade Name	Adult Oral Dose	Mechanism of Action	Cautions/ Contraindications [b]	Therapeutic Considerations (including side effects and drug interactions) [b]	PharmaCare Coverage	Annual Cost (cost per tablet/capsule)
Naltrexone [c] **(ReVia®)** *(Approved indication: treatment of alcohol dependence to support abstinence and decrease relapse risk)*	50 mg once daily (start at 25 mg once daily to minimize side effects)	Blocks the action of endorphins when alcohol is consumed.	Must be opioid free for 7 to 10 days before initiating and must stop for 7 days if opioid therapy required. Liver failure, current or anticipated opioid use, hypersensitivity.	Some side effects include: nausea, vomiting, headache, fatigue, somnolence, hepatotoxicity. Drug interactions: opioids, medications that can also contribute to hepatocellular injury (i.e. NSAIDS)	Limited coverage[d]	Annual cost = $1952.50 (50 mg tablet = $5.30)
Acamprosate **(Campral®)** *(Approved indication: maintenance of abstinence from alcohol in patients who are abstinent at treatment initiation)*	666 mg three times daily 333 mg three times daily if mild to moderate renal impairment	Restores the imbalance of neuronal excitation and inhibition caused by chronic alcohol use.	Severe renal impairment, pregnancy, hypersensitivity.	Some side effects include: diarrhea, nausea, headache, depression. Suicidal ideation (rare) Can be used in patients with liver disease Drug interactions: naltrexone	Limited coverage[d]	Annual cost = $1817.70 (333 mg tablet = $0.80)
Compounded disulfiram **(Antabuse® no longer available)** *(Approved indication: deterrent to alcohol use/abuse)*	Maintenance: 250 mg once daily Range: 125 to 500 mg once daily	Blocks alcohol metabolism causing an aversive reaction to alcohol when it is consumed. Reaction: flushing, nausea, vomiting, headaches, palpitations, hypotension.	Total abstinence is needed. Do not give to intoxicated individuals or within 36 hours of alcohol consumption. Cardiac disease, cerebrovascular disease, renal/ hepatic failure, pregnancy, psychiatric disorders, alcohol consumption, hypersensitivity.	DO NOT ADMINISTER WITHOUT PATIENT'S KNOWLEDGE. Alcohol reaction can occur up to two weeks after last dose and symptoms (severe) can include: hepatoxicity, peripheral neuropathy, respiratory depression, psychotic reactions, optic neuritis. Some common side effects include: drowsiness, metallic taste, impotence, headache. Drug interactions: alcohol containing medications, metronidazole, warfarin, diazepam, amitriptyline. phenytoin.	Regular Benefit	Annual cost = $146 (125 mg capsule = $0.30) (250 mg capsule = $0.40) (500 mg capsule = $0.80)

PSYCHOSOCIAL STRATEGIES

Potential interventions at different stages of treatment				
	Stage of treatment			
	Engagement	Persuasion	Active treatment	Relapse prevention
Case management	X	X	X	X
Family work	X	X	X	X
Pharmacological treatment	X	X	X	X
Assertive outreach	X	X	X	
Coerced or involuntary interventions	X	X	X	
Residential programmes		X	X	
Motivational interviewing		X	X	
Persuasion groups		X	X	
Cognitive-behavioural counseling		X	X	X
Social skills training		X	X	X
Vocational rehabilitation		X	X	X
Active treatment groups			X	X
Self help groups			X	X
From Noordsy *et al.,* 2015				

Psycho-social approach

•**Engagement** – regular contact and development of a therapeutic alliance, and meeting basic needs.

• **Persuasion** – motivational techniques to enhance motivation to change (reduce substance use).

•**Active treatment** – from harm reduction to abstinence-oriented approaches.

• **Relapse prevention** – identification of highrisk situations for relapse and management of future relapses.

Benzodiazepines

Benzodiazepines

- **Therapeutic dose vs. illicit**
- **Early/mild dependence:** minimal interventions
- **Dependence user**: gradual dose reduction of prescribed benzodiazepine
- **Problematic withdrawal symptoms on reduction:** Switching from a short half-life benzodiazepine to a long half-life benzodiazepine before gradual taper
- **Carbamazepine**: Withdrawals
- **Chronic Insomnia**: Gradual reduction + CBT (85%) vs. Gradual reduction (48%)
- **Panic Disorder**: Gradual reduction + CBT (76%) vs. Gradual reduction (25%)

The management of BZD withdrawal syndrome:

1. Gradual tapering of the BZD

2. Switching to an equivalent dose of a long half-life (Diazepam) BZD before gradual tapering of the latter

3. the use of adjuvant medications:

Carbamazepine 400mg bid, Valproate 250mg – 500mg bid

4. Treatment of the underlying conditions(i.e., SSRIs for anxiety) prior to detoxification and continuing these medications after BZD discontinuation

5. Non-pharmacological treatments of underlying conditions

BENZODIAZEPINE EQUIVALENT DOSES

5 mg of *diazepam* is equivalent to:		
0.5mg	of *alprazolam*	**For example:** If the patient is using *4 mg of lorazepam* per day, this is equivalent to *40mg of diazepam* per day. If the patient is using *60 mg of temazepam* per day, this is equivalent to *30mg of diazepam* per day
3mg	of *bromazepam*	
10mg	of *clobazam*	
1mg	of *flunitrazepam*	
0.5mg	of *lorazepam*	
0.75mg	of *lormetazepam*	
5mg	of *nitrazepam*	
15mg	of *oxazepam*	
2.5mg	of *midazolam*	
10mg	of *temazepam*	
0.25mg	of *triazolam*	

Clonazepam 0.25 -5mg

WHO, 2009

Benzodiazepine dose reduction regime

Patients using less than 40mg/day diazepam eq				
	Time of dose			Total dail
	08:00	12:00	20:00	
Starting dose	5mg	5mg	5mg	15mg
1st reduction	5mg	2.5mg	5mg	12.5mg
2nd reduction	5mg	-	5mg	10mg
3rd reduction	2.5mg	-	5mg	7.5mg
4th reduction	-	-	5mg	5mg
5th reduction	-	-	2.5mg	2.5mg

WHO, 2009

Antidepressant side effects

	Anti-cholin-ergic	Cardiac	Nausea	Sed-ation	Over-dose	Pro-convuls-ant	Sexual dys-function
Tricyclics	+++	++	+	++	++	+	++
(Es)citalopram (Cipramil/Cipralex)	O	O	++	O	O	O	++
Fluoxetine	O	O	++	O	O	O	++
Paroxetine (Seroxat)	O	O	++	O	O	O	+++
Sertraline (Lustral)	O	O	++	O	O	O	++
Mirtazapine (Zispin)	O	O	O	++	O	O	O
Reboxetine (Edronax)	+	+	+	O	O	O	O
Duloxetine (Cymbalta)	O	O	++	O	?	?	++
Trazodone (Molipaxin)	+	+	+++	++	+	O	++
Venlafaxine (Efexor)	O	++	+++	+	?	+	++
Bupropion (Zyban)	+	O	+	O	++	+++	O
MAOIs	++	++	++	O/+	++	O	+
Agomelatine (TBA)							

ANTIDEPRESSANT SWAPPING

TO / FROM	MAOIs		TCA	SSRIs				Related	Reversible MAOI	Other		
	Hydrazines	Tranyl-cypromine	Tricyclics	Citalopram	Fluoxetine	Paroxetine	Sertraline	Trazodone	Moclobemide	Reboxetine	Venlafaxine	Mirtazapine
MAOIs-Hydraziness		14	14	14	14	14	14	14	14	14	14	14
Tranyl-cypromine[f]	14		14	14	14	14	14	14	14[a]	14	14	14
Tricyclics	7	7	CT Cautiously	Taper to 25-50mg Add SSRI and discontinue TCA over 5-7 days[b]	Taper to 25-50mg Add SSRI and discontinue TCA over 5-7 days[b]	Taper to 25-50mg Add SSRI and discontinue TCA over 5-7 days[b]	Taper to 25-50mg Add SSRI and discontinue TCA over 5-7 days[b]	Taper to 25-50mg Add SSRI and discontinue TCA over 5-7 days[b]	7	CT Cautiously	CT Cautiously start Venlafaxine 37.5mg/daily	CT Cautiously
Citalopram	7	7	CT Cautiously [b]		0 start Fluoxetine 10mg/day titrate up after 7 days	0 start Paroxetine 10mg/day titrate up after 7 days	0 start Sertraline at 25mg/day titrate up after 7 days	CT Cautiously Titrate up Trazodone	14	CT Cautiously	0 start Venlafaxine 37.5mg/day & increase v.slowly	CT Cautiously
Paroxetine	14	7	CT cautiously with v.low dose of tricyclic [b]	0	0		0 then Setraline at 25mg/day	CT Cautiously start titration of Trazodone	14	CT Cautiously	0 start Venlafaxine at 37.5mg/day & increase v.slowly	CT Cautiously
Fluoxetine [c]	35-42	35-42	4-7 days Start tricyclic at v.low dose & increase slowly	4-7 days. start Citalopram at 10mg/day & increase slowly		4-7 days start Paroxetine at 10mg/day	4-7 days start Sertraline at 25mg/day	4-7 days start low dose Trazodone and titrate up	35	0 start Reboxetine at 2mg bd & increase cautiously	4-7days start Venlafaxine at 37.5mg/day increase v.slowly	0 start Mirtazapine cautiously
Sertraline	14	14	CT cautiously with v.low dose of tricyclic [b]	0	0	0		CT Cautiously start titration of Trazodone	14	CT Cautiously	0 start Venlafaxine at 37.5mg/day	CT Cautiously
Trazodone	7	7	CT cautiously with v.low dose tricyclic	0	0	0	0		7	0 start 2mg BD & increase cautiously	0 start Venlafaxine at 37.5mg/day	CT Cautiously
Moclobemide	1	1	1	1	1	1	1	1		1	1	1
Reboxetine	7	7	CT Cautiously	CT Cautiously	CT cautiously	CT cautiously	CT cautiously	CT cautiously	7		CT cautiously	CT cautiously
Venlafaxine	7	7	CT cautiously with v.low dose of tricyclic [b]	CT cautiously start with 10mg/day	CT cautiously start with 20mg every other day	CT cautiously start with 10mg/day	CT cautiously start with 25mg/day	CT cautiously	7	CT cautiously		CT cautiously
Mirtazapine	7	7	0	0	0	0	0	7	0	0	0	
STOPPING [d] **- Reduce over _ wks**	4 weeks	4 weeks	4 weeks	4 weeks	20mg/day = just stop 40mg/day = 2 wks	4 weeks or longer if necessary [e]	4 weeks	4 weeks	4 weeks	4 weeks	4 weeks or longer if necessary [e]	4 weeks

MAUDSLEY GUIDELINES, 10TH Edition

HIV MEDICATIONS & PSYCHOTROPIC EFFECTS (MAUDSLEY GUIDELINES, 10TH Edition)

Table Psychotropic effects of antiretrovirals

Diagnosis	*Implicated agent*
Depression	Abacavir[39] Amprenavir[40] Efavirenz[36,40,41] Enfuvirtide* Indinavir[42] Nevirapine[43] Ritonavir/lopinavir* Saquinavir* Stavudine* Zidovudine*
Mania	Didanosine[44] Efavirenz[45,46] Zidovudine[47–49]
Psychosis	Abacavir[35,39] Efavirenz[36,50–52] Nevirapine[43]
PTSD	Efavirenz[53]
Vivid dreams	Abacavir[54] Enfuvirtide* Entricitabine* Nevirapine[55] Efavirenz[56]
Suicidal ideation	Abacavir[39] Efavirenz[55,56]
Miscellaneous symptoms (anxiety, sleep disturbance, emotional lability, etc.)	Efavirenz[56,57] Ritonavir/lopinavir* Stavudine* Zalcitabine*

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