Diagnostic Considerations

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Disclosures

• Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.
Outline: Key Points

- *What* exactly are we trying to diagnose? Disorders and substance-related harms
- Addiction syndrome as bi-axial and dimensional
- SUD phenomenology varied; clinical presentation heterogeneous
- Like other disorders, early detection and intervention improves prognosis
- Reliable easy to use methods available for diagnosis
- SUD can mask, and masquerade as, other diagnoses – methods to disentangle
Definition and Brief History of Construct: Terminology

- Addiction
- Substance use disorder
- Dependence
- Abuse
- Misuse
- Hazardous/harmful use
How do substances cause harm?

Mediators of substance-related harm: Toxicity, Intoxication, and Addiction

Patterns of Use

Toxic Effects

intoxication

Addiction

Average volume

Chronic Disease

Accidents/injuries (acute disease)

Acute social problems

Chronic Social problems

(Adapted from: Babor et al, 2010)
In brackets, increased risk at 20g/day compared with not drinking

- Oral cavity & Pharynx (86%)
- Larynx (43%)
- Oesophagus (39%)
- Breast (25%)
- Liver (19%)
- Rectum (9%)
- Colon (5%)

Source: Corrao et al 2009
What is “addiction”? 

Addiction is a genetically influenced disease of the brain characterized by impairments in the neurocircuitry of reward, memory, motivation, impulse control, and judgement.
What is “addiction”?

Impaired control over a reward-seeking behavior from which harm ensues

“Substance use disorder” clinically significant impairment or distress as manifested by 2 or more of 11 symptoms...
Formulations and definitions (Jellinek, 1960, pg 33)

• “....there are more definitions of ‘definition’ than there are alcoholism. This may be consolation for students of alcoholism who complain about the plethora and conflict of definitions or so-called definitions in their field. On the other hand it should impress them that definition is nothing sacred and unalterable. One cannot question whether definitions are right or wrong, unless they go against the rules of the defining process, but one may debate their utility.”
Monothetic classification: characteristics that are both necessary and sufficient in order to identify members of that class. (“Aristotelian” definition of a class).

Polythetic classification: broad set of criteria neither necessary nor sufficient. Each member of the category must possess a certain minimal number of defining characteristics (e.g., 2/11), but none must be present.

Monothetic = all members identical on all characteristics. Polythetic = all members are similar, but not identical.

DSM system (post DSM III) is based on polythetic system of classification.

Clinical implications?
Heterogeneity gives rise to a search for subtypes – identification of clinically meaningful subtypes challenging...

- Silkworth (1939)
- Jellinek (1960)
- Cloninger (1981)
- Babor (1992)
- Del Boca (1994)
- Del Boca (1996)
- Hesselbrock (2006)
- Moss (2007)
- Anton (2008)
- Kranzler (2014)
Why derive typologies?

• To guide phenotypic characterization for identification of SUD candidate genes
• Assist in characterization of human molecular targets for pharmacotherapy
• Guide ascertainment criteria for clinical trials of behavioral and pharmacotherapy interventions

Source: Moss et al, 2007 Drug and Alcohol Dependence
Why assess/diagnose? SUD remission achieved quicker the sooner people get tx

Cumulative Survival

Source: Dennis et al, 2005.
DSM Development
DSM (1952) Description of “Alcoholism” and “Addiction”

000–x64  Addiction

Addictions will be classified as defined below.

000–x641  Alcoholism

Included in this category will be cases in which there is well established addiction to alcohol without recognizable underlying disorder. Simple drunkenness and acute poisoning due to alcohol are not included in this category.

000–x642  Drug addiction

Drug addiction is usually symptomatic of a personality disorder, and will be classified here while the individual is actually addicted; the proper personality classification is to be made as an additional diagnosis. Drug addictions symptomatic of organic brain disorders, psychotic disorders, psychophysiologic disorders, and psychoneurotic disorders are classified here as a secondary diagnosis.
Essential postulates:

1. The syndrome may be recognized by the clustering of certain elements. Not all elements need always be present or present in the same degree, but with mounting intensity the syndrome is likely to show increasing coherence.

2. The syndrome is not all-or-none, but occurs with graded intensity.

3. Its presentation will be shaped by the pathoplastic influence of personality and culture (and thus is variable).

4. A bi-axial concept is introduced, with the dependence syndrome constituting one axis and alcohol-related problems the other.
Bi-axial Depiction of original formulation of the Dependence Syndrome

Addiction severity

Substance-related problems
(physical and mental health; housing; social relations; education and employment; meaning/purpose)
ADS Key Elements (Edwards & Gross, 1976)

- **Narrowing of repertoire**: repertoire expands initially but narrows as dependence increases: individual begins to drink the same whether it’s a workday/weekend & irrespective of mood, social context

- **Salience**: stereotyping of drinking pattern leads to giving **priority to maintaining alcohol intake** - overrides other considerations

- **Increased tolerance**: Able to hold doses that may kill naïve drinkers

- **Withdrawal**: Tremor, sweating, nausea, mood disturbance, DTs/grand mal seizures

- **Relief/avoidance of w/d sxs by further use**: subtle at first; becomes extreme

- **Subjective awareness of compulsion to use**: Loss of control over use/inability to stop

- **Reinstatement after abstinence**: syndrome reoccurs despite long abstinence (more rapid reinstatement with higher severity)
DSM-IV “Abuse” Criteria

• A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:
  – **Role impairment:** recurrent substance use resulting in a failure to fulfill major role obligations at work, school, home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
  – **Hazardous use:** recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)
  – **Legal problems:** recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct)
  – **Continued use despite social problems:** continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights)
• The symptoms have never met the criteria for Substance Dependence for this class of substances.
DSM-IV defines “dependence”

- A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:
  - **tolerance**, as defined by either of the following:
    - a need for markedly increased amounts of substance to achieve intoxication or desired effect
    - markedly diminished effect with continued use of same amount of substance
  - **withdrawal**, as manifested by either of the following:
    - the characteristic withdrawal syndrome for substance
    - the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
  - substance often taken in **larger amounts/over a longer period than intended**
  - **persistent desire or unsuccessful efforts to cut down** or control substance use
  - **great deal of time is spent** in activities to obtain, use, or recover from its effects
  - important social, occupational or recreational **activities given up/reduced**
  - the substance **use is continued despite** knowledge of having a persistent or recurrent **physical or psychological problem** that is likely to have been caused or exacerbated by the substance (e.g., continued drinking despite recognition that an ulcer was made worse by alcohol consumption)
Rationale for combining “abuse” and “dependence”: “abuse” does not appear first in relation to consumption intensity... suggesting continuum

Source: Li, Hewitt & Grant, ADS 30 Years Later: A commentary, Addiction, 2007, 102, 10, 1522-1530
Rationale for combining “abuse” and “dependence”: “abuse” does not appear first in relation to consumption intensity... suggesting continuum

But just because these consequences are correlated with “dependence” doesn’t necessarily mean they are “dependence” any more than psychosocial impairments correlated with cancer constitute “cancer”.

Source: Li, Hewitt & Grant, ADS 30 Years Later: A commentary, Addiction, 2007, 102, 10, 1522-1530
“This one goes to 11” - DSM V “Substance Use Disorder”

A. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by 2 (or more) of the following, occurring within a 12-month period:

1. recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
2. recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)
3. continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights)
4. tolerance, as defined by either of the following:
   a. a need for markedly increased amounts of the substance to achieve intoxication or desired effect
   b. markedly diminished effect with continued use of the same amount of the substance (Note: Tolerance is not counted for those taking medications under medical supervision such as analgesics, antidepressants, anti-anxiety medications or beta-blockers.)
5. withdrawal, as manifested by either of the following:
   a. the characteristic withdrawal syndrome for the substance (refer to Criteria A and B of the criteria sets for Withdrawal from the specific substances)
   b. the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms (Note: Withdrawal is not counted for those taking medications under medical supervision such as analgesics, antidepressants, anti-anxiety medications or beta-blockers.)
6. the substance is often taken in larger amounts or over a longer period than was intended
7. there is a persistent desire or unsuccessful efforts to cut down or control substance use
8. a great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects
9. important social, occupational, or recreational activities are given up or reduced because of substance use
10. the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance
11. craving or a strong desire or urge to use a specific substance

Severity specifiers:
Mild: 2-3; Moderate: 4 or 5; Severe 6+
Current systems for diagnosis based on (mostly self-reported) observable symptoms and signs (e.g., DSM/ICD)

These observable manifestations occur typically in later stages of the illness (brain changes occur before outward manifestation) and early detection and treatment can help offset harms

Dxs over-specified; too many distinct diagnosis implying unique pathophysiologies suggesting distinct treatments; yet these are often heterogeneous (polythetic categories)

RDoC are designed to identify common factors (e.g., biotypes) that may underlie psychopathologies through genetic, neurobiological, and behavioral analyses

Goal is to identify more homogeneous groupings to enhance tx response “precision medicine”

Making progress... not ready for prime time yet...
RDoC (NIMH)

MRI scans showed that people with psychosis had different patterns of reduced gray matter – neurons and their connections, the brain’s working tissue (orange/yellow) – depending on their biotype. Derived from clusters of other biomarkers, the biotypes identify distinct subgroups of psychosis, likely involving different illness processes.

These subsets of biomarkers differentiated groupings of psychosis cases from each other considerably better than did traditional clinical diagnoses.

Several instruments available to formally assess diagnosis...

<table>
<thead>
<tr>
<th>S9. Detailed Substance Use Disorder Worksheet</th>
<th>For Staff Use Only</th>
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<tbody>
<tr>
<td>(If this is a self-administered assessment, please ask for staff assistance in completing the following information.)</td>
<td>1 2 3 4 5 6 7 8 9 99</td>
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</table>

For each of the problems endorsed in S9h-u, ask:
- Can you tell me which substance...(Read from below)?
- About when did that happen? (Using Card B)
- Have you ever had this problem with any other substance(s)?
- Repeat for each Sx in S9 until no more are reported

Record time code (3=past month, 2=2-12 months ago, 1=1+ years ago, 0 or blank means never).

### DSM-IV Abuse Criteria

- h. repeatedly caused you not to meet your responsibilities?
- i. you repeatedly used in unsafe situations?
- k. caused you to have repeated problems with the law?
- m. did you keep using even though it was leading to fights or getting you into trouble with other people?

### DSM-IV Dependence Criteria

- n. you have needed more of to get high?
- p. you have had withdrawal problems from?
- q. you have used more of or longer than you meant to?
- r. you have been unable to cut down on or stop using?
- s. you spent a lot of time getting or using?
- t. caused you to give up activities or caused problems?
- u. you kept using despite medical or psychological problems?

### Clinical Significance (for each drug with 1+ Abuse/Dependence criteria ask...)

- v. At what age did you first use... (for alcohol, read "At what age did you first get drunk")?

- w. How do you usually take... (1-oral, 2-smoking, 3-inhalation, 4-intramuscular, 5-intravenous, 6-NA, 7-other)?
Several instruments available to formally assess diagnosis...

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<tr>
<th>S9c. Detailed Substance Use Disorder Worksheet</th>
<th>Alcohol</th>
<th>Amphetamine</th>
<th>Cannabis</th>
<th>Cocaine</th>
<th>Hallucinogen</th>
<th>Inhalant</th>
<th>Opioid</th>
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<th>Sed &amp; Hyp-Aux</th>
<th>Other</th>
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Choosing Your Screening Tool...

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<th>Test</th>
<th>Description</th>
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<tr>
<td>AUDIT (WHO)</td>
<td>Alcohol use Disorders Identification Test</td>
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<td>AUDIT-C (WHO)</td>
<td>Alcohol Use Disorders Identification Test - Consumption</td>
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<td>SASQ (Single alcohol screening Question; NIAAA)</td>
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<td>CAGE (lacks sensitivity to pick up on less severe problems)</td>
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<td>CRAFFT (Car, Relax, Alone, Forget, Friends, Trouble; adolescent specific)</td>
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<td>DAST (Drug abuse screening test)</td>
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<td>ASSIST (all drugs) (WHO)</td>
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<td>Biomarkers (e.g., for alcohol: EtG, GGT, CDT, MCV)</td>
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AUDIT-C

Please circle the answer that is correct for you.

1. How often do you have a drink containing alcohol?
   - Never (0)
   - Monthly or less (1)
   - Two to four times a month (2)
   - Two to three times per week (3)
   - Four or more times a week (4)
   
   **SCORE**

2. How many drinks containing alcohol do you have on a typical day when you are drinking?
   - 1 or 2 (0)
   - 3 or 4 (1)
   - 5 or 6 (2)
   - 7 to 9 (3)
   - 10 or more (4)
   
   **SCORE**

3. How often do you have six or more drinks on one occasion?
   - Never (0)
   - Less than Monthly (1)
   - Monthly (2)
   - Two to three times per week (3)
   - Four or more times a week (4)

**TOTAL SCORE**
Add the number for each question to get your total score.

Maximum score is 12. A score of ≥ 4 identifies 86% of men who report drinking above recommended levels or meets criteria for alcohol use disorders. A score of > 2 identifies 84% of women who report hazardous drinking or alcohol use disorders.
AUDIT-C Brief Screen

What are the chances that alcohol will harm you?

Audit-C Score (in points)
- Severe Risk (8-12 pts)
- High Risk (6-7 pts)
- At Risk (4-5 pts for males)
  (3-5 pts for females)
- Low Risk (1-3 pts for males)
  (1-2 pts for females)
- No Risk (0 pts)

1 in 100 males

The AUDIT-C is a questionnaire given to thousands of patients. This triangle shows how your drinking compares to theirs. Men who score 5 or higher and women who score 4 or higher are likely to be harmed from drinking.
Several Dimensional Assessments available too that yield degree of substance involvement/severity

- AUDIT/AUDIT-C/SADQ/MAST
- LEEDS/ASSIST/DAST
Major issues

• SUD may **masquerade** as other psychiatric illness:
  – Patients presenting with anxiety/mood/psychotic complaints/symptoms, may be due to substance use

• SUD may **mask** other psychiatric illness:
  – Patients presenting with SUD may also have typical anxiety/mood symptoms, but these may persist beyond 4-6 weeks of abstinence indicated an independent disorder

• SUD will present differently in different people (pathoplasticity):
  – Symptom quality/quantity and manifestation differ by personality, culture, context, age, gender....
Differential Diagnosis of Independent Co-occurring Disorders

- Primary/secondary distinction based on relative onset helpful in predicting remission of psych sxs; has predictive validity (Winokur et al, 1995)
- Monitoring sxs in context of abstinence aids appropriate tx decisions (e.g., with BDI-II/PHQ9); abstinence period of at least 4-6 wks necessary to determine degree of sxs remission (Brown, Inaba, Gillin, et al, 1995; Schuckit, 2009)
- Use of timeline aids assessment (e.g., SUD disorder above and psych below with life events). Look for relative onset and for psych symptoms during periods of abstinence
### The Timeline Technique in Dual Diagnosis

**Drugs:**
- Cocaine
- Stimulants
- Sedative/Hypnotics
- Opioids
- Cannabis
- Hallucinogens
- PCP
- Other
- Alcohol

**Unsuccessful Attempts to cut down/ withdrawal**

**Legal consequences/**

**Cocaine use**

**Dealing coke**

**Abstinent for 4 months age 31 years**

**Inpatient Tx (Alc)**

**AGE**
- 14
- 17
- 19
- 21
- 23
- 24
- 25
- 31
- 32
- 33
- 34
- 34.5

**1stDUI**

**2nd DUI**

**Juvenile Hall**

**In trouble at home and at school for breaking the rules; bullying kids at school; fighting; hurting animals; setting fires (2x)**

**Multiple jobs of less than 3 months**

**Unemployed**

**Arrest (armed robbery)**

**Began getting depressive symptoms (feeling down, sleeping a lot)**

**No significant sxs of de**

**Inpt 1 Dep**

**Inpt 2 Dep**

**MDE**

**Symptoms:**
- Depression
- Anxiety
- Psychosis
- Mania
- Antisocial
- Cognitive Impairment
Outline: Key Points

• *What* exactly are we trying to diagnose? Harm vs disorder

• Addiction syndrome as bi-axial and dimensional

• SUD phenomenology varied; clinical presentation heterogeneous

• Like other disorders, early detection and intervention improves prognosis

• Reliable easy to use methods available for diagnosis

• SUD can mask, and masquerade as, other diagnoses – methods to disentangle