Redefining Recreational Drug User Population in Human Abuse Potential Studies: Considerations of Diagnostic Differences between DSM-IV-TR and DSM 5

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Disclosure

Employee of INC Research
Agenda
Topics of Discussion

1. DSM publications to date

2. Utility of DSM-IV-TR in current human abuse potential studies

3. DSM 5: Changes to substance use disorders criteria

4. Impact of DSM 5 on human abuse potential studies
DSM Publications

- Diagnostic and Statistical Manual of Mental Disorders (DSM) published by the American Psychiatric Association (APA)

- DSM I - first publication in 1952

- DSM-IV - published in 1994

- DSM-IV-TR (text revision) update in 2000
  - currently used in human abuse potential studies
  - differentiates between substance “dependence” vs “abuse” diagnoses

- DSM 5 – published in May 2013
  - no longer differentiates between substance “dependence” vs “abuse” diagnoses
DSM 5
- Not just an update but a complete overhaul of diagnostic criteria including Substance Use Disorders (SUD)
- Currently not adopted for use in human abuse potential studies due to significant changes to the diagnosis of SUD
Relevance of DSM 5 for HAP Trials

- DSM 5 redefined Substance Use Disorders - substance dependence and abuse are no longer valid diagnoses

- Major implications for study populations in clinical trials investigating human abuse potential (HAP)

- Subject population in HAP studies
  - Non-dependent recreational drug users
    (FDA Draft Guidance, HAP, 2010; FDA Guidance, AD Opioids, 2015)
  - Assessed by DSM-IV-TR substance dependence clinical interviews as exclusionary criteria during screening phase of a study for subject eligibility
What Changed? DSM-IV-TR to DSM 5

**DSM-IV-TR**
- 2 separate diagnoses
  - Substance Dependence = 7 total criteria
  - Substance Abuse = 4 total criteria

**DSM 5**
- 1 diagnosis
  - Substance Use Disorders = 11 total criteria

- Omitted legal problems from abuse criteria (due to limited diagnostic utility)
- Addition of new criterion of “craving”
### Comparing DSM-IV-TR vs DSM 5

<table>
<thead>
<tr>
<th>DSM-IV-TR Abuse</th>
<th>DSM-IV-TR Dependence</th>
<th>DSM 5 SUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Role obligation failure</td>
<td>√</td>
<td>—</td>
</tr>
<tr>
<td>Continued use despite social/interpersonal</td>
<td>√</td>
<td>—</td>
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<tr>
<td>Recurrent use in hazardous situations</td>
<td>√</td>
<td>—</td>
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<tr>
<td>Repeated legal problems</td>
<td>√</td>
<td>—</td>
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<tr>
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<td>√</td>
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<tr>
<td>Sacrificing activities</td>
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</tr>
<tr>
<td>Continued use despite physical/psychological</td>
<td>—</td>
<td>√</td>
</tr>
<tr>
<td>Tolerance</td>
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<td>√</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>—</td>
<td>√</td>
</tr>
<tr>
<td>Craving (New)</td>
<td>N/A</td>
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DSM 5 Severity Scale

Substance Use Disorders

Continuum

Mild

Moderate

Severe

2-3 criteria

4-5 criteria

6+ criteria
Rationale for Changes to DSM 5

• Diagnostic “orphans” (e.g., 2 dependence criteria) – no diagnosis
• ~50% of individuals diagnosed with abuse disorder with only 1 criterion: hazardous use
• Hierarchy assumed with substance abuse to be the milder than dependence
• Abuse thought to be prodromal to substance dependence
• All cases of dependence assumed to meet criteria for abuse
• Therefore, DSM 5 introduced with concept that abuse and dependence are unidimensional to solve “problems” with abuse in DSM-IV-TR

DSM 5 includes 3 of 4 abuse criteria from DSM-IV-TR
DSM 5: Implications for HAP Studies

- Creation of a new subject pool with 2+ criteria for substance use disorder
- Requires rethinking the definition of “non-dependent” recreational drug user population
- DSM 5 criteria are not all created equal but weigh the same
How to Classify DSM 5 Mild SUD?

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Person 1:
- Meets min 2 criteria from previous "abuse" criteria
  a) Hazardous use
  b) Continued use despite social/interpersonal problems
- More “abuse” rather than “dependence”

Person 2:
- Meets min 2 criteria from previous "dependence" criteria
  a) Tolerance
  b) Great deal of time spent
- More of “dependent” rather than “abuse”

Same diagnosis fits all?
Who is the recreational drug user in HAP studies using DSM 5 criteria?

- Mild SUD?
- Moderate SUD?
- Exclude all categories of SUD (i.e., mild, moderate and severe)?
- Create our own criteria for “non-dependent” recreational drug users?
Working Group Task Force

- Comprised of psychiatrists, addiction specialists, clinical neuropsychologists and pharmacologists has been created to address the transition from DSM-IV to DSM 5 in HAP studies

- Tasked with redefining the recreational drug user population to determine valid criteria that would be most suitable for HAP studies
Conclusions

- DSM 5 changes to SUD has significant implications for HAP studies for recreational drug users, but also for dependent populations
- No HAP studies using DSM 5 to date – need to define the population
- Re-evaluation and consensus between pharmaceutical industry and regulatory agencies needs to occur based on empirical findings to determine the optimal solution
References


Discussion Points
Discussion Points

- Should clinical trials investigating HAP continue using the DSM-IV as exclusionary criteria for non-dependent recreational drug users instead of adopting the DSM 5?

- Should we drop DSM all together for another form of assessing SUD in HAP studies?

- Should we change the name from human abuse potential to something else to reflect the changes in DSM 5?
Criteria Grouping in DSM 5

**Impaired Control**
1) Use in larger amounts
2) Desire to cut down
3) Time spent
4) Craving (new)

**Social Impairment**
5) Role obligation failure
6) Use despite social problems
7) Sacrificing regular activities

**Risky Use**
8) Use in hazardous situations
9) Use despite knowledge of physical/psychological issues

**Pharmacological Criteria**
10) Tolerance
11) Withdrawal

Red = DSM-IV abuse criteria