

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

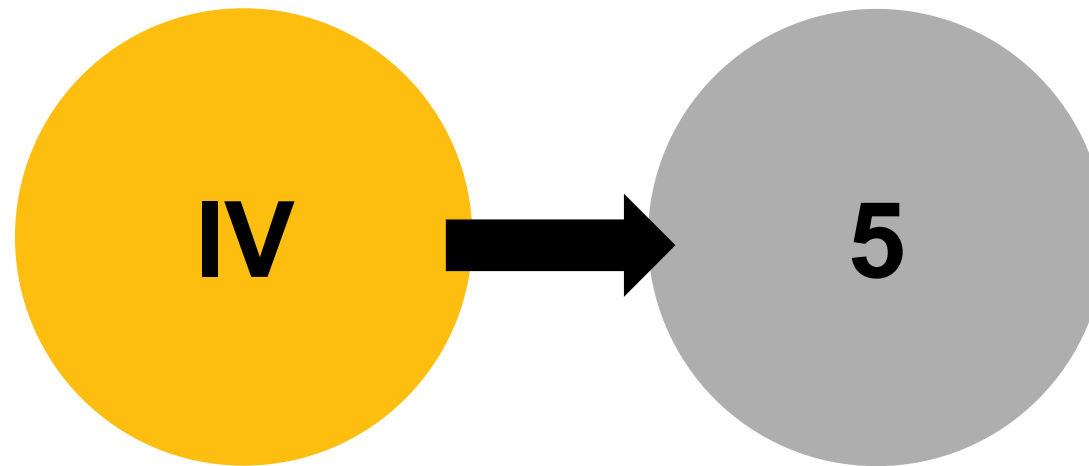
Agenda

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- DSM 5 redefined Substance Use Disorders - substance *dependence* and *abuse* are no longer valid diagnoses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(FDA Draft Guidance, HAP, 2010; FDA Guidance, AD Opioids, 2015)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

Dependence &
Abuse

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

	DSM-IV-TR Abuse	DSM-IV-TR Dependence	DSM 5 SUD
• Role obligation failure	√	—	√
• Continued use despite social/interpersonal	√	—	√
• Recurrent use in hazardous situations	√	—	√
• Repeated legal problems	√	—	X
• Use in larger amounts or longer period than intended	—	√	√
• Desire or unsuccessful effort to cut down	—	√	√
• Great deal of time spent	—	√	√
• Sacrificing activities	—	√	√
• Continued use despite physical/psychological	—	√	√
• Tolerance	—	√	√
• Withdrawal	—	√	√
• Craving (New)	N/A	N/A	√

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

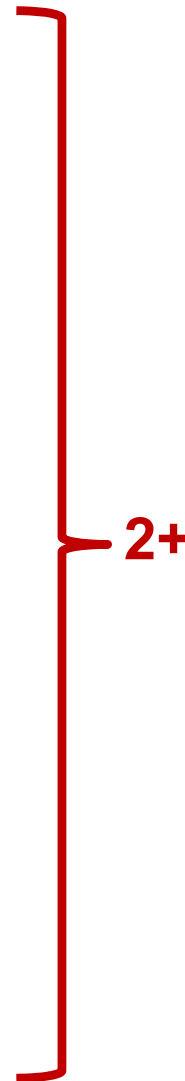
DSM 5 includes 3 of 4 abuse criteria from DSM-IV-TR

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?

DSM 5 SUD
Role obligation failure
Continued use despite social/interpersonal
Recurrent use in hazardous situations
Use in larger amounts or longer period than intended
Desire or unsuccessful effort to cut down
Great deal of time spent
Sacrificing regular activities
Continued use despite physical/psychological problems
Tolerance
Withdrawal
Craving (New)



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?

DSM 5: Redefining Recreational Drug Users

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

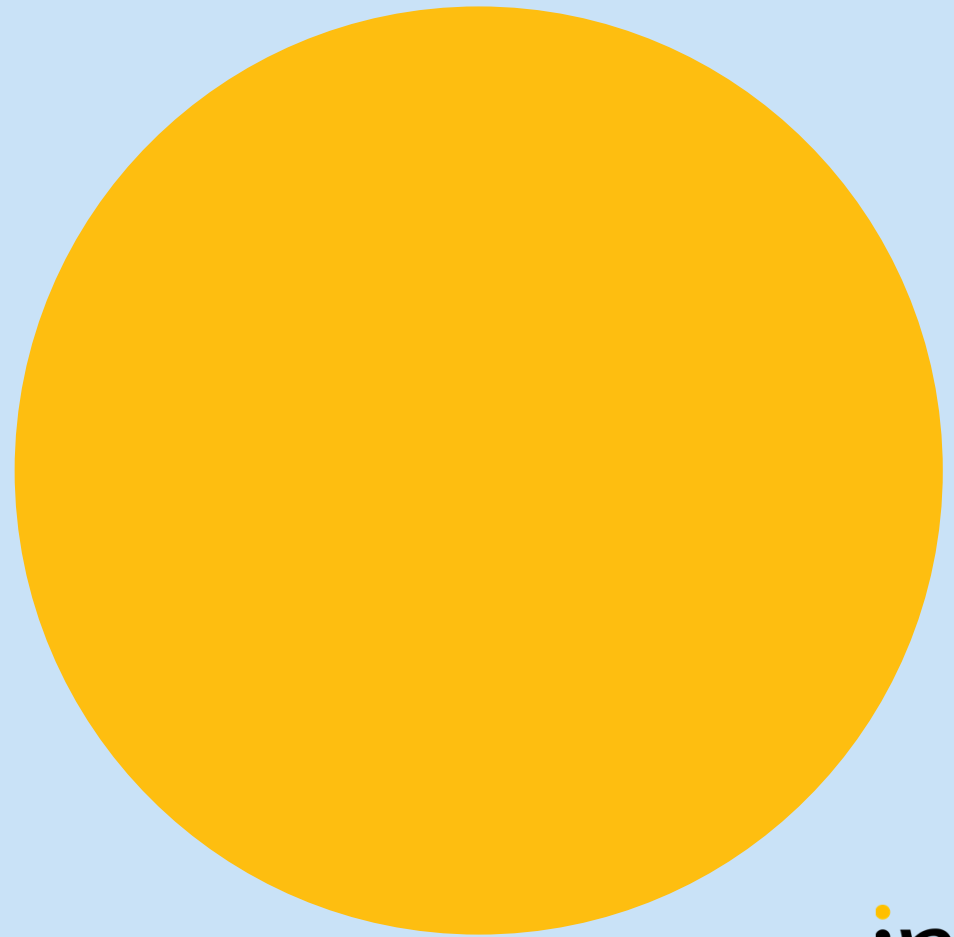
Conclusions

- 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

1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC, American Psychiatric Association, 2000.
2. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Washington, DC, American Psychiatric Association, 2013.
3. FDA Draft Guidance for Industry: Assessment of Abuse Potential of Drugs (2010), CDER.
4. Hasin et al. (2013). DSM 5 Criteria for Substance Use Disorders: Recommendations and Rationale. American Journal of Psychiatry, 170(8): 834-851.

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
- 5) 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