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"I'm still using meth, but only once this week". What does this mean?! This NIDA study bravely took a step towards understanding what a reported reduction in methamphetamine (MA) or cocaine use might mean for people with stimulant use disorder (do). It found that at about three months' time "Reduced Use" of stimulants- defined as going from high frequency use (5+ days per month) to low frequency use (1-4 days per month) was associated with lower self-reported ratings for problems from other drug and alcohol use, less depression, better clinical global impression ratings and lower cravings. There were not significant changes in ratings of family/social function or psychiatric symptoms, nor had people achieved low HIV risk behaviors or "problem free functioning". Those who became abstinent, however, experienced improvements in all of the above, and to a greater degree.

The study includes a relatively healthy group of people as evidenced by their symptom scores –those participating in clinical trials often are. This is a limitation of the work, as is its exploratory nature. In addition, some of the associations here may actually be causal (are reduced cravings a cause or effect of using less?), in other cases, obvious (patient reporting on severity of use at the same time that they report they've reduced use), and are relatively short term in the life of a use disorder. Still, it's encouraging to see development in the vocabulary of harm reduction. Working to define a clinically meaningful reduction in stimulant use, with an understanding of how it compares to abstinence, will offer nuance to the care we give and stands to improve the quality and sensitivity of research.

Please read on for a deeper look at this new angle,

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Title: In people with stimulant use disorders, reducing from high frequency to low frequency stimulant use is associated with reported improvements in substance use and mental health symptoms.

Citation: Aminesmaeili M, Farokhnia M, Susukida R, Leggio L, Johnson RM, Crum RM, et al. Reduced
drug use as an alternative valid outcome in individuals with stimulant use disorders: Findings from 13 multisite randomized clinical trials. Addiction. 2024. https://doi.org/10.1111/add.16409

Link: https://pubmed.ncbi.nlm.nih.gov/38197836/

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METHODS

This is a secondary data analysis that 'harmonized' data from 13 RCTs studying pharmacologic treatments for people with cocaine or MA use disorders. The original studies were NIDA funded trials in sites across the US. Participants were approximately 1/3 female, mean 40yrs, and 45% white. Trials were between 8-15wks, but mostly 12wks in duration.

The authors defined three mutually exclusive categories of participants, based on use at the end of the study: No Reduced Use, Reduced Use- defined as going from high frequency use (5+ days per month) to low frequency use (1-4 days per month), and Abstinent. Abstinence data was corroborated by a UDT at the end of treatment. The investigators compared differences between these groups on clinical indicators using validated survey instruments, including the Addiction Severity Index-lite (ASI-lite), HAM-D (a depression measure), clinical global impression, and cravings scales. They also asked about HIV risk behaviors and functioning. Data were adjusted for baseline differences and a number of potential confounders.

MAIN RESULTS

Overall n=2062, of which 1196 had cocaine use do and 866 MA use do. 72% had data available at the end of trial. Missing data was excluded and assumed to be at random.

Overall, 14% were abstinent and 18% had "Reduced Use" by the end of study period. ASI scores for other substance use were generally low (score range is 0-1, with 1 most severe; range in this study was 0-0.17). The ASI asks about frequency of use, how "troubled" a person is by their use and how much they feel the need to seek treatment for it. Note the ASI for stimulants was not included in the analysis because it would overlap with the outcome. Similarly, the HAM-D was low, scoring 3-4 for all groups, where normal is 0-7 and max score is 52. Global impressions range from 1-7, where 1 is normal, 7 severely ill. Here, means were 3-4.6.

This table shows the differences in clinical indicators for the Reduced Use, No Reduced Use and Abstinent groups compared to one another:

	Comparison of different patterns[a]					
	Reduced use vs no reduced use		Abstinence vs no reduced use		Abstinence vs reduced use	
	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P
ASI composite score						
ASI-other drugs	−0.28 (−0.37 to −0.20)	<0.001	−1.18 (−1.40 to −0.97)	<0.001	−0.90 (−1.09 to −0.71)	<0.001
ASI-alcohol	−0.18 (−0.34 to −0.02)	0.025	−0.35 (−0.70 to 0.01)	0.053	−0.16 (−0.52 to 0.19)	0.360
ASI-legal	−0.63 (−1.15 to −0.11)	0.018	−1.66 (−2.44 to −0.88)	<0.001	−1.03 (−1.97 to −0.10)	0.031
ASI-family/social	−0.05 (−0.21 to 0.11)	0.556	−0.43 (−0.71 to −0.16)	0.002	−0.39 (−0.66 to −0.11)	0.006
ASI-psychiatry	−0.18 (−0.42 to 0.05)	0.128	−0.67 (−1.12 to −0.22)	0.004	−0.48 (−1.00 to 0.03)	0.067
Depression severity (HAM-D)[b]	−0.16 (−0.30 to −0.02)	0.022	−0.52 (−0.67 to −0.38)	<0.001	−0.36 (−0.55 to −0.17)	<0.001
Severity of use-self rated[b,c]	−0.24 (−0.31 to −0.16)	<0.001	−0.55 (−0.64 to −0.45)	<0.001	−0.31 (−0.41 to −0.21)	<0.001
Global improvement-self rated[b,c]	−0.33 (−0.40 to −0.26)	<0.001	−0.66 (−0.74 to −0.59)	<0.001	−0.34 (−0.42 to −0.25)	<0.001
Severity of use-observer rated[b,c]	−0.24 (−0.28 to −0.19)	<0.001	−0.61 (−0.70 to −0.52)	<0.001	−0.37 (−0.46 to −0.29)	<0.001
Global improvement-observer rated[b,c]	−0.34 (−0.41 to −0.27)	<0.001	−0.63 (−0.72 to −0.55)	<0.001	−0.29 (−0.38 to −0.20)	<0.001
Severity of seeking primary drug-observer rated[b,c]	−0.30 (−0.36 to −0.23)	<0.001	−0.65 (−0.77 to −0.53)	<0.001	−0.35 (−0.48 to −0.23)	<0.001
Craving for primary drug (BSCS)[b]	−0.58 (−0.73 to −0.42)	<0.001	−1.38 (−1.74 to −1.02)	<0.001	−0.80 (−1.18 to −0.43)	<0.001
Craving for secondary drug (BSCS)[b]	−0.13 (−0.22 to −0.04)	0.006	−0.16 (−0.28 to −0.04)	0.009	−0.03 (−0.18 to 0.12)	0.686

Reduced vs No reduced Abs vs No Reduced Abs vs Reduced

	n	Weighted %[d]	n	Weighted %[d]	n	Weighted %[d]	Adjusted OR (95% CI)		Adjusted OR (95% CI)		Adjusted OR (95% CI)	
Problem-free functioning	101	57.8	128	46.2	351	39.3	1.25 (0.91–1.71)	0.170	3.14 (2.12–4.66)	<0.001	2.52 (1.62–3.93)	<0.001
Stimulants in urine at follow-up[b,e]	13	11.2	120	66.6	550	78.6	0.50 (0.35–0.71)	<0.001	0.03 (0.02–0.07)	<0.001	0.07 (0.03–0.15)	<0.001
HIV risk behavior	89	49.0	154	60.5	532	61.1	1.01 (0.76–1.33)	0.967	0.44 (0.27–0.71)	0.001	0.44 (0.25–0.75)	0.003

In a number of indicators (other substance use, depression, global impression) Reduced Use was better off than No Reduced Use, and Abstinence was better off than both Reduced and No Reduced Use. Note thought, that while Reduced Use didn't have better family/social or psychiatric impact than those who didn't reduce use, Abstinence scored significantly better in both domains that did those who reduced (and than those who didn't). Also, Abstinence were more likely to meet criteria for low HIV risk behaviors and "problem free functioning" than either of the other groups. Abstinent and Reduced Use participants scored the same for cravings for secondary drug. Abstinent was no different the other groups on the ASI for alcohol, which may have been related to low power for this outcome.

CONCLUSION

Among people with MA and cocaine use disorders, those reducing use from more than 5 times per month to 1-4 times per month had fewer problems related to other substance use and overall appeared 'better' after adjustment for baseline scores and characteristics. They also had lower scores on a depression scale but unlike those who achieved abstinence, those with Reduced Use did not have improvement on a more general psychiatric survey, or in family /social function, nor did they achieve low HIV risk behavior or meet criteria for problem free functioning.

COMMENTS

Validity: Does this study say what it says it says?

Internal validity

This study relies heavily on mathematical models to put relationships together. Not being a statistician, it's hard to say if that was done well, but any time modeling is done there is the possibility of drawing relationships that don't exist. The consistency of the findings however, and sensitivity analyses were reassuring. Refreshingly, there is a clear statement that this was exploratory (ie, no hypothesis laid out ahead of time), and that multiple comparisons were not adjusted, so there is the possibility that these relationships are based on chance. Again, however, the consistency of findings argues against that.

29% of participants were excluded because of missing data. This may affect results if treatment dropout differentially affected the relationship between reported improvement and other measures of improvement. It's hard to make a strong case for this.

A strength of this study is that it captures other drug use and mental health symptoms such that it might pick up on the 'whack a mole' phenomenon, of stopping one drug but starting another.

External validity

This population appears relatively healthy – with low scores on multiple scales measures of other substance use and mental health symptoms, and well enough to complete a clinical trial. Because of this, the findings may not apply to populations with greater impairments including those with significant polysubstance use.

Also, this is a study based almost entirely on self report (minus a UDT to help verify accuracy of report of abstinence). Translating this to clinical care might change the validity of the self-report to be more or less accurate, depending on the nature of the provider-patient relationship. If a patient is reporting a greater reduction than they are actually having, the associations here would then not apply.

Finally, the definition of Reduced Use here was a change from high frequency use (5 or more uses in the past 30days) to low frequency (1-4 uses in the past 30days). This is not inherently problematic, but worth noting, as we might all have different ideas of what a lot and a little is. And important to remember is that these impacts can not necessarily be applied to other substances. Notable is that no differences were found in results when MA and cocaine use disorders were separately analyzed.

Final thoughts:

This study is a foray into defining and understanding reduced substance use. It gives us a definition to work with in those using stimulants, and backs up our hunch that reduced use is indeed a positive step. Further understanding and defining outcomes like this will give depth to our work, and ultimately a better understanding of how to balance risks and benefits of treatment. In the mean-time, maybe it will help clinicians shape questions about stimulant use, knowing that getting from 10 times a month to 4times a month seems to come with benefits, and that abstinence likely promises more.