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Synthetic Cannabinoids: Undesirable Alternatives to Natural Marijuana

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Despite decreasing prevalence of use of synthetic cannabinoids (a.k.a.: “Spice” and “K2” drugs) in the US (1), adverse health outcomes associated with use have increased. According to an annual nationally representative survey of high school students in the United States (US), in 2011, 11.4% of high school seniors reported using synthetic cannabinoids; however, prevalence of 12-month use decreased to 5.2% in 2015 (1,2). Despite this reduction in prevalence, reported poisonings related to use in the US have recently skyrocketed from 2,668 in 2013 to 7,369 in 2015 (through November 30th) (3). The majority of poisonings were in New York City (NYC) (3,4), with more than 120 poisonings related to synthetic cannabinoids reported within a single week in April of 2015 (5). While frequency of use or amount used in these poisoning cases is unknown, there have been clusters of poisonings within short periods of time (5), which may imply that some synthetic cannabinoid compounds—or batches or mixtures of compounds—may be becoming more dangerous.

Self-reported emergency treatment access rates also indicate that synthetic cannabinoids are significantly more dangerous than cannabis (marijuana). For example, in a global survey, the relative risk of seeking emergency medical treatment following a use episode was 30 (95% CI: 17.5-51.2) times higher for synthetic cannabinoids compared with marijuana (6). Given continued evidence of harms from synthetic cannabinoid use and the greater risk of harm per episode of use, an improved understanding of motivations for use of both synthetic cannabinoids and natural marijuana is necessary to inform prevention and intervention programs.

The manuscript *Comparison of Outcome Expectancies for Synthetic Cannabinoids and Botanical Marijuana* by Lauritsen and colleagues in this latest issue of *The American Journal of Drug and Alcohol Abuse (AJDAA)* compares self-reported outcome expectancies and reasons for use of natural cannabis (marijuana) and synthetic cannabinoids (7). Participants reported very different reasons for use of synthetic cannabinoids compared to reasons for use of natural marijuana. The most common reasons for marijuana use were reportedly relief of psychological/psychiatric symptoms (25%), relaxation (16%), and relief of bodily pain (12%). In contrast, the authors found that the primary reported reasons for use of synthetic cannabinoids were wider availability compared to natural marijuana (19%), use to avoid screening positive on a drug test (12%), curiosity (12%), perceived legality (10%), and cost (9%).

Thus, whereas the primary reasons for natural marijuana use were traditional reasons for using marijuana (or some other drugs), the most prevalent reasons listed for synthetic cannabinoid use were largely related to circumventing legal issues associated with use or possession of natural marijuana. Like any illicit drug, the illegality of marijuana can sometimes limit availability of the substance, and this may increase the risk of a user resorting to a more dangerous alternative (i.e., synthetic cannabinoids). Others reported using synthetic

cannabinoids because they are (or are perceived to be) legal and others were worried about failing a drug test. These reasons imply that these users preferred real marijuana, but resorted to this more dangerous substance in order to avoid arrest, keep their job or comply with rehabilitation or probationary orders. Others in this sample reported using synthetic cannabinoids because they cost less than marijuana. The finding by Lauritsen et al. that twice as many individuals who used synthetic cannabinoids were unemployed than users of natural marijuana further supports this reason for use.

Lauritsen and colleagues asked participants to type in reasons for use and the authors later categorized and quantified these responses. As the authors acknowledge, while this method is limited as a list of reasons was not available for participants to check off (e.g., as items on lists can serve as reminders), this method allowed participants to type in reasons that perhaps seemed most relevant. The same method was used by Barratt et al. (8) to obtain reasons for first use of synthetic cannabinoids in an Australian online purposive sample, whereas Palamar et al. (9) obtained reasons for use of marijuana using a checklist among a nationally representative sample of high school seniors.

In order to compare Lauritsen et al.'s findings to these existing works, their data needed to be transformed into percentage of respondents, instead of percentage of responses. After conducting that transformation, we find that the reasons for synthetic cannabinoid use were broadly comparable between Lauritsen et al. and Barratt et al., although Barratt et al. found that curiosity was a more important reason (consistent with their emphasis on reasons for first use), low cost did not motivate synthetic cannabis use in Australia (consistent with market differences between Australia and USA), and recreational effects were mentioned in Barratt but did not feature in the top 5 reasons reported by Lauritsen. In contrast, our comparison between Lauritsen's findings on reasons for botanical marijuana use and those of Palamar et al.'s nationally representative sample of high school seniors who reported using marijuana in the last year (also published here in the *AJDAA*) indicated marked differences. Over two thirds of Lauritsen's sample reported using cannabis to relieve psychological symptoms and one third to relieve bodily pain, while only a fifth reported use for enhancing mental state and even less reported use for fun. In the national sample analyzed by Palamar et al., the majority reported marijuana use to feel good or get high, to have a good time and for experimentation or curiosity. Only use for relaxation was comparable between the two groups.

Lauritsen et al. do not attempt to interpret their findings about the reasons for natural marijuana use in relation to previous studies in their paper. A likely explanation, which the authors do note as a limitation of their analysis, is that their sample was biased towards members of botanical cannabis advocacy groups. The majority of their sample report use of cannabis for medical purposes (to relieve psychological problems and bodily pain), including

those who have access to medical-grade cannabis. Such a group is quite different from young adults who use marijuana mainly for recreational purposes, which is perhaps why the sample analyzed by Palamar et al. above and these sampling differences may account for the discrepancies in results.

Another main finding of this paper was that users and non-users of synthetic cannabinoids alike felt that negative outcomes were more likely to occur due to its use, and positive outcomes were less likely to occur, compared to the use of natural marijuana. This is consistent with results from previous studies in which adverse health outcomes related to synthetic cannabinoid use have generally been more serious than those related to natural marijuana use (10-12).

Some of the most interesting findings of Lauritsen et al. are presented in Table 2, which compares descriptive statistics regarding use of synthetic cannabinoids and natural marijuana. Despite the lack of significance tests, differences (or trends) are at least implied for many variables. For example, it appears that those reporting synthetic cannabinoid use were more than four times likely to report decreased use over time than those who only reported use of natural marijuana, and synthetic cannabinoid use was reportedly used only on average of about five days in the last month, compared to natural marijuana use which was reported on average of more than 20 days in the last month. Likewise, synthetic cannabinoids were reportedly used less often per day (when used), which may imply higher potency or perhaps greater dislike. Not a single participant in this study reported use of synthetic cannabinoids but not marijuana, and this corroborates larger studies in which all or almost all synthetic cannabinoid users (e.g., 99.0%, 99.5%) also reported use of natural marijuana (2,12).

Perhaps the most public health-relevant descriptive statistic in Table 2 is that those who reported being approved to receive medical marijuana were three times more likely to report no lifetime use of synthetic cannabinoids. This adds to the argument that many individuals who use synthetic cannabinoids simply resort to use—often due to fear of arrest for possessing an illicit substance. Given the negative outcome expectancies associated with use, it is of concern that so many individuals appear to be willing to suffer the potential adverse effects associated with synthetic cannabinoid use—all to apparently avoid arrest or a positive drug test.

Larger studies, in different populations are needed to investigate this study's findings further. As the authors clearly state, as the recruitment method was via Internet websites, its generalizability is limited. For example, "marijuana" websites tend to have more experienced users, so results derived from those recruited on these sites are likely not generalizable to less dedicated users. In addition, some participants appear to have been recruited from Bluelight.org, an international harm reduction website in which many individuals highly experienced with use of novel psychoactive substances (NPS) post reviews of NPS' effects.

O'Brien et al. (13) have described members of Bluelight and similar websites as cyber-psychonauts: individuals who take drugs with the intention of subjectively exploring their effects, often doing so at home alone, and documenting their experiences to share with other psychonauts online. Psychonauts are often experienced with specific synthetic cannabinoid compounds, but they tend to be knowledgeable and somewhat careful regarding their experimentation. Thus, psychonauts are a different type of user than the typical user in the US (e.g., an urban male who purchases unknown compounds of a particular brand in a bodega or corner store).

In sum, this paper adds to the dearth of literature by comparing synthetic cannabinoids and natural marijuana with regard to outcome expectancies and reasons for use. The results of this paper add to previous studies that have found that most marijuana users prefer natural marijuana compared to synthetic cannabinoids as it tends to be associated with fewer adverse effects (12). While these negative outcomes might explain why most synthetic cannabinoid use is only experimental in nature (2), further research is needed on specific compounds and associated effects. By 2015, at least 134 synthetic cannabinoid compounds had been discovered throughout Europe alone (14), and it is relatively unknown which compounds (and in what amount used) are most associated with specific adverse health outcomes. In addition, the typical user may have no idea what synthetic cannabinoid(s) he or she is smoking or ingesting, regardless of the information on the label. Despite the lack of research and user knowledge about synthetic cannabinoids, epidemiology researchers and users alike tend to simply collapse all synthetic cannabinoid compounds and brands into the simple category of "synthetic cannabinoids." This is problematic, in part, because some compounds can produce very different effects than others. Despite the limitations of collapsing all compounds into a single category, survey results suggest some relative consistency in reported effects and outcome expectancies. Even though researchers and users are often not aware what compounds have been used, research is needed to continue to examine drug effects as well as outcome expectancies and reasons for use in order to guide prevention and harm reduction efforts.

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