and families can understand can be challenging," said Peters. "I've seen this done best by a team of professionals, having a medical professional and a counselor meet with the patient together," she said. If the patient wishes, a family member or loved one can be there as well, and ideally, there should be a case manager to help the patient consider continuing care needs.

Despite the appeal of this comprehensive patient-centered shared decision-making process, it's frequently not possible due to the patient's resources, level of care, type of treatment facility and staffing, and the patient's motivation, said Peters. "Reducing harm, preventing death, and keeping the patient engaged in some kind of care are, of course, key," she said, noting that Hazelden's COR-12 curriculum is helpful for providers in expanding MAT within the framework of 12-Step programs. (For more on COR-12, see "Study finds MAT combined with 12-Step residential treatment is effective," *ADAW*, Sept. 30, 2019; https://onlinelibrary.wiley.com/doi/10.1002/adaw.32492.)

"One piece of education that always needs to be provided is overdose prevention," said Peters. "It's important to offer naloxone to clients with OUD and their families or help them obtain it elsewhere, and to provide education on recognition of signs/symptoms of overdose and how to use naloxone."

SAMHSA recommendations

In TIP 63 from the Substance Abuse and Mental Health Services Administration (SAMHSA), the recommendation is clear: People with OUD should be informed about pharmacotherapy, including all three FDA-approved medications. They should also be informed of risks and benefits of these treatments, and risks and benefits of non-pharmacotherapy treatments, according to SAMHSA. There is also language about informing patients of the "nature of the disorder," which could include requiring the provider to discuss the risks of overdose and recurrent substance use (for TIP 63, go to https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP21-02-01-002.pdf).

"We do not know of any cases by patients with OUD who sought help at a program that did not use MOUD or advise people about the pros and cons of the different treatment approaches. But it's quite conceivable that someone will bring that claim."

Sally Friedman

Legal ramifications

If a patient does not get medications, and overdoses after abstinence-based treatment, is the treatment center liable? "We do not know of any cases by patients with OUD who sought help at a program that did not use MOUD or advise people about the pros and cons of the different treatment approaches," Sally Friedman, vice president of legal advocacy at the Legal Action Center, told *ADAW*. "But it's quite conceivable that someone will bring that claim." •

For more information on:

- statistics on prevalence of use, overdoses and deaths, go to https://www.hhs.gov/opioids/about-the-epidemic/index.html;
- risks of the health consequences of OUDs, go to https://www.uptodate.com/contents/opioid-use-disorder-epidemiology-pharmacology-clinical-manifestations-course-screening-assessment-and-diagnosis, and for a video from the Centers for Disease Control and Prevention on symptoms of OUDs, risks of use and misuse, and treatment, go to https://www.cdc.gov/opioids/patients/index.html;
- options for OUD and evidence-based treatment, that includes both methadone and buprenorphine and different levels of care, go to https://www.psychiatry.org/patients-families/addiction/opioid-use-disorder; and
- how to get and use naloxone to reverse overdoses, go to https://www.drugabuse.gov/publications/drugfacts/naloxone.

Psilocybin: Next to treat depression, OCD and nicotine addiction

First it was the plant, cannabis. How could this be made into a saleable profit-making commodity when it grows in the ground? Witness the marijuana (a chemical from the plant) industry, which lobbied to make sure laws in states that legalized it banned people from growing more than a few plants.

Now it's psilocybin, which comes from mushrooms, which also grow in the ground. As Shayla Love detailed in *Vice* last winter, in "The Race to Patent Psychedelics Is Just Getting Started," investors are very interested in this (and other) psychedelics, which "now appear in patent applications for Philip Morris e-cigarettes, periodontal

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disease, hair loss, weight loss, and food allergies."

There are other companies interested as well. And the National Institutes of Health — mainly the National Institute of Mental Health (NIMH), but most recently the National Institute on Drug Abuse (NIDA) — is issuing grants to study psilocybin as a therapy for various things, including addiction. In fact, Philip Morris is one of the sponsors interested in psilocybin for the treatment of, of all things, nicotine addiction. A grant issued to Matthew Johnson, M.D. (see tweet below) of Johns Hopkins — which recently established a Center for Psychedelic and Consciousness Research — will be on just this (NIDA is not ready to talk about its psychedelics portfolio yet but confirmed this grant). As for NIMH, it is focusing on research using psilocybin to treat depression and obsessive compulsive disorder.

Where there is NIH funding, there will be institutes, research and industry.

And there will also be patents, as the *Vice* article shows. "In many respects, the for-profit psychedelic field is behaving the same as other biotech companies have before — they're taking notice of potentially beneficial compounds and research, and trying to patent "novel" uses to build profitable patent libraries," Love wrote.

This business situation is far from the mind-opening, "mystical" experience psychedelics are supposed to bring to patients.

However, she noted that while researchers are showing promising results, there is concern about "psychedelics becoming price gouged or monopolized through intellectual property."

This business situation is far from the mind-opening, "mystical" experience psychedelics are supposed to bring to patients.

Rick Doblin, the founder and executive director of the Multidisciplinary Association for Psychedelic Studies, is opposed to patents for methylenedioxymethamphetamine (MDMA), which his group has been focused on. The "open science" approach, however, is not one favored by investors. Whether a substance grows in the ground or is a synthetic, people like Doblin think it should be public domain.

Mental health treatment

Two years ago, the American Psychological Association held what was part of a continuing series of discussions on psychedelics as treatment medications for mental health disorders (see "Psychedelics gradually gaining attention as potential mental health therapies," *ADAW*, Aug. 20, 2018; https://onlinelibrary.wiley.com/doi/10.1002/adaw.32073).

This was, however, the first time the talk was of treatment, not the pathology of abusable drugs.

Striking research findings about the potential therapeutic effects of compounds such as MDMA and psilocybin are changing the perspective of some treatment professionals, at least in the mental health arena.

An important development in research regarding psychedelics occurred in 2006 when two large randomized controlled trials conducted in different parts of the country reported significant benefits from use of psilocybin to treat symptoms of anxiety associated with terminal illness. Yet he added that research into MDMA is furthest along in terms of approaching the point at which a formal indication for its use could occur in the next few years.

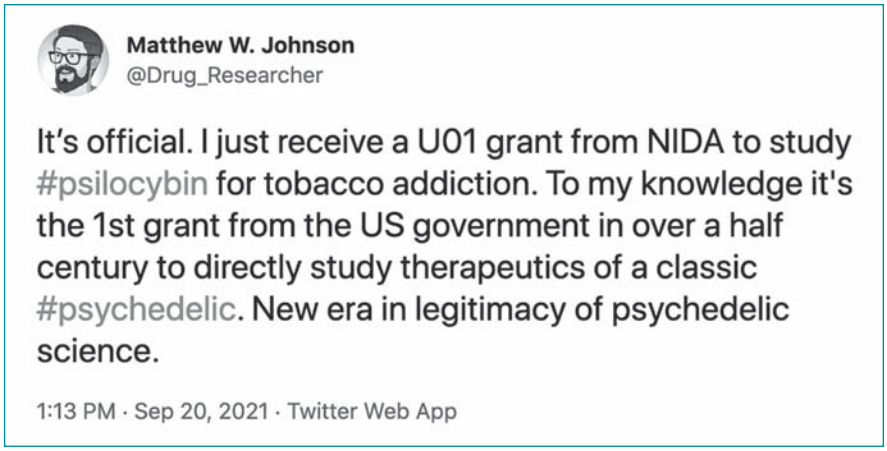
Typically, *ADAW* has covered psychedelic drugs as substances of abuse. They are illegal, for the most part, on Schedule I of the Controlled Substances Act. But clinical trials are continuing.

For example, MDMA has been found effective in reducing PTSD symptoms.

However, the sessions are time-consuming and costly.

Ketamine is another substance — now legal in the form of esketamine (Spravato), approved by the Food and Drug Administration (FDA) in 2019 for treatment-resistant depression (see "Esketamine for depression

The first researcher to get psilocybin grant from NIDA



faces real-world barriers," *ADAW*, Oct. 9, 2019; https://onlinelibrary.wiley.com/doi/10.1002/adaw.32501) — which is a combination of a painkiller and a hallucinogen. Barriers to treatment include the effects of the drug — and the same can be said for psilocybin.

The most obvious effect of psychedelics is dissociation — a detachment from reality. At once therapeutic and potentially dangerous, dissociation is the reason these medications must be taken in a doctor's office, not at home.

The infrastructure needed to administer the therapy requires extra space, clinical staff to monitor patients after administration and a system for buying and storing the Schedule III drug and reporting data to an FDA-mandated Risk Evaluation and Mitigation Strategy.

To use Spravato as an example of what happens when a medication transitions from illegal to legal, look at cost: Spravato costs $590 to $885 per treatment visit, or an estimated $7,080 to $10,620 (excluding physician, facility and other nondrug charges) for the initial two-month treatment episode.

In addition, studying treatments for major depressive disorder (MDD), which affects 10.4% of Americans within a year and 20.6% over a lifetime, is difficult. Spontaneous recovery and placebo effects can mar the cleanness of results, making clinical trials very difficult.

Exercise and improved nutrition are increasing as treatment approaches, but patients with MDD may not be motivated to do them — lack of motivation being a core symptom.

However, unlike other antidepressants, which take six to eight weeks to produce the full effect, esketamine works in hours or days. But it is more difficult for patients to access and clinicians to provide, the authors wrote. It is a self-administered nasal spray, but it must be used at a health care facility. Mental status and vital signs must be monitored for two hours after administration, and no driving is allowed until the next day.

Reimbursement issues

Treating patients with psychedelics would require fundamental changes in the way psychiatrists practice and bill. They generally don't want to be employed by hospitals or participate in large group practices, with one-third solo practitioners and most of the rest in small group practices. This is different from other specialties. In many cases, the patients would have to pay high out-of-pocket prices for treatment.

So the wealthiest patients may be the ones who get access to the treatments — hardly something investors would find distasteful.

But psychedelics clinics operated by nonphysicians could take over, with a possible result in overprescribing, with concomitant diversion and other problems.

Some studies have found that the use of psychedelics is related to higher levels of spirituality, which, psychiatrists say, can lead to greater emotional stability.

Finally, like psychotherapy, "treatment" with psychedelics can lead to greater insight, self-awareness and better relationships with others. They don't need to be just for treating disease, experts say. In addition to helping smokers quit, psilocybin could help them understand themselves better. To many, that sounds worth paying for. •

Non-opioid veterinary sedative xylazine implicated in OD deaths

Xylazine, a veterinary drug for sedation, is not approved by the Food and Drug Administration (FDA) for humans. A central nervous system depressant, it has been used as a toxic adulterant in illicit fentanyl and heroin, and it may increase the risk of fatal overdose. It's not an opioid, so naloxone won't reverse its effects. Now, several states are reporting the presence of xylazine in drug overdose deaths.

In the Sept. 17 issue of *Morbidity and Mortality Weekly Report*, the Centers for Disease Control and Prevention warn of the presence of xylazine in drug overdose deaths, using data from 38 states in 2019.

Among 45,676 overdose deaths in 2019, 1.8% were positive for xylazine and 1.2% were "xylazine-involved" (based on data from the scene).

Xylazine was listed as a cause of death in 64.3% of deaths in which it was detected. Among all xylazine-involved deaths, one or more other drugs, particularly illicit drugs, were also listed as a cause of death, and 98.7% of xylazine-positive deaths and 99.1% of xylazine-involved deaths had fentanyl (including analogs) listed as a cause of death. Cocaine and heroin were listed as a cause of death in 32.1% and 26.0% of xylazine-positive deaths, respectively, and in 29.6% and 28.4% of xylazine-involved deaths, respectively.

Those numbers may be underestimates, the CDC wrote. "Data reviews revealed instances where xylazine presence was noted at the scene of the overdose but not detected on postmortem toxicology," because routine toxicology panels might not even include tests for xylazine.

"No pharmaceutical antidote is specific to xylazine, and immediate supportive care, especially respiratory and cardiovascular support, is critical in the event of an overdose when the presence of xylazine is suspected," according to the CDC. Implementing routine standardized postmortem toxicology testing protocols for xylazine could help better elucidate the role of xylazine in drug overdose deaths. •

For the full report, go to https://www.cdc.gov/mmwr/volumes/70/wr/mm7037a4.htm.