

SCIENCE & TECH SPOTLIGHT:

# OPIOID VACCINES

SEPTEMBER 2019

## WHY THIS MATTERS

The ongoing opioid epidemic in the United States impacts lives on both a personal and national level. More than 10 million people abused opioids in 2017, with more than 47,000 opioid-related deaths — a nearly six-fold increase since 1999. Opioid vaccines could offer advantages over current treatment options..

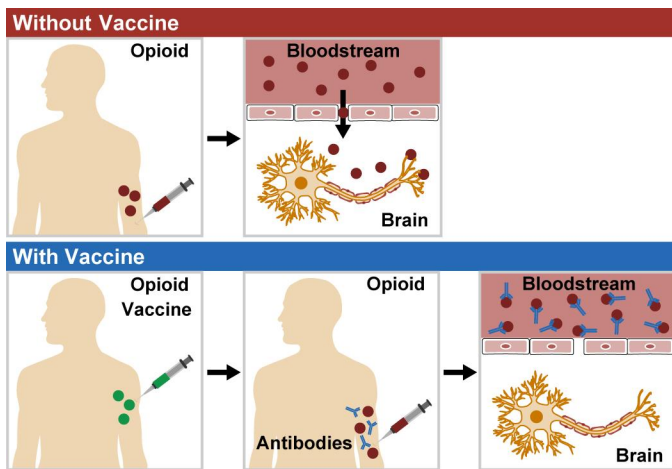
### /// THE TECHNOLOGY

#### What is it?

Opioid vaccines are medical therapies designed to block opioids, such as heroin and fentanyl, from entering the brain or spinal cord, thus preventing addiction and other negative effects. While none are approved for use yet, they could be useful for at-risk individuals, patients in drug recovery programs, or first responders who might accidentally come into contact with deadly opioids that can be absorbed through the skin. This approach offers advantages over some current treatment methods, including requiring minimal medical supervision and no potential for abuse.

#### How does it work?

When opioid molecules bind to receptors in the central nervous system (the brain and spinal cord), they can cause psychotropic effects (e.g., hallucination, euphoria), addiction, and overdose. Opioid molecules have specific chemical structures. Opioid vaccines are designed to trigger an immune response to these structures when injected into a patient. Similar to vaccines for infectious diseases, such as polio or measles, when a patient is treated with an opioid vaccine, their immune system learns to identify the targeted opioid as a dangerous foreign substance so it can respond if that opioid enters the bloodstream in the future.



Source: GAO. | GAO-19-706SP

**Figure 1.** When an opioid enters the bloodstream (top), it crosses into the brain, where it can act on the target receptor to cause psychotropic effects, addiction, and overdose. Opioid vaccines (bottom) trigger the body to create antibodies that bind to opioid molecules and prevent them from entering the central nervous system, thus preventing negative effects.

After the body has learned to target an opioid molecule, it naturally forms antibodies that can bind to it. These opioid-specific antibodies stick to opioid molecules in the bloodstream, forming a unit that is too large to enter the central nervous system.

Without entering the central nervous system, the molecule is not able to produce the negative effects associated with opioids. The antibody-bound opioid will eventually be excreted via urine without harming the exposed individual.

#### How mature is it?

As of 2019, the Food and Drug Administration (FDA) has not approved any opioid vaccines for use. While opioid vaccine studies were initially proposed as early as the 1970s, clinical trials have thus far been unsuccessful. Currently, at least three early-stage clinical trials of potential opioid vaccines are underway, including one that the Walter Reed Army Institute of Research is conducting on a heroin vaccine.

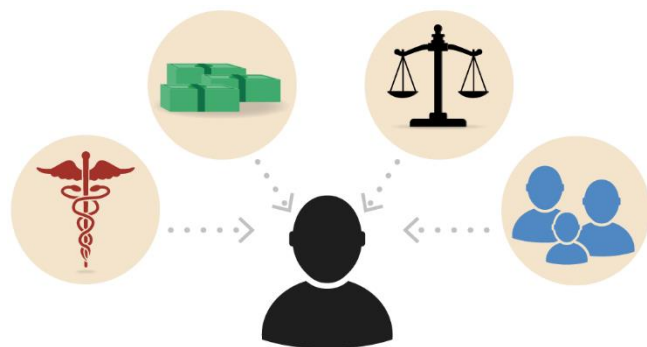
Recently the National Institutes of Health and the National Institute of Allergy and Infectious Diseases released a broad agency announcement to fund the development of opioid vaccines against heroin and fentanyl. This funding is set to begin in August 2020. Other academic researchers continue to publish studies focusing on development and preclinical testing of opioid vaccines.

### /// OPPORTUNITIES

- **Treat at-risk patients.** Unlike some current treatment options, opioid vaccines do not carry the risk of abuse. This could allow for more effective treatment of patients at high risk of abusing another medication, such as methadone.
- **Medical advantages.** The vaccines have a long duration (months to years) of action and require limited medical supervision.
- **Compatible with other therapies.** Vaccines currently in development are targeted to illicit use of opioids such as heroin and fentanyl, and therefore do not interfere with most drug treatment or pain management therapies.
- **Protection against accidental exposure.** Vaccines could be administered prophylactically to individuals at risk of accidental exposure to opioids, such as law enforcement, military, and first responders.

### /// CHALLENGES

- **Lack of broad-based effect.** Current opioid vaccines are designed against the specific chemical structure of each opioid; therefore, multiple vaccines would be needed to provide broad-spectrum immunity. In addition, opioids such as fentanyl can be easily altered into a series of similar molecules called analogs, further complicating vaccine development.
- Less effective in immune-compromised patients. Patients with opioid use disorders often have other infections and altered immune responses that may limit the effectiveness of vaccines.
- Mechanism not well understood. The current biological mechanism of opioid vaccines is not as well understood as that of vaccines for infectious diseases.
- Patient consent. Consent issues could arise for people who might receive an opioid vaccine. For example, some might question a parent's right to compel their child to take a vaccine against a non-infectious agent, or an addicted person's ability to understand potential long-term effects of an opioid vaccine.
- Interference with medical care. If vaccines were developed against legal opioids that are used for pain management, vaccinated individuals would have a reduced risk of addiction but would also be unable to use those medications as effective treatments.
- Insurance and payment. Recent refusals to provide insurance to individuals who carry naloxone, used to counter opioid overdose, highlight the insurance issues surrounding opioid-related treatments. Would insurance cover an opioid vaccine? What might be the baseline costs?



Source: GAO. | GAO-19-706SP

**Figure 2.** Opioid vaccines will likely have a wide range of social and economic effects that could impact the individual.

### /// POLICY CONTEXT AND QUESTIONS

PGS use in forensic analyses is increasing, but PGS results reportedly can be used with only limited confidence under certain circumstances. Some key questions for consideration include:

- In what situations is PGS useful, and when should it be avoided or used with caution?

- What are the gaps in empirical evidence that need to be filled to increase confidence in PGS results for use in criminal or civil trials, and what is the cost and feasibility of addressing these gaps?
- How are federal agencies evaluating and using PGS, and what should the federal role be?
- What additional validation work is needed to expand use of PGS?

### /// SELECTED GAO WORK

- Drug Policy: Assessing Treatment Expansion Efforts and Drug Control Strategies and Programs, GAO-19-535T
- Opioid Crisis: Status of Public Health Emergency Authorities, GAO-18-685R
- Opioid Use Disorders: HHS Needs Measures to Assess the Effectiveness of Efforts to Expand Access to Medication-Assisted Treatment, GAO-18-44
- Opioid Addiction: Laws, Regulations, and Other Factors Can Affect Medication-Assisted Treatment Access, GAO-16-833

### /// REFERENCES

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Janda, Kim D., and Jennifer B. Treweek. "Vaccines Targeting Drugs of Abuse: Is the Glass Half-empty or Half-full?" *Nature Reviews Immunology* 12, no. 1 (2011): 67-72. doi:10.1038/nri3130.

Liang, X., Liu, R., Chen, C., Ji, F., & Li, T. (2016). Opioid System Modulates the Immune Function: A Review. *Translational perioperative and pain medicine*, 1(1), 5–13.

"NOT-AI-19-052: Broad Agency Announcement (BAA): Development of Vaccines for the Treatment of Opioid Use Disorder BAA-DAIT-75N93019R00009." National Institutes of Health. August 01, 2019.

Pravetoni, Marco, and Sandra D. Comer. "Development of Vaccines to Treat Opioid Use Disorders and Reduce Incidence of Overdose." *Neuropharmacology*, 2019, 107662. doi:10.1016/j.neuropharm.2019.06.001.

### GAO SUPPORT:

GAO meets congressional information needs in several ways, including by providing oversight, insight, and foresight on science and technology issues. GAO staff are available to brief on completed bodies of work or specific reports and answer follow-up questions. GAO also provides targeted assistance on specific science and technology topics to support congressional oversight activities and provide advice on legislative proposals.

**Timothy M. Persons, Ph.D., Chief Scientist, [personst@gao.gov](mailto:personst@gao.gov)**

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This document is not an audit product and is subject to revision based on continued advances in science and technology. It contains information prepared by GAO to provide technical insight to legislative bodies or other external organizations. This document has been reviewed by the Chief Scientist of the U.S. Government Accountability Office.