



March 21, 2018

Francis Collins, MD, PhD
Director
National Institutes of Health
1 Center Drive
Bethesda, MD 20892

Dear Dr. Collins:

Opioid use disorder is a rapidly evolving national public health crisis. Dramatic increases in deaths from opioid overdoses have gained widespread attention in the media and scientific community. Infectious diseases (ID) are a substantial and increasing consequence of the opioid epidemic, yet they remain underreported. Hepatitis C virus (HCV) infection rates have increased almost 300 percent, along with increases in new infections with hepatitis B virus (HBV) and HIV. Serious, life-threatening bacterial and fungal infections, including infective endocarditis, are also increasing in those who inject opioids.

The Infectious Diseases Society of America (IDSA), the HIV Medicine Association (HIVMA), and the Pediatric Infectious Diseases Society (PIDS) appreciate that NIH is supporting a wide range of research projects on pain and addiction to provide scientific solutions to help end the opioid crisis. However, more needs to be done to combat the concurrent epidemics of morbid and life-threatening infectious diseases and to address outstanding research gaps in this area. Below, we highlight priority research questions at the intersection of opioids and ID and offer recommendations for the NIH Institutes and Centers (ICs) to address these challenges.

Understand the scope of ID morbidity and mortality as a complication of injection drug use and evaluate best practices for management of people who inject drugs (PWID)

Currently, there is a lack of longitudinal data on morbidity and mortality from life-threatening bacterial and fungal infections associated with injection drug use (IDU) such as infective endocarditis. This is, in part, because there is no tracking system in place for reporting such infections. Aside from anecdotal experiences and scattered reports documenting increasing mortality, the scope of the problem on a national level remains unknown. Along with improved disease monitoring, vital research is needed to understand best practices for management of PWID. This is particularly relevant to care transitions following hospitalization. The existing HIV epidemiological infrastructure provides a good model of a surveillance system for identifying and tracking serious bacterial and fungal complications of injection drug use. To support the development of robust opioid epidemic surveillance, NIH should fund research to determine the continuum of care that occurs with opioid-related infections.

De-couple NIH opioid grant money from OAR HIV requirements

For researchers outside of NIAID, it is difficult to know where to submit IDU-related grants that do not pertain to HIV. The National Institute on Drug Abuse (NIDA) has been reluctant to use its non-HIV funding for hepatitis B and C and other comorbid infectious diseases, and NIAID has not allocated significant funding for opioid-related research. Researchers have been consistently counseled that unless a research protocol related to injection drug use has the word “HIV” in the title, it is unlikely to get funded. The Office of AIDS Research (OAR) coordinates and approves all HIV-related funding for other NIH ICs, which limits research funding available for other ID in opioid-using populations. We

encourage NIH to work with OAR to increase funding flexibility for grant applications that seek to study ID complications of opioid misuse that may not directly link to HIV/AIDS. As one example, there is an urgent need to learn more about effective prevention and treatment modalities of infective endocarditis in individuals who inject drugs given the growing rates of IDU-linked infective endocarditis, and the increased morbidity, mortality, and personal and healthcare-associated costs due to this condition.

Fund implementation research on evidence-based interventions aimed at preventing opioid use disorder-associated infections in addition to HIV and hepatitis C

Historically, HIV and HCV have been the primary drivers of morbidity and mortality among people who inject drugs. As the epidemic is shifting with effective treatments available for both viral infections, more attention needs to be paid to preventable infections associated with injection drug use, including hepatitis B and life-threatening bacterial and fungal infections for which there is little current support. Additional research funding aimed at understanding how to help PWID protect themselves against these injection-related infections is needed.

As federal agencies increase their attention to opioid use disorder, there is a corresponding need to fund implementation research linking patients with providers to identify other evidence-based interventions, including PrEP to prevent HIV infection, improved opioid use disorder treatment, and syringe services programs to prevent viral and bacterial infectious diseases. Studying the use of long-acting glycopeptides for endocarditis may also yield more effective treatments and lower recommended antibiotic doses, thereby improving patient care and decreasing the risk of antimicrobial resistance. More information is needed on the creation (and ultimately, expansion) of models of co-located and fully integrated health care, particularly in resource-limited rural areas – similar to the Ryan White HIV/AIDS Program model of care that evolved in response to the HIV public health crisis. NIH is currently funding K-level grants evaluating the co-located delivery of care. The Institutes and Centers can expand these efforts to an R-level grant via U grant mechanisms that assess how the coupling of medication-assisted treatment and infectious diseases services can effectively and efficiently be combined in different settings.

Increase research on vulnerable and underrepresented groups

It is critical that NIH also funds research on affected underrepresented groups such as incarcerated individuals and rural populations. Health disparities are commonly experienced by persons within the criminal justice system, yet there is limited research on how to best address these issues. Understanding the epidemiology and current standards of care for inmates with infections is essential – especially as incarcerated populations represent a reservoir for continued spread of infections after release. More attention must be paid to the processes of effectively transitioning people with chronic infections like HIV and hepatitis B from jails or prisons to ongoing outpatient medical care, and ensuring uninterrupted access to HIV and HBV medications, curative HCV treatment, and intravenous antibiotics for persons with serious bacterial infections who no longer require hospitalization.

We recommend that NIH fund infectious diseases-focused quality improvement and/or implementation science research on concurrent opioid use disorders in these and other vulnerable populations. It can be difficult for young investigators to find homes for research proposals where the vulnerable patients do not have HIV. By expanding its focus on implementation science, NIH can cast a wider net to capture data from vulnerable and underrepresented populations with opioid-related infectious diseases. Much as NIDA's JJ-TRIALS Cooperative Research Centers utilize implementation science to prevent and treat substance use disorders in the criminal justice system, future NIH-funded studies could facilitate enhanced coordinated treatment between infectious disease clinicians and addiction medicine professionals.

Evaluate the integration of ID treatment and addiction services

As injection-related infections increase, more research is needed on what outcomes can be improved when co-locating or integrating care across disparate systems (e.g., provider training for buprenorphine, bringing methadone into different clinical settings). The integration of ID and addiction medicine is essential to successfully address these questions and the opioid epidemic at large. We recommend that NIH support research that assesses the infectious diseases, public health, and cost-effectiveness of care integration and push federal agencies and patient care facilities to coordinate their resources accordingly.

IDSA, HIVMA, and PIDS appreciate the opportunity to provide recommendations on the use of NIH research funding to target the infectious diseases syndromes associated with the opioid epidemic. We recognize that addressing this growing national emergency will require a collaborative effort by stakeholders, NIH, and other federal agencies. We stand ready to aid NIH as it focuses its research efforts on this topic. Should you have any questions or concerns about these comments, please feel free to contact Jaelyn Levy, IDSA Senior Program Officer for Science and Research Policy, at jlevy@idsociety.org or 703-299-1216.

Sincerely,



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**CC: Eunice Kennedy Shriver National Institute of Child Health and Human Development
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National Institute of Allergy and Infectious Diseases
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute on Drug Abuse
National Institute on Minority Health and Health Disparities**