



# Using Science to Battle Stigma in Addressing the Opioid Epidemic: Opioid Agonist Therapy Saves Lives

In 1965, Dole and Nyswander<sup>1</sup> published the first study of methadone maintenance treatment for opioid use disorder. On the basis of research conducted at The Rockefeller Institute for Medical Research with Kreek, they described the treatment of 22 individuals with methadone for chronic heroin addiction. In this landmark study, they reported the notable findings of craving relief, blockade of the euphoria of subsequent heroin use, and a Lazarus-like effect on psychosocial functioning, with treated subjects resuming schooling, work, and relationships. Over the past 50 years, the evidence base for opioid agonist therapy, first with methadone and now with buprenorphine, has grown exponentially. The lifesaving impact of these medications is so dramatic that the World Health Organization added both to its list of essential medications. Across the globe, opioid agonist therapy has been embraced by countries as diverse as Israel, Iran, and China.

Despite the evidence supporting the use of opioid agonist therapy, only 8% of injecting drug users currently receive treatment, with tremendous variability across the globe ranging from 90% treated in the United Kingdom, compared with 3% in India, and none in Russia.<sup>2</sup> In the United States, even if every treatment slot for methadone and buprenorphine were filled, there would still be an excess of 914,000 individuals with opioid use disorder unable to access treatment.<sup>3</sup> These disparities in treatment access reflect the continued philosophical debate about opioid agonist therapy that has existed since methadone was first discovered.

Mutual help organizations and psychosocial programs sometimes are opposed to medication treatment. In many Narcotics Anonymous groups, individuals receiving pharmacotherapy are restricted from certain types of participation. Disparaging comments by members can be found in online forums, such as “Methadone is a drug, treating

addiction with it is like lightly hosing a fire with gasoline” or we “demand that we draw the line on using drugs and calling it recovery.”<sup>4</sup> Some recovery programs, for example, halfway houses, may not allow participants to be on agonist therapy. Even the language clinicians use, including terms such as “medication-assisted treatment” or “opioid substitution,” implicitly suggest that pharmacotherapy is a corollary to treatment or simply represents replacing one drug with another.<sup>5</sup> In the lay press, this stigma has been further enhanced by articles such as a recent National Public Radio piece entitled “When Drug Treatment for Narcotic Addiction Never Ends,” which provides a description of physicians who provide opioid agonist therapy as “legit drug dealers.”<sup>6</sup>

Contrary to what this rhetoric would suggest, scientifically there is no debate about the efficacy and safety of maintenance treatment with opioid agonist therapy. Treatment outcomes for behavioral interventions alone for opioid use disorder are dismal, with more than 80% of patients returning to drug use.<sup>7</sup> In contrast, treatment with opioid agonists when adequately dosed results in retention rates of 60% to 80%, with only 15% of those treated continuing to use illicit opioids.<sup>7,8</sup> A recent statewide study comparing those who received agonist therapy with those who received behavioral treatments found a 50% reduction in relapse among those treated with pharmacotherapy.<sup>9</sup> Opioid agonist therapy also has been shown to reduce new human immunodeficiency virus and hepatitis C virus infection and overdose death.<sup>10-12</sup>

A growing body of evidence has answered the clinical questions of appropriate dosing, expected treatment duration, and timing of treatment initiation. Numerous studies have confirmed that flexible as opposed to fixed dosing strategies and higher dosages for both buprenorphine and methadone maintenance are more effective.<sup>8,13,14</sup> Adequate treatment duration is a key to success, with tapering strategies of various lengths showing high rates of relapse. Long-term studies of methadone maintenance have demonstrated outcomes that improve with treatment duration. Among those treated for less than 6 months, 67% continue to use heroin compared with only 8% of those treated for more than 4.5 years.<sup>15</sup> A recent study of

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buprenorphine treatment outcomes at 42 months found that 62% of treated individuals were abstinent from opioids, with 30% continuing on opioid agonist therapy.<sup>16</sup> Last, several recent studies have shown that proactive and rapid initiation of opioid agonist therapy, particularly in medically complex patients, can be effective, whereas long wait times for treatment markedly increase the risk of death.<sup>17-19</sup>

Methadone and buprenorphine are not just clinically efficacious, but also cost-effective. Total healthcare costs for patients on methadone maintenance are 50% to 62% lower.<sup>20</sup> Adherence to buprenorphine is associated with lower outpatient, inpatient, emergency department, and total healthcare costs, and buprenorphine treatment reduces annual total healthcare costs by approximately \$20,000.<sup>21,22</sup> A recent cost-effectiveness analysis found that every additional dollar spent on opioid agonist therapy would save \$1.80 and that treating 10% of untreated individuals in New England would generate more than \$550 million in regional societal savings.<sup>23</sup>

Decades of research support opioid agonist therapy as a cornerstone of effective treatment that is crucial in the fight to end the opioid epidemic. Clinicians, medical systems, public health officials, and patients can be assured that opioid agonist therapy's benefits are robust and far outweigh the risks of treatment. Early treatment initiation and adequately dosed long-term maintenance strategies can be fully endorsed, recognizing the benefits for promoting abstinence, reducing overdose, and preventing new human immunodeficiency virus and hepatitis C virus infections. Opioid agonist therapy can be supported as a cost-effective treatment tool that reduces total healthcare spending. Our main barrier in battling this epidemic is the lack of dissemination, understanding, and adoption of this science-based treatment strategy. As we have done in other epidemics, most recently with human immunodeficiency virus/acquired immune deficiency syndrome, the medical community can and must take a leadership role in ensuring our approach is driven by science and not stigma.

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