Analysis of the National Academies of Sciences, Engineering and Medicine Report, "Medications for Opioid Use Disorder Save Lives"

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EXECUTIVE SUMMARY

The National Academies' Report is grounded and is well referenced. It is published at a time when the nation continues to grapple with unceasing opioid related deaths and a changing epidemic.

The strength of the Report is its view that Medication-Assisted Treatment for Opioid Use Disorder should be considered a first line method of confronting the epidemic.

There are other parts of the Report that question the efficacy of using behavioral therapies in conjunction with such medications.

Medication-Assisted Treatment should be a first line opportunity to treat Opioid Use Disorder. One of the most significant aspects of the Report is moving away from the term Medication-Assisted Treatment and describing current practices as being Medication-Based Treatment. The shift in language is significant. More than 15 years ago, SAMHSA and other agencies coined the term Medication-Assisted Treatment, indicating that when medications were used to treat Opioid Use Disorder, clinical support services should be used in conjunction with the medication.
The Report makes a very good point in explaining one of the knowledge gaps in how we have provided access to federally approved medications to treat this disorder.

> Because each medication has a distinct mechanism of action, the most appropriate medication and dosage varies across patients and may vary in the same patient over the course of treatment. The existing medications are very effective, but they are not perfect; for example, evidence gaps remain about how to choose the most effective medication for a particular patient and how best to retain people in treatment, which is itself a significant problem. Moreover, because OUD has complex behavioral and social causes and consequences, it is not yet known which behavioral interventions might be most appropriate to help restore patients to full functionality.

Herein lies the rub. The Report clearly reflects an understanding of the complex nature of the disease in that OUD is simply not a neurological disorder. Like most complex illnesses, it has a number of behavioral components. One might argue this represents a contradiction in the approach of medication being the treatment.

There is a seventh conclusion, which is an integral part of the Report's approach in dealing with this public health crisis. "Current regulations around methadone and buprenorphine, such as waiver policies, patient limits, restrictions on settings where medications are available, and other policies that are not supported by evidence or employed for other medical disorders."

There have also been a number of policy approaches, which argue for the elimination of the SAMHSA/DEA regulations governing OTPs as a method of expanding access to the treatment system. The argument in this case is that the existence of these regulations restricts access to care. This is not the case. The true limitation to access to the availability of OTPs are based on zoning board restrictions, legislative interventions, moratoriums on opening new OTPs and the lack of third-party reimbursement.

The second chapter in this Report discusses how medications are used. There are descriptions about the major medications used to treat this disorder. There is an interesting issue in the section that discusses buprenorphine,

> Because it is a partial agonist, buprenorphine also has less of an effect on respiratory depression, so it has a lower risk of overdose than methadone and other opioids (Dahan et al., 2006), and a therapeutic dose may be achieved within a few days (Connery, 2015).

What is interesting about this section is that it never describes the dosage ceiling effect of buprenorphine. Buprenorphine is an effective medication and people by the thousands have gotten access to such care through DATA 2000 practices. The point here is that in such a scientific paper with so much evidence and so many references, the dosage ceiling limitation of burprenprohine is never discussed.

There is a brief but important section in the second chapter, which talks about patient preferences.

> Patients' preferences about medications to treat OUD are fundamental in determining whether they start and stay on treatment for OUD, but those preferences have yet to be fully explored. Some informative data about patients' medication preferences are available from Rhode Island's correctional system and the state of Vermont. In both populations, methadone is the most common choice among people receiving medication for OUD (between 60 and 70 percent), with buprenorphine preferred by the remainder of patients.

What is not stated in this chapter but is also important, is the difference in how patients get access to certain medications in different environments, not based on patient preference but based on the preference of policymakers, who have no idea about how to clinically treat Opioid Use Disorder. The issue of patient preference, as stated in the Report, is paramount in leading to treatment retention and effective care in the long term.

The bottom-line is that the National Academies Report is thoughtful and comprehensive. It provides an important inflection point in how we treat Opioid Use Disorder in the United States.

The deregulation of the treatment system depends on where you happen to sit. From a public health, harm reduction point of view, which does not necessarily take into account the issues of treating this disorder through clinical methodologies, the issue of removing all barriers makes sense. With regard to how the treatment system actually functions in reality and how patients are treated, with what medications and under what circumstances and what treatment environment, is a completely different matter.

INTRODUCTION

The National Academies' Report is grounded and is well referenced. It is published at a time when the nation continues to grapple with unceasing opioid related deaths and a changing epidemic.

The strength of the Report is its view that Medication-Assisted Treatment for Opioid Use Disorder should be considered a first line method of confronting the epidemic. It also places emphasis on increasing access to such medications in the criminal justice setting and through innovative treatment models.

There are other parts of the Report that question the efficacy of using behavioral therapies in conjunction with such medications. What will be interesting about this particular Report is how SAMHSA and NIDA will respond to the conclusions of this Report, which challenges over 40 years of research and clinical practice. In other words, over four decades of research and clinical practice have clearly made the case of the value of behavioral therapies, working in conjunction with federally approved medications to treat this disorder, producing better patient outcome. The Report seems to contradict this body of evidence.

This analysis will follow the order of the Report's summary findings as a method of easily referencing back to the document.

REPORT SUMMARY

The summary hits on all of the major findings of the Report, "Efforts to date have made no real headway in stemming this crisis, in large part because tools that already exist—like evidence-based medications—are not being deployed to maximum impact." This is a reasonable observation but the Report does not discuss the recent expansion in the use of such medications to treat Opioid Use Disorder over the course of the past 10 years.

MAT AS "FIRST LINE" METHOD OF TREATING OPIOID USE DISORDER

Medication-Assisted Treatment should be a first line opportunity to treat Opioid Use Disorder. One of the most significant aspects of the Report is moving away from the term Medication-Assisted Treatment and describing current practices as being Medication-Based Treatment. The shift in language is significant. More than 15 years ago, SAMHSA and other agencies coined the term Medication-Assisted Treatment, indicating that when medications were used to treat Opioid Use Disorder, clinical support services should be used in conjunction with the medication (SAMHSA TIP #43 – 2005)[(1)][1]. This approach was based on the fact that many of the patients would cross the threshold of treatment facilities such as Opioid Treatment Programs, with a number of comorbidities, including HIV infection, Hepatitis B and C, depression and anxiety disorders in addition to a number of other health problems.

This point was made in an article, which was published in the Heroin Addiction and Related Clinical Problems Journal in February 2019 [(2)], since it referenced many of the research studies and policy statements that supported the value of having behavioral therapies used in conjunction with Medication-Assisted Treatment. The NASEM Report makes a very clear statement in this regard.

> Although Medication-Assisted Treatment (MAT) is a term commonly used to describe treatment programs for Opioid Use Disorder (OUD) that include any of the three opioid agonist or antagonist medications, the committee chose to use the term "medication-based treatment for OUD" rather than MAT throughout this Report. This change in nomenclature aligns with the committee's conceptual framework of OUD as a chronic disorder for which medications are first-line treatments that are often an integral part of a person's long-term treatment plan, rather than complementary or temporary aids on the path to recovery.

Soon after this statement appears, there is a "Summary of Conclusions" in Box S-2, "A lack of availability of behavioral interventions is not a sufficient justification to withhold medications to treat Opioid Use Disorder". In this statement, the National Academies' Report veers away from established evidence and gets into forming an opinion about public policy. One can argue against the backdrop of a major public health epidemic of Opioid Use Disorder in the U.S. that people do need immediate access to care to prevent death. The defining issue is what kind of care is the person going to receive? In the view of the National Academies' Report, the treatment is the medication. In this approach, the Report shifts the paradigm of treatment of having medications as a first line

[1] TIP #43 was recently removed from the SAMHSA website.

of treatment to the issue that medication is the treatment itself. This is a marked departure in how Opioid Use Disorder treatment has operated for more than 50 years.

It is useful to reference NIDA's *Principles of Drug Addiction Treatment,* published in 2012, "effective treatment attends to multiple needs of the individual, not just his or her drug abuse. To be effective, treatment must address the individual's drug abuse and any associated medical, psychological, social, vocational, and legal problems." (3)

It is also useful to reference SAMHSA's Treatment Improvement Protocol #43, which was published in 2005.

> Discussions about whether addiction is a medical disorder or a moral problem have a long history. For decades, studies have supported the view that Opioid Use Disorder is a medical disorder that can be treated effectively with medications, administered under conditions consistent with their pharmacological efficacy, when treatment includes comprehensive services, such as psychosocial counseling, treatment of co-occurring disorders, medical services, vocational rehabilitative services, and case management services. (4)

8 One might reasonably argue that the Report's recommendation is related to increasing access to medication as a public health/harm reduction approach to treating the illness.

INCREASING ACCESS TO TREATMENT IN CRIMINAL JUSTICE SETTINGS

Later on in the Report, there is a recommendation to increase access to the use of medications to treat Opioid Use Disorder in the criminal justice setting. This setting would include drug courts, probation and parole offices and correctional facilities. As many people know, such facilities have been very reluctant to support the use of medications in such settings. There is increasing interest in doing so in Drug Courts and in correctional facilities at present, however, the individuals, who make such policy determinations tend to be conservative. It is uncertain that such conservative policymaking officials would support the increased use of Medication-Assisted Treatment as a first and only line of treatment in criminal justice settings, without insuring that other therapies are in place to support the medications. One might argue that the approach in the NASEM Report will run counter to the effort of trying to increase access to the use of such medications in such conservatively based environments. This approach can also affect groups that are considering the use of federally approved medications to treat this disorder for the very first time. Such entities may reject the use of medications without the availability of clinical support services.

WHAT IS THE BEST MEDICATION TO TREAT A PARTICULAR PATIENT?

The Report makes a very good point in explaining one of the knowledge gaps in how we have provided access to federally approved medications to treat this disorder.

> Because each medication has a distinct mechanism of action, the most appropriate medication and dosage varies across patients and may vary in the same patient over the course of treatment. The existing medications are very effective, but they are not perfect; for example, evidence gaps remain about how to choose the most effective medication for a particular patient and how best to retain people in treatment, which is itself a significant problem. Moreover, because OUD has complex behavioral and social causes and consequences, it is not yet known which behavioral interventions might be most appropriate to help restore patients to full functionality.

Herein lies the rub. The Report clearly reflects an understanding of the complex nature of the disease in that OUD is simply not a neurological disorder. Like most complex illnesses, it has a number of behavioral components. One might argue this represents a contradiction in the approach of medication being the treatment. The statement does reflect reasonable issues with regard to gaps in knowledge. More research is clearly needed to compare the medications and to best understand which medications are used for people at different points of their disease. It is also reasonable to suggest that we do not know which particular kind of counseling or behavioral intervention would work best with such medications for different patients. These are complex questions. On the other hand, we need to be careful about eliminating the use of behavioral therapy when such medications are used to treat this disorder. The field has been criticized in a number of reports when treatment is perceived to be substandard (GAO Report – March 1990 – Methadone Maintenance – Some Treatment Programs Are Not Effective; Greater Federal Oversight Needed) [(5)]. In such cases, the public support of MAT, while still uncertain, could be further compromised. The Report produces some evidence and then makes some leaps into policy but may not fully appreciate the complex nature of what our culture and its institutions will accept in terms of how people are treated. The summary section makes an interesting point in its fourth conclusion.

> Behavioral interventions, in addition to medical management, do not appear to be necessary as treatment in all cases. Some people may do well with medication and medical management alone. However, evidence-based behavioral interventions can be useful in engaging people with Opioid Use Disorder in treatment, retaining

> them in treatment, improving outcomes, and helping them resume a healthy functioning life. There is inadequate evidence about which behavioral interventions provided in conjunction with medications for Opioid Use Disorder are most helpful for which patients, including evidence on how effective peer support is; more research is needed to address this knowledge deficit.

Once again, this is a reasonable conclusion for the Report to make. The problem is that it marginalizes the use of counseling in the public health debate of providing increased access to MAT.

CONFRONTING MAJOR BARRIERS TO THE USE OF MEDICATIONS TO TREAT OUD

There is a seventh conclusion, which is an integral part of the Report's approach in dealing with this public health crisis. "Current regulations around methadone and buprenorphine, such as waiver policies, patient limits, restrictions on settings where medications are available, and other policies that are not supported by evidence or employed for other medical disorders."

This simple statement brings together a number of complex policy debates. One of the debates is the basis for having regulatory oversight of OTPs, which is fairly extensive at the federal and state level versus the lack of oversight for the use of buprenorphine in DATA 2000 practices. These points were raised in the article published in the Heroin Addiction and Related Clinical Problems Journal in February 2019. (6)

There have also been a number of policy approaches, which argue for the elimination of the SAMHSA/DEA regulations governing OTPs as a method of expanding access to the treatment system. The argument in this case is that the existence of these regulations restricts access to care. This is not the case. The true limitation to access to the availability of OTPs are based on zoning board restrictions, legislative interventions, moratoriums on opening new OTPs and the lack of third-party reimbursement.

At the point of writing this analysis, there are just over 1,600 OTPs in the United States. The great expansion over the past 10 years has come through proprietary investment rather than the investment of public funds. This is not an opinion but a matter of fact. There has also been a significant expansion of DATA 2000 practices, which primarily use buprenorphine to treat opioid use disorder.

The issue of not providing adequate third-party reimbursement for the use of all federally approved medications in OTPs, is a major barrier. This has nothing to do with regulation, as much as it has to do with how state legislatures and executive offices within state government move to increase access to important issues like Medicaid reimbursement. There are still 11 states[2] that do not provide any Medicaid reimbursement for Medicaid eligible patients

[2] • Arkansas, Idaho, Iowa, Kansas, Louisiana, Mississippi, Montana, North Dakota*, Oklahoma, Tennessee, Utah.

participating in OTPs. Accordingly, patients have to make "out of pocket payments" to remain in treatment. This is a real barrier to care.

The second chapter in this Report discusses how medications are used. There are descriptions about the major medications used to treat this disorder. There is an interesting issue in the section that discusses buprenorphine,

> Because it is a partial agonist, buprenorphine also has less of an effect on respiratory depression, so it has a lower risk of overdose than methadone and other opioids (Dahan et al., 2006), and a therapeutic dose may be achieved within a few days (Connery, 2015).

What is interesting about this section is that it never describes the dosage ceiling effect of buprenorphine. Buprenorphine is an effective medication and people by the thousands have gotten access to such care through DATA 2000 practices. The point here is that in such a scientific paper with so much evidence and so many references, the dosage ceiling limitation of burprenprohine is never discussed. That might be perceived as a shortcoming given what is known about the pharmacologic properties of the medication.

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This same chapter makes another statement, which has a questionable point of view.

> While buprenorphine maintenance treatment is at least as effective as methadone in suppressing the use of illicit opioids among people who remain in treatment, it appears to be slightly less effective than methadone maintenance treatment at retaining people in treatment. (Mattick et al., 2014).

This is a simple statement that may describe, inadequately, a more complex issue. The first issue is the difference in the pharmacology of the medication. Methadone maintenance, as a pure agonist, does not have a dosage ceiling effect. The dose can be increased to the point where the use of other opioids will not have any particular effect. Buprenorphine as a partial agonist is effective in treating a long-term opioid dependent person to a point. That is why it has a dosage ceiling effect with a better patient safety profile when compared to methadone.

It is also important to reference a report from the Cochrane Collaboration, "Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence (Review)" as authored by Mattick and Breen. This report reviewed 24 randomized clinical studies which were evaluating buprenorphine and methadone maintenance in treating opioid dependence. "Buprenorphine can reduce heroin use compared with placebo although it is less effective than methadone". [(7)]

* North Dakota was using STR funds to pay for Medicaid eligible patients but that is not the same as Medicaid reimbursement, which is why they are included on the list.

Additionally, little is known about what occurs in DATA 2000 practices in addition to the prescription of buprenorphine. An article, "Patterns and Quality of Buprenorphine Opioid Agonist Treatment in a Large Medicaid Program" [8] by Dr. Adam Gordon did a retrospective review of Medicaid claims for DATA 2000 patients in the state of Pennsylvania. A small percentage of claims involved the use of behavioral counseling. OTPs must provide a comprehensive array of services in treating the patient in addition to all of the medications that might be used, depending on reimbursement. One might argue that retention through an OTP, which primarily uses methadone maintenance, might be higher compared to buprenorphine use in the DATA 2000 practice, is also related to the services that are offered to the patients.

REAL WORLD EVIDENCE ON PATIENT PREFERENCES

There is a brief but important section in the second chapter, which talks about patient preferences.

> Patients' preferences about medications to treat OUD are fundamental in determining whether they start and stay on treatment for OUD, but those preferences have yet to be fully explored. Some informative data about patients' medication preferences are available from Rhode Island's correctional system and the state of Vermont. In both populations, methadone is the most common choice among people receiving medication for OUD (between 60 and 70 percent), with buprenorphine preferred by the remainder of patients.

Generally speaking and at present, the use of extended release naltrexone is not preferred by patients with Opioid Use Disorder. What is not stated in this chapter but is also important, is the difference in how patients get access to certain medications in different environments, not based on patient preference but based on the preference of policymakers, who have no idea about how to clinically treat Opioid Use Disorder. The issue of patient preference, as stated in the Report, is paramount in leading to treatment retention and effective care in the long term. The Report makes the point that methadone maintenance has the best overall retention for patients in treatment. The reason for raising this issue is not tot criticize any of the three federally approved medications that are used to treat opioid use disorder. It is simply to point out that the effectiveness of the medication may, at times, be in the eyes of the beholder and the most important beholder is the patient.

INNOVATIVE SETTINGS FOR OUD TREATMENT

The Report provides a number of illustrations about innovative approaches on treating this disorder. It discusses the issue of mobile medication units to provide Medication Based Treatment in addition to group-based treatment and physician/pharmacist collaboration models.

It also references the developing Hub and Spoke Model, which has been championed in Vermont, Rhode Island and Maryland.

CONCLUSION

The bottom-line is that the National Academies Report is thoughtful and comprehensive. It provides an important inflection point in how we treat Opioid Use Disorder in the United States. How this Report gets translated into policy at the federal and state level remains to be seen. As stated earlier in this analysis, there are points that can be challenged, especially with regard to using behavioral interventions in conjunction with medications.

The deregulation of the treatment system depends on where you happen to sit. From a public health, harm reduction point of view, which does not necessarily take into account the issues of treating this disorder through clinical methodologies, the issue of removing all barriers makes sense. With regard to how the treatment system actually functions in reality and how patients are treated, with what medications and under what circumstances and what treatment environment, is a completely different matter. The National Academies Report does have some limitations when it veers away from talking about evidence into making some policy pronouncements. One might argue that the policy pronouncements are divorced from the evidence stated in the Report and there are contradictions in different sections of the recommendations.

Nevertheless, the Report has great value and should be widely read. This is an issue for many countries in the World and the United Nations Office on Drugs and Crime in conjunction with the World Health Organization is looking to promulgate standards of care, which embrace the use of medications and behavioral therapies. Some of the questions raised in the Report will be helpful in providing recommendations to other nations.

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