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A Community's Response to the Opioid Epidemic: Methadone Maintenance and Mercer County

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Abstract

This study analyzes the severity of the opioid epidemic in Mercer County, WV and the use of methadone maintenance treatment for opioid use disorder, positing that the use of methadone further perpetuates the opioid epidemic in the county. Taking into consideration economic and demographic factors, as well present policy implementation and existing literature on the risk of addiction, diversion, and impact of long-term methadone maintenance. This study concludes that the use of methadone is perpetuating the opioid crisis. The perpetuation of the crisis is due to methadone's pharmacological makeup coupled with disparities outlined in literature regarding "Diseases of Despair" which include racial demographics, income, educational attainment and rates of depression and mental illness. While there is no exact date that pinpoints the beginning of the opioid epidemic in the United States, the general consensus is that it began in the mid-1990's when Purdue Pharmaceuticals unveiled their slow-release oxycodone formula Oxycontin[1,2.] According to the Centers for Disease Control, West Virginia leads the nation in overdose deaths. Data released shows poisoning deaths in the state increased from 28.9 per 100,000 in 2010 to 52 per 100,000 in 2016[3]. Mercer County, WV was fourth in the state for opioid related overdose deaths from 2001 to 2015[4]. Director of Community Connects, a Mercer County based non-profit that focuses on the opioid epidemic in the region, Greg Puckett claims that per capita Mercer leads the state in OD deaths [5] and the county is considered to be a high intensity drug trafficking area[6]. Both the state and county have implemented policies aimed at countering the impact of the epidemic. This includes a prescription monitoring program overseen by the state Board of Pharmacy, Substance Abuse Early Intervention targeting youth between the ages of 14 and 17. Both Adult and Teen Court programs, as well as Screening, Brief Intervention, Referral and Treatment (SBIRT), they have also pledged increased investment in treatment centers and the softening of regulation on those who operate Medication Assisted Treatment (MAT) programs. These policies have had a measured effect on the prescription rates of opiate derived pharmaceuticals, from 190.4 per 100 residents in 2007[7] to 119.3 prescriptions per 100 residents in 2016[8]. Yet the question remains: why has the county, like the state, seen an increase in opioid related overdose deaths? In 2015 the county suffered 57.2 deaths per 100,000 persons, which increased to 65.2 deaths per 100,000 persons in 2016[9]. With policies from all levels of government focusing on curtailing the issue, it persists.

1. Literature

In an effort to understand the causes of the opioid crisis researchers have identified possible drivers. It is not uncommon to see companies such as Purdue Pharmaceuticals Inc., the maker of OxyContin (oxycodone) come under fire by government officials and residents. The earliest lawsuits found their way into the legal system in the early 2000s with individuals filing personal injury suits and have since spread to include all levels of government across the nation filing suit in an attempt to recoup the financial losses they have incurred because of the epidemic[10], Mercer County being one of the entities filing suit.

The claim is that manufacturers such as Purdue misled physicians and patients with marketing tactics that downplayed the possibility of addiction and pushed for opioids use as a first line of treatment for chronic pain. Because of these tactics, areas were saturated by the prescription medications causing a public nuisance. These lawsuits also include wholesale distributors. Distributors shipped over 20 million opioids over a period of a decade (2006- 2016) to a southern West Virginia town of 2,900 people in Mingo County. Pharmacies in the Southern West Virginian counties of Wyoming, which borders Mercer County and Logan, where a pharmacy in a town of 1,800 received 1.1 million hydrocodone pills in 2008[11]. However, the claim that pharmaceutical companies could so easily mislead physicians about the addictive nature of opioid derived prescription medications is questionable due to the fact that the medical community has known about the addictive nature of opium for generations.

Another driver is the role that insurance companies have played in the epidemic. Schatman and Weber note that the impact of insurance companies has been their lack of coverage for interdisciplinary pain treatment, including behavioral health therapy[12]. Because of this the number of behavioral health treatment centers has been drastically reduced, this coupled with the companies pushing doctors to prescribe methadone, a highly addictive opioid, for treatment of chronic pain because of its cheap cost, has laid the foundation for disaster. However, in Mercer County, where only 6.7% of the population under 65 does not have healthcare coverage[13], they have access to two behavioral health treatment centers and numerous doctors who provide behavioral health counseling the are covered by their Medicaid insurance. One of the centers offers income-based payment as well, which allows even those who do not have insurance access to their services.

In discussing the drivers directly linked to the healthcare system, there is a thread that links all of them, profit. This includes the physicians, as noted by Manchikanti et. al.[14]. Because of the introduction of new pain management standards, which put priority on prescribing opioids for pain management and the deregulation of opioids by state medical boards, physicians took advantage of the regulatory environment and prioritized profit over patient well-being. Profit-seeking was reflected in the prescription rates in Mercer County. Since 2011 however, the state has increased monitoring of opioid prescriptions. The database is monitored by the Board of Pharmacy and track every prescription written for opioid medications, however there are opportunities for physicians to waive the obligation to submit the information electronically. The state has also set a limit on the number of days for which a physician can write a prescription. As previously noted the prescription rate in Mercer County has fallen considerably to 119 per 100 residents[8].

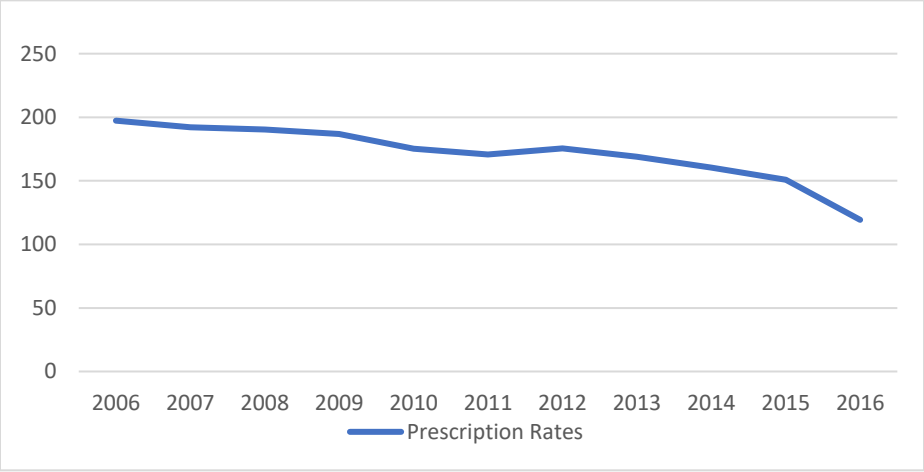

Figure 1. Mercer county prescription rates 2006-2016

Figure 1. Opioid prescription rates per 100 persons in Mercer County, West Virginia per the CDC

However, the epidemic persists and keeps West Virginia among the highest in the nation for opioid related overdoses and deaths.

This study suggests that the use of methadone maintenance treatment (MMT) is aiding in the perpetuation of the opioid epidemic in Mercer County due to the relationship between its pharmacological makeup and social and economic upheaval.

2. History of Methadone Maintenance Treatment

Medication Assisted Treatment (MAT) has gained popularity in the last twenty years, including from the United State Surgeon General, the United Nations and the World Health Organization as an effective way to treat opioid addiction. There are multiple models to the programs, some of which use medications such as Naltraxone. Naltraxone is an opioid antagonist which blocks the receptors which keep the user from achieving a euphoric effect from any other opioid they consume. Another popular medication used in MAT is methadone, an opioid agonist which activates the opioid receptors and was traditionally used to treat chronic pain. Methadone as a pain reliever is also posited as a prescription that helped fuel the epidemic.

Using methadone hydrochloride as a treatment for opioid addiction was first tested by Vincent Dole and Marie Nyswander. The first test was conducted on 22 patients who were addicted to heroin and Dole and Nyswander found that the medication reduced "narcotic hunger" and sufficiently blocked the euphoric effect of heroin[15]. In the decades since their initial research Medication Assisted Treatment (MAT) including Methadone Maintenance Treatment (MMT) or Opioid Treatment Programs (OTPs) have become the industry standard. In 2016 the U.S DHHS published "Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs and Health". In the section Treatment under the subheading Methadone they conclude that "More than 40 years of research support the use of methadone as an effective treatment for opioid use disorder", claiming that abstinence only philosophies are not scientifically supported. "The research clearly demonstrates that MAT leads to better treatment outcomes compared to behavioral treatments alone"[16].

Much of the literature, produced for both peer review and public consumption lean heavily on the fact that methadone keeps the user from experience any symptoms of opioid withdrawal for a period of 36 hours. Symptoms can include muscle aches, sweating, diarrhea and vomiting. But as noted by the National Institutes of Health, while the symptoms are uncomfortable, they are usually not life-threatening[17].

Studies have shown that MMT is more effective in a long-term setting, and the recommended minimum for treatment is 12 months[18]. The general function of MMT is as follows: The patient is admitted to the treatment center, the physician prescribes a dose high enough to stabilize the patient as to stave off symptoms of withdrawal, this is a critical and at time dangerous step which varies from patient to patient. The patient and physician will proceed with a regime to taper or wean the patient off the methadone. However, patients can be on the medication for years and in some cases decades. According to Nora Volkow, director of the National Institutes of Health on Drug Abuse opioid addiction should be viewed as a chronic disease akin to diabetes and some patients may have to be on methadone maintenance for the remainder of their lives[19].

There is controversy that surrounds the use of methadone and the umbrella term "harm reduction" that methadone falls under. It is easy to equate harm reduction with enabling. Clean needle exchange programs are a good example of this. However, while clean needle programs can be used as a tool to build relationships with addicts that may facilitate them to move into to treatment, they do not attempt to hide what they are doing. They are supplying clean needles to addicts who use illicit drugs intravenously. Philippe Bourgois notes the language change that takes place when discussions of methadone arise "The 'dope' become 'medication' the 'addict' became a 'patient' and 'addiction' became 'treatment'"[20]. In his view this is an attempt to legitimize the use of an addictive substance to treat addiction a form of social control and enforced dependency. It is important to question whether the use of methadone is simply a social band aid if the main contributing drivers are social and economic depression and the influx of addictive opiates into vulnerable populations.

3. Diseases of Despair

The second school of thought regarding the main causes of the opioid crisis are the underlying social and economic issues. In their seminal research Anne Case and Angus Deaton examined the growing mortality rate of middle-aged, white non-Hispanic Americans. They noted the increase in suicides, chronic liver disease, and drug and alcohol poisonings, highlighting the increasing deaths associated with the opioid crisis, deeming these issues as "Diseases of Despair"[21]. Counties with the lowest levels of social capital have suffered the highest rates of overdoses and the diseases increase as economic status decreases[22]. The Appalachian Regional Commission (ARC) applied this research to Mercer County, concluding that the region faces disparities related to educational attainment, unemployment, income, and multiple health outcomes[23]. When applying these factors to the use of methadone in treatment concerns arise. The lower than average per capita income may fuel diversion of the methadone, while the higher rate poverty, as well as the dipartites in income, educational attainment, and increased feelings of hopeless, isolation, and depression

underpin the abuse of the prescription. Methadone is a full agonist synthetic opioid akin to morphine and is therefore highly addictive and subject to abuse.

4. Demographic information of Mercer County

Mercer County is located in Northern Central Appalachia and is considered to be an "at risk" economy with eight distressed areas[24]. Per capita income is lower than the national average of $49,246, with an income of $34, 063. Mercer County has a poverty rate of 21.1% and an unemployment rate of 6.5%, higher than the nation average of 4.9%[25]. Education attainment in lower in Mercer in comparison to the nation average. The national average of attainment of a high school diploma or more is 87%, while the average in Mercer County is 83%. Despite access to two four-year institutions (Bluefield State College and Concord University) within Mercer County and a four-year institution less than a half mile over the state line in Virginia (Bluefield College) Mercer also has a lower average completion rate for those who obtain bachelor's degrees, with an average of 19.5% compared to the national average of 30.3%[26]. According to WV DHHR Mercer County is 91.1% non-Hispanic White, with a Medinan age of 42.5 years old. The depression rate in Mercer County is significantly higher than that of the state with Mercer reporting a depression rate of 26% compared to the state average of 21.6%. With 8% of the county population reporting at least one major depressive episode in the past year. Reports of general mental illness are also higher in Mercer County, with a reported rate of 23.2% compared to the state average of 21.7%. It is also important to note the significantly higher rate of suicide in Mercer County of 25.1 per 100,000 persons compared to the state 17.4 per 100,000 persons[27].

5. Pharmacological and Regulatory Information on Methadone

5.1 Addiction and Withdrawal

"This is why I've spent half a lifetime on mmt, outta fear of this shit, literally no other reason. YEARS of paws tho, wtf."

This is a statement made by Reddit user C21H27NO in response to a post about a user who had been out of methadone treatment for 2 years and is still dealing with Post-Acute Withdrawal Symptoms or PAWS. The symptoms associated with PAWS are psychological and mood related. According to the American Addiction Centers, PAWS is not an official medical diagnosis and is a controversial topic in the medical industry[28]. But for those going through PAWS, the symptoms are as real as the physical effects of acute withdrawal. Proponents of MMT readily make the claim that acute withdrawal from methadone is not as severe as that of heroin, however Gossop and Strang state that this claim goes against the experience of those going through withdrawal which showed that patients going through in-patient gradual methadone reduction reported more severe withdrawal responses than those going through heroin withdrawal in both the acute phase and the recovery phase[29]. The duration of methadone withdrawal also exceeds that of other opioids[30]. This is contributed to the long half-life of methadone which can range from 15-55 hours in comparison the half-life of heroin is 0.1-0.25 hours[31].

5.2 Regulation and Oversight

Both the Federal and State government require MMT clinics to be registered with SAMHSA and the WV DHHR. West Virginia requires each MMT clinics to have an onsite licensed physician, who must conduct an initial health screening before a prescription can be administered. Because of the complexity of methadone treatment including half-life, metabolization, and previous opioid use, the physician must construct a treatment plan specific to each patient. There are two phases of methadone treatment which policy is constructed around. Phase 1 includes patients who have been in compliance with treatment for a duration less than 12 months, Phase 2 includes patients who have been in compliance with treatment for longer than 12 months. For patients in Phase 1 WV law dictates that they should receive a minimum of 4 hours of behavioral therapy per month, with 1 hour of that in individual therapy with a counselor who holds a minimum of a master's degree in human services. Patients in Phase 2 are required to attend a minimum of 1 hour of therapy a month. Phase 1 patients are required to undergo two randomly timed drug screenings per month, with patients in Phase two are required to submit 1 random drug screening a month[32].

Initial dosing of methadone is the most dangerous phase for patients and it is during this time that a high number of deaths occur, because of this WV DHHR advises that a patients initial dose should be based on risk of toxicity and opioid abstinence, with the initial dose being no more than 30 mg and the dosage the first day being no more than 40 mgs unless the physician deems a high dose necessary. with a dosage increase of 5-10 mg per day until stabilization is achieved with the optimal dose range between 60-120mg per day[33].

The state outlines prescription dosing rate for patient who have missed treatment days, requiring patients who have missed 3 or more to have administration of medication halted until the physician can reassess the patient's needs[32]. However, discharge from the program is completely up to the clinic and patients can be discharged for a variety of reasoning including positive drug screenings, missed days, and behavioral issues and criminality. Studies have found that a majority of MMT patients are discharged within the first 12 months of treatment and that there is an increased risk of overdose for those prematurely discharged[34].

Unlike other Schedule II opiates, methadone administered in a MMT setting is not required to be reported to the state PDMP, this is due to federal regulations regarding an increased level off privacy for those in OTPs[35].

5.3 Tapering and Detox

Although the state advises that optimal dose range for stabilization can reach 120 mg, it has been shown that doses that exceed 100 mg/day can lead to an increased craving for illicit drug use[36]. Long-term enrollment in MMT can also lead to an increase in methadone tolerance and therefore daily dosage[37] and those receiving between 60-100 mg are less likely to have sustained success in tapering[38]. Local officials in Mercer County highlight that the absence of policy requiring the initiation of tapering is an issue and their concern for profit-driven prescribing[5].

5.4 Diversion and self-treatment

West Virginia State code as well as Federal code define take home allowances for patients enrolled in MMT programs. During the second 90-day period of treatment patients are allotted 1 day of medication, plus one additional day for clinic closure, such as Sunday closures. After 12 months of compliance patients may receive 2 weeks of take-home supply[39]. Diversion of methadone has been a topic of controversy surrounding the practice and when there were methadone clinics purposed for Mercer County, there was substantial backlash from the community[40,41]. Diversion of the medication is a prime concern for community members and in 2006 there were an estimated 400 patients traveling from Mercer County to the clinic in Raleigh County to receive treatment[41]. Patients can sell their take-home doses to those looking to achieve euphoric effects or those who are self-treating for opioid addiction. It has been found that methadone maintenance is the largest contributor to illicit methadone use[42,43,44].

6. Discussion

Because of the significant disparities in per capita income, educational attainment, poverty, and depression as well as the racial makeup of the area, Mercer County is more susceptible to drug abuse than other parts of the state and nation. Due to the addictive nature of methadone, the increased chances of overdose in the initial treatment stage and opiate naïve persons due to the long-half life and differences in metabolic processing, the use of methadone in treating OUD can be counterintuitive to the efforts in curbing the opioid crisis there.

Even with the moratorium on new methadone clinics, West Virginia has recently filed a successful Medicaid exemption that will allow methadone used for OUD to be covered by the insurance signaling that the state is willing to expand access to the medication.

The use of methadone of OUD has been hailed as the gold standard for MMT, however there are alternatives available that may be superior. Another popular medication utilized in opioid dependence therapy is Buprenorphine (Suboxone). BUP is a partial opioid agonist in comparison to methadone which is a full opioid agonist. Typically prescribed in partnership with naloxone, BUP has been shown to be just as effective as methadone in treating OUD, but it has certain properties that make it superior to the overall health and positive outcome of patients.

Because BUP is a partial agonist it is less severe than methadone and when administered along with naloxone, patients report that it produced less craving for illicit drug use such as heroin. The pharmacology of the medication also blocks the euphoric effects of other opioids more effectively than methadone and has a lower chance of overdose due to the ceiling effect or maximum effect achievable leading to a lower chance of respiratory depression[45].

Patients also claim that BUP is easier to withdrawal from, suffering less severe physical symptoms than methadone and the tapering regime for BUP can be done in a much shorter time period[46].

Another conversation that is taking place is the potential use of medical marijuana in treating OUD. Philippe Lucas discusses the rationale behind the use of marijuana citing the increased public health due to the substitution effect in the context of harm reduction and an increase in public safety with studies showing areas that have legalized the medication have shown a decrease in homicides, violent crimes, and vehicle related fatalities[47].

In examining the policy surrounding MAT, Mercer County is limited to the policy they can enact, having to rely on and implement state and federal policies. However, nonprofits such as Community Connections can utilize their resources to better understand the local impact that methadone is having on the community and should use this information to inform policy makers on the state and federal level. Because of the poverty rate in Mercer County, the concern for diversion is higher than other wealthier suburban areas in the country. This is driven by not only the need to secure income, but also the altruistic nature of community members who may divert their take home doses to those they know are suffering from withdrawal symptoms from illicit substance use but cannot afford MAT themselves. Because of this and the increased cravings that may come with sustained methadone maintenance, urine testing should be more frequent among patients with take-home privileges than regulation currently calls for.

The county should also push for more oversight in the areas of tapering and length of retention in treatment programs. While it is understandable that some patients may need to be on maintenance longer than most, there should be an appeal process in which the clinic is required to give a comprehensive reason why a patient needs to be enrolled in the process longer than 24 months. This process may cut down on concerns of profit motives expressed by county officials and ensure the patient is receiving the best possible chance of achieving detoxification and abstinence.

Another area of focus should be the privacy levels of patients enrolled in MAT and if there can be a balance struck between patients and regulators. Methadone dispensed in the clinic setting should be reported to the state PDMP to aid regulators in understand the scope and saturation of the medication in the local area. This would also aid law enforcement and state agencies in tracking diversion and overdose rates.

Clinics should also have to justify discharging patients that have not gone through detoxification and patients should not be able to be discharged due to missed payments. The ability to discharge patients, especially those who have been in treatment for longer than 12 months should be subject to increased oversight due to the increased chance of relapse and overdose.

Speaking on more structural changes that should ne entertained, the state should heavily consider increasing the minimum wage as an increase has been shown to improve physiologic well-being and job satisfaction, and a lower rate of income inequality leading to lower rates of depression and a reduced feeling of isolation and hopelessness[48].

7. Conclusion

Methadone Maintenance Treatment has been shown to have numerous benefits for those suffering from OUD. This includes a sense of reintegration into personal and professional relationships, a reduced use of illicit opioids such as heroin and prescription medications, and the ability to stave off withdrawal symptoms.

However, the literature also shows that there are drawbacks to the utilization of the medication including increased tolerance in patients enrolled in long term maintenance, increased cravings exhibited in patients on higher doses, as well as the public safety risks due to diversion. The extended withdrawal symptoms of methadone when compared to other mediations utilized in MMT is also a concern if the goal of MAT is in fact abstinence and not just retention in the program, which some local officials doubt. The underlying structural socio-economic disparities enhance the risk of abuse and diversion, even if that diversion is altruistic in nature. While Mercer County does not have a methadone clinic located within its territory, the clinic in Raleigh County is regularly attended by Mercer County residents and therefore Mercer is directly impacted by its use in OUD treatment.

This study is not making the argument that methadone is the main driver of the opioid crisis in Mercer County or even that there are not other factors which make the issue more severe. But, the use of methadone seems counterintuitive and the risks seems to out weight the long-term benefits, if the goal is in fact a healthy, stable population.

The prospect of utilizing medical marijuana in OUD is promising and other, less severe medications already approved for treating OUD such as buprenorphine have been shown to be just as effective as methadone is treatment with a decreased risk of overdose and overall higher patient satisfaction. Further research on the impact of phycological disorders and treatment for OUD is needed.

8. References

1. HHS, U.S. 2018. *opioids.* September 19. https://www.hhs.gov/opioids/about-the-epidemic/index.html.

2. Jangi, Sushrut. 2016. "Why did the opioid epidemic get so bad?" *The Boston Globe*. March 29. Accessed October 20,2018. https://www.bostonglobe.com/magazine/2016/02/29/how-did-opioid-epidemic-get-bad/qkb8DnUzwYLjWSQsZgGpqJ/story.html.3. “Opioid Overdose.” 2017. *Centers for Disease Control and Prevention*. https://www.cdc.gov/drugoverdose/data/statedeaths.html (December 3, 2018). 2010-2016 Increases

4. Bureau of Public Health, and Rahul Gupta. West Virginia Overdose Deaths Historical Overview 2001-2015 *West Virginia Overdose Deaths Historical Overview 2001-2015*. Charleston, WV: Bureau for Public Health. https://dhhr.wv.gov/oeps/disease/ob/documents/opioid/wv-drug-overdoses- 2001_2015.pdf 5.Interview with County Commissioner and Director of Community Connections, May 24, 2018

6. Department of Justice. 2018. “HIDTA Counties by State.” *National HIDTA Assistance Center*. http://www.nhac.org/news/HIDTA_Counties.htm (December 3, 2018).

7. “Opioid Overdose.” 2017. *Centers for Disease Control and Prevention*. https://www.cdc.gov/drugoverdose/maps/rxcounty2007.html (December 3, 2018).
Interactive Map

8. “Opioid Overdose.” 2017. *Centers for Disease Control and Prevention*. https://www.cdc.gov/drugoverdose/maps/rxcounty2016.html (December 3, 2018).
Interactive Map

9. Goff, Mike, Nathan Wood, and Mohsin Mahar. 2017. West Virginia Board of Pharmacy Prescription Opioid Problematic Prescribing Indicators County Report Mercer County *West Virginia Board of Pharmacy Prescription Opioid Problematic Prescribing Indicators County Report Mercer County*. https://dhhr.wv.gov/vip/county-reports/CountyReports/Mercer_PfS County Reports_Final.pdf.

10. Haffajee, Rebecca L., and Michelle M. Mello. 2017. “Drug Companies’ Liability for the Opioid Epidemic.” *New England Journal of Medicine*377(24): 2301–5. https://www.nejm.org/doi/full/10.1056/NEJMp1710756.

11. Eyre, Eric. 2018. “Drug Firms Shipped 20.8M Pain Pills to WV Town with 2,900 People.” *Charleston Gazette-Mail*. https://www.wvgazettemail.com/news/health/drug-firms-shipped-m-pain-pills-to-wv-town-with/article_ef04190c-1763-5a0c-a77a-7da0ff06455b.html (December 4, 2018).

12. Schatman, Michael, and Lynn Webster. 2015. “The Health Insurance Industry: Perpetuating the Opioid Crisis through Policies of Cost-Containment and Profitability.” *Journal of Pain Research*8: 153–58. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4370920/.

13. US Census Bureau. 2014. “Search Results.” *Census Bureau QuickFacts*. https://www.census.gov/search-results.html?q=mercer county, wv health insurance coverage&page=1&stateGeo=none&searchtype=web&cssp=SERP&_charset_=UTF-8 (December 4, 2018).

14. Manchikanti, Laxmaiah et al. 2012. “Opioid Epidemic in the United States.” *Pain Physican*15: ES9–ES38. http://www.painphysicianjournal.com/current/pdf?article=MTcwNA==&journal=68.

15. Dole, Vincent P., and Marie Nyswander. 1965. “A Medical Treatment for Diacetylmorphine (Heroin) Addiction.” *Jama*193(8): 646–50.

16. “Treatment.” 2016. In *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, Health*, Washington, DC: U.S Department of Health and Human Services. essay, 4–22-4–23.

17. Geneva: World Health Organization. 2009. “Clinical Guidelines for Withdrawal Management and Treatment of Drug Dependence in Closed Settings.” *Withdrawal Management*4. https://www.ncbi.nlm.nih.gov/books/NBK310652/.

18. Walsh, Lynn. 2015. “Methadone.” *Stages of Community Readiness | SAMHSA*. https://www.samhsa.gov/medication-assisted-treatment/treatment/methadone (December 4, 2018).

19. Glenza, Jessica. 2016. “Russia's 'Cold Turkey' Approach Highlights Global Divide over Drug Treatment at UN.” *The Guardian*. https://www.theguardian.com/world/2016/apr/20/ungass-russia-drug-treatment-heroin-methadone (December 4, 2018).

20. Bourgois, Philippe. 2000. “Disciplining Addictions: The Bio-Politics of Methadone and Heroin in the United States.” *Culture, Medicine and Phychiatry*24(2): 165–95. Disciplining Addictions: The Bio-politics of Methadone and Heroin in the United States.

21. Case, Anne, and Angus Deaton. 2015. "Rising Morbidity and Mortality in Midlife among White Non-Hispanic Americans in the 21st Century." *Proceedings of the National Academy of Science of the United States of America*112(49): 15078–83. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4679063/.

22. Dasgupta, Nabarun, Leo Beletsky, and Daniel Ciccarone. 2018. "Opioid Crisis: No Easy Fix to Its Social and Economic Determinants." American Journal of Public Health108(2): 182–86. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5846593/.

23. Appalachian Regional Commission et al. 2017. Appalachian Disease of Despair *Appalachian Disease of Despair*. NORC. https://www.arc.gov/assets/research_reports/appalachiandiseasesofdespairaugust2017.pdf.

24. Appalachian Regional Commission. 2018. County Economic Status and Number of Distressed Areas in West Virginia, Fiscal Year 2019 *County Economic Status and Number of Distressed Areas in West Virginia, Fiscal Year 2019*. https://www.arc.gov/images/appregion/economic_statusFY2019/CountyEconomicStatusandDistressAreasFY2019WestVirginia.pdf.

25. Appalachian Regional Commission. 2017. "Socioeconomic Data: Mercer County, West Virginia." https://www.arc.gov/reports/socio_report.asp

26. Appalachian Regional Commission. "Education – High School and College Completion Rates, 2012–2016." *Subregions in Appalachia - Appalachian Regional Commission*. https://www.arc.gov/reports/region_report.asp?FIPS=54999&REPORT_ID=72 (December 4, 2018).

27. "Mercer County: Behavioral Health Epidemiological County Profile." 2016. https://dhhr.wv.gov/bhhf/Sections/programs/ProgramsPartnerships/AlcoholismandDrugAbuse/Documents/County EPI Profiles 2017/2016 Mercer County Profile.pdf

28. Crane, Marisa. "Post-Acute-Withdrawal Syndrome (PAWS): An In-Depth Guide." *American Addiction Centers*. https://americanaddictioncenters.org/withdrawal-timelines-treatments/post-acute-withdrawal-syndrome (December 4, 2018).

29. Gossop, Michael, and John Strang. 1991. "A Comparison of the Withdrawal Responses of Heroin and Methadone Addicts during Detoxification." *British Journal of Psychiatry*158(05): 697–99. https://www-cambridge-org.proxy177.nclive.org/core/services/aop-cambridge-core/content/view/D6AB3D1564A31A4B466F27E2835105E3/S0007125000023837a.pdf/comparison_of_the_withdrawal_responses_of_heroin_and_methadone_addicts_during_detoxification.pdf.

30. "How to Get off Methadone." *American Addiction Centers*. https://americanaddictioncenters.org/withdrawal-timelines-treatments/methadone (December 4, 2018).

31. ARUP Laboratory. 2017. "Drug Plasma Half-Life and Urine Detection Window." https://www.aruplab.com/files/resources/pain-management/DrugAnalytesPlasmaUrine.pdf

32. West Virginia Department of Health and Human Services. 2018. "CHAPTER 504 SUBSTANCE USE DISORDER SERVICES." Methadone: Page 15-20 https://dhhr.wv.gov/bms/Provider/Documents/Manuals/Chapter%20504%20Substance%20Use%20Disorder%20Services%20Manual%20FINALwithoutwatermark.pdf

33. Berry, James H. 2013. "Medication Assisted Treatment: Tools of the Trade." Page 27 http://dhhr.wv.gov/bhhf/Documents/2013 IBHC Presentations/Day 2 Workshops/MAT- WVIBH 2013.pdf

34. Reisinger, Heather Schacht et al. 2009. "Premature Discharge from Methadone Treatment: Patient Perspectives." *Journal of Psychoactive Drugs*41(3): 285–96.

35. Email Correspondence with Michael Goff, Executive Director of the West Virginia Board of Pharmacy, October, 24,2018

36.Curran, H. Valerie, Judi Bolton, Shamil Wanigaratne, and Ciaron Smyth. 1999. "Additional Methadone Increases Craving for Heroin: A Double-Blind, Placebo-Controlled Study of Chronic Opiate Users Receiving Methadone Substitution Treatment." *Addiction*94(5): 665–74.

37. Gutwinski, Stefan et al. 1999. "Opioid Tolerance in Methadone Maintenance Treatment: Comparison of Methadone and Levomethadone in Long-Term Treatment." *Addiction*94(5): 665–74. https://0-search.proquest.com.wncln.wncln.org/docview/199658703?accountit-8388.

38. Nosyk, Bohdan et al. 2012. "Defining Dosing Pattern Characteristics of Successful Tapers Following Methadone Maintenance Treatment: Results from a Population-Based Retrospective Cohort Study." *Addiction*107(9): 1621–29.

39. *MEDICATION-ASSISTED TREATMENT - OPIOID TREATMENT PROGRAMS*. 2017. (http://www.pdmpassist.org/pdf/2017 WV REG TEXT 430992 (NS).pdf).
West Virginia DEPARTMENT OF HEALTH AND HUMAN RESOURCES , Page 57
40. Toler, Tammie. 2014. "PRINCETON - A Proposed Mercer County Methadone Clinic Will Officially Go up for Debate Nov. 28 in Charleston." *ptonline.net*. https://www.ptonline.net/news/local_news/princeton-a-proposed-mercer-county-methadone-clinic-will-officially-go/article_8a87ec79-8da5-59b3-a56e-5ae96da0ba27.html (December 4, 2018).
41. Toler, Tammie. 2006. "Methadone Plan Meets with Praise, Protest." *Bluefield Daily Telegraph*. https://www.bdtonline.com/archives/methadone-plan-meets-with-praise-protest/article_9200bf13-9108-5d0d-b0b9-18c1c311dfd5.html (December 4, 2018).
42. Spunt, Barry, Dana E. Hunt, Douglas S. Lipton, and Douglas S. Goldsmith. 1986. "Methadone Diversion: A New Look." *Journal of Drug Issues*16(4): 569–83.
43. Weppner, Robert S., and Richard C. Stephens. 1973. "The Illicit Use and Diversion of Methadone on the Street as Related by Hospitalized Addicts." *Journal of Drug Issues*3(1): 42–47.
44. Duffy, Paul, and Adam John Mackridge. 2013. "Use and Diversion of Illicit Methadone – under What Circumstances Does It Occur, and Potential Risks Associated with Continued Use of Other Substances." *Journal of Substance Use*19(1-2): 48–55.
45. Hill, Duncan R. 2015. "A Comparison of Methadone and Buprenorphone-Naloxone as Opioid Substitution Therapy: the Patient Perspective in NHS Lanarkshire." *Journal of Substance Use*20(3): 168–77.
46. Ling, Walter, Larissa Mooney, and Matthew Torington. 2012. "Buprenorphine Implant for Opioid Addiction." *Pain Management*2(4): 345–50.
47. Lucas, Philippe. 2017. "Rationale for Cannabis-Based Interventions in the Opioid Overdose Crisis." *Harm Reduction Journal*14(1).
48. Leigh, J. Paul. 2016. "Could Raising the Minimum Wage Improve the Public's Health?" *American Journal of Public Health*106(8): 1355–56.