Task 3: Annotated Bibliography

April Bounacos

Old Dominion University

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Dr. Sharon Silverberg

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Oesterle, T. S., Thusius, N. J., Rummans, T. A., & Gold, M. S. (2019). Medication-Assisted Treatment for Opioid-Use Disorder. *Mayo Clinic Proceedings*, *94*(10), 2072–2086. https://doi.org/10.1016/j.mayocp.2019.03.029

This article reviews the three primary medications used in treating people with opioid-use disorders such as methadone, buprenorphine, and naltrexone. The article states that the clinical efficacy of buprenorphine (Suboxone) for the treatment of opioid-use disorder has been well established and it is associated with improved rates of sobriety, decreased criminal activity outcomes, and reduction on accidental overdoses. One study of individuals randomly assigned to either methadone, buprenorphine, or naloxone showed that 33.2% had achieved 5-year abstinence from heroin, which was better than the "no treatment" group. It is suggested that even though MAT is proven to help, it is being underused in our society and we should be using any tool at our disposal to help fight this epidemic. I think that this article is relevant to my evaluation because it helps to give me an idea of what other studies have shown on how Medication-Assisted Treatment is working in our society.

Ghanem, N., Dromgoole, D., Hussein, A. M., & Jermyn, R. T. (2022a). Review of medication-assisted treatment for opioid use disorder. *Journal of Osteopathic Medicine*, *122*(7), 367–374. https://doi.org/10.1515/jom-2021-0163

This article was written to educate healthcare providers on the use of MAT for the treatment of opioid-use disorder and that it needs to be more available to the community which will allow there to be more access to the treatment. In doing so, it can help to set a standard for accessibility of MAT treatment in the future. Among 1,186 enrollees with OUD receiving MAT, the mean travel distance to prescribers ranged from 0.8 to 395.9 miles and the distance to the nearest MAT prescriber showed significant association to likelihood of receiving any MAT ($p<0.001$). This information is relevant to one of my evaluation questions in the sense that now I have a perspective of what could be causing people to not have access to the services or what may hinder them from being successful in the program. Ghanem et al. (2022), concluded that new medications and devices need to be explored and that improved outcomes may motivate changes in social attitudes towards opioid-use disorder.

Williams, A. R., Nunes, E. V., Bisaga, A., Levin, F. R., & Olfson, M. (2019). Development of a Cascade of Care for responding to the opioid epidemic. *American Journal of Drug and Alcohol Abuse*, *45*(1), 1–10. https://doi.org/10.1080/00952990.2018.1546862

Williams et al. (2019) stated in the past 2 years, dramatically improved outcomes have been demonstrated for patients who initiate buprenorphine to treat opioids-use disorder in emergency departments. Published studies suggest demographic characteristics (e.g., age, race, sex) are less important than addiction severity (e.g., progression to heroin use, injection, overdose history, comorbid cocaine use) and treatment history (e.g., multiple failed attempts at tapers in the past) in predicting long-term retention and outcomes.

Patients with OUD are difficult to identify, track, and engage in treatment due to their marginalized status, so in response, community-based and low threshold outreach strategies are needed for success in MAT in the future. I think that the information that was provided in the journal article will be useful for my evaluation because it gives insight to the how and why Medication-Assisted Treatment is a work in progress and also the ways that this type of treatment can move forward in the future.

Amura, C. R., Sorrell, T. R., Weber, M. B., Alvarez, A., Beste, N., Hollins, U., & Cook, P. F. (2022). Outcomes from the medication assisted treatment pilot program for adults with opioid use disorders in rural Colorado. *Substance Abuse Treatment Prevention and Policy*, *17*(1). https://doi.org/10.1186/s13011-021-00424-4

The article focuses on a study of a pilot medication for opioid use disorder (MOUD) program was developed to increase the number of NPs and PAs providing medication for opioid-use disorder in order to bring this evidence-based treatment to 2 counties showing disproportionally high opioid overdose deaths. Over the first 18 months, the MOUD Pilot Program led to 15 new health care providers receiving MOUD waiver training and 1005 patients receiving MOUD from the 3 participating organizations. Under state-funded law (Colorado Senate Bill 17–074), three rural agencies submitted de-identified patient-level data at baseline (N = 1005) and after 6 months of treatment (N = 190, 25%) between December 2017 and January 2020. The Addiction Severity Index, PhQ9 and GAD-7 with McNemar-Bowker, and Wilcoxon Signed Rank tests analysis were used to measure patient outcomes across after participation in the program. This study shows decreased

substance use, improved physical and mental health, and reduced symptoms after 6 months of MOUD. Although more research on retention and long-term effects is needed, data shows improved health outcomes after 6 months of MOUD. Lessons learned from implementing this pilot program informed program expansion into other rural areas in need to address some of Colorado' major public health crises. This information is relevant to my evaluation because it will be able to give me an idea of how other places have done with a program like this, where the program was not available in the community before the facility came along.

Ma, J., Bao, Y., Wang, R., Su, M., Liu, M., Li, J., Degenhardt, L., Farrell, M., Blow, F. C., Ilgen, M. A., Shi, J., & Lu, L. (2019). Effects of medication-assisted treatment on mortality among opioids users: a systematic review and meta-analysis. *Molecular Psychiatry*, *24*(12), 1868–1883. https://doi.org/10.1038/s41380-018-0094-5

Ma et al. (2019) explained a recent meta-analysis estimated mortality rate of periods during and after opioid substitution treatment and found that receiving methadone and buprenorphine treatment was associated with substantial reductions in the mortality of those with OUDs. The methodological quality of the studies was independently assessed using the nine-star Newcastle–Ottawa scale (NOS) by two authors. Each study was evaluated based on eight items with a total score of 9, containing some perspectives about sample selection, comparability of cohorts, and outcome assessment for cohort studies. Studies with a score of 7 or greater were defined as high quality This study provided strong quantitative evidence that links mortality rate and mortality risk to different

characteristics of MAT, further highlighting the importance of MAT in the prevention of premature death among individuals with OUDs. The results of this study were Individuals with OUDs had higher risks of all-cause death and overdose death after terminating MAT than that while receiving MAT. I think that this information is relevant to my evaluation because it shows that MAT can be successful if people use the program correctly.

Fink, D., Schleimer, J. P., Sarvet, A. L., Grover, K., Delcher, C., Castillo-Carniglia, A., Kim, J. M., Rivera-Aguirre, A., Henry, S. G., Martins, S. S., & Cerdá, M. (2018). Association Between Prescription Drug Monitoring Programs and Nonfatal and Fatal Drug Overdoses. *Annals of Internal Medicine*, *168*(11), 783–790. https://doi.org/10.7326/m17-3074

This study is an observational study, done in The United States, that examined an association between prescription drug monitoring programs implementation and nonfatal or fatal overdoses. 2 investigators independently extracted data from and rated the risk of bias (ROB) of studies by using established criteria. Consensus determinations involving all investigators were used to grade strength of evidence for each intervention. Low-strength evidence from 10 studies suggested a reduction in fatal overdoses with prescription drug monitoring programs implementation. Program features associated with a decrease in overdose deaths included mandatory provider review, provider authorization to access PDMP data, frequency of reports, and monitoring of nonscheduled drugs. Evidence that PDMP implementation either increases or decreases

nonfatal or fatal overdoses is largely insufficient, as is evidence regarding positive associations between specific administrative features and successful programs. Moving forward from this study, the authors concluded, research is needed to identify a set of "best practices" and complementary initiatives to address these consequences.

Mariolis, T., Bosse, J., Martin, S., Wilson, A., & Chiodo, L. (2019). A systematic review of the effectiveness of buprenorphine for opioid use disorder compared to other treatments: implications for research and practice. *J Addict Res Ther*, *10*(2), 1000379.

Prior systematic reviews have compared the relative effectiveness of buprenorphine (BUP), methadone (MET) and other medications and treatments for opioid use disorder (OUD). Literature searches were conducted using nine databases. Articles were limited to quantitative reports of studies conducted with adult human subjects in an outpatient, non-residential treatment settings in the United States, in peer-reviewed journals. The results suggest BUP is highly effective for reducing illicit opioid use and retaining people in treatment. The current review extends these prior reviews by synthesizing research, which compares BUP and buprenorphine and naloxone (BUP/NX) to several treatments in addition to MET on several primary and secondary outcomes. MET was found to be superior to buprenorphine (BUP) in helping patients adhere to and remain in treatment, while BUP was superior to MET for achieving abstinence from opioids. BUP was found to be superior to behavioral treatment alone, extended-release naltrexone (XR-NTX), an absence of any treatment, and placebo. The study found that buprenorphine (BUP) is an effective treatment option for achieving abstinence from opioids, and with emerging

treatment guidelines, may be easier to access than other forms of treatment. Further, flaws in research designs make it difficult for providers to determine the best medication treatment in order to improve outcomes. Future research is necessary to determine the effectiveness of BUP when administered according to the most current protocols. This information is relevant to my evaluation because it shows that MAT can be successful and the studies that need to be done to make it more effective.

Kennedy, A. E., Wessel, C. B., Levine, R. E., Downer, K., Raymond, M., Osakue, D., Hassan, I., Merlin, J. S., & Liebschutz, J. M. (2021). Factors Associated with Long-Term Retention in Buprenorphine-Based Addiction Treatment Programs: a Systematic Review. *Journal of General Internal Medicine*, *37*(2), 332–340. https://doi.org/10.1007/s11606-020-06448-z

Kennedy et al. (2021) conducted a systematic review to determine what factors were associated with longer retention in buprenorphine treatment. Articles were restricted to randomized controlled trials on human subjects which contained ≥ 24 weeks of objective data on retention in buprenorphine treatment. They assessed whether dose of buprenorphine, treatment setting, or co-administration of behavioral therapy was associated with retention rates. Three studies compared doses of buprenorphine between 1 and 8 mg and showed significantly higher rates of retention with higher doses (p values < 0.01). All other studies utilized buprenorphine doses between 8 and 24 mg daily, without comparison. No study found a significant difference in retention between buprenorphine alone and buprenorphine plus behavioral therapy (p values > 0.05).

Initiating buprenorphine while hospitalized or within criminal justice settings prior to outpatient treatment programs was significantly associated with retention in buprenorphine treatment (p values < 0.01 respectively). In conclusion, setting of treatment initiation and a higher buprenorphine dose are associated with improved long-term treatment retention. To move forward, more objective data on buprenorphine treatment programs are needed, including a standardized approach to defining retention in buprenorphine treatment programs. I think that this information is useful to my evaluation because it shows how or why people would stay on MAT longer than other people in different situations.

Piske, M., Thomson, T., Krebs, E., Hongdilokkul, N., Bruneau, J., Greenland, S., Gustafson, P., Karim, M. N., McCandless, L. C., Maclure, M., Platt, R. W., Siebert, U., Socías, M. E., Tsui, J. I., Wood, E., & Nosyk, B. (2020). Comparative effectiveness of buprenorphine-naloxone versus methadone for treatment of opioid use disorder: a population-based observational study protocol in British Columbia, Canada. *BMJ Open*, *10*(9), e036102. https://doi.org/10.1136/bmjopen-2019-036102

Piske et al. (2020) objective is to determine the comparative effectiveness of methadone versus buprenorphine/naloxone, both overall and within key populations, in a setting where both medications are simultaneously available in office-based practices and specialized clinics. We will determine the effectiveness of buprenorphine/naloxone vs methadone using intention-to-treat and per-protocol analyses—the former emulating flexible-dose trials and the latter focusing on the comparison of the two medication

regimens offered at the optimal dose. Sensitivity analyses will be used to assess the robustness of results to heterogeneity in the patient population and threats to internal validity. Retention in buprenorphine was less effective than methadone when dosing was flexible, however, these differences were not observed when buprenorphine dosages were fixed at medium (7–16 mg/day) and high (≥16 mg/day) doses. I think that this information is useful to my evaluation because it shows how different medications can be more successful depending on the circumstances or dosages that are being given.

Jakubowski, A., Norton, B. L., Hayes, B. J., Gibson, B. E., Fitzsimmons, C. K., Stern, L. S., Ramirez, F., Guzman, M., Spratt, S. E., Marcus, P., & Fox, A. P. (2021). Low-threshold Buprenorphine Treatment in a Syringe Services Program: Program Description and Outcomes. *Journal of Addiction Medicine*, *16*(4), 447–453. https://doi.org/10.1097/adm.0000000000000934

Jakubowski et al. (2021) aimed to describe the treatment philosophy, practices, and outcomes of a low-threshold syringe services program (SSP)-based buprenorphine program developed through an SSP-academic medical center partnership. They included all SSP participants who received 1 or more buprenorphine prescription from Feb 5, 2019 to October 9, 2020. They collected data on patient characteristics, substance use, buprenorphine prescriptions, and urine drug tests (UDTs). They evaluated buprenorphine treatment retention using prescription data and buprenorphine adherence using UDTs. The median percentage of days covered with buprenorphine prescriptions through 180 days was 43% (interquartile range 8%–92%). Of the 82 patients who completed 2 or

more UDTs, the median percentage of buprenorphine-positive UDTs was 71% (interquartile range 40%–100%). In an SSP-based low-threshold buprenorphine treatment program, approximately one-third of patients continued buprenorphine treatment for 180 days or more, and buprenorphine adherence was high. In other words, SSPs can be a pathway to buprenorphine treatment for patients at high risk for opioid-related harms. I think that this information is useful and relevant to my evaluation because it shows that Buprenorphine can be helpful to people in early sobriety to stay sober.