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## **A Relevant Comparison Between Buprenorphine And Methadone in Various Aspects**

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### **Abstract**

In 1974, FDA approved Methadone, an opioid agonist for Methadone Maintenance Therapy (MMT), a well-known rehabilitation program for opioid use disorder. Due to severe side effects of Methadone including withdrawal, relapse, respiratory depression, and death, FDA restricted MMT to be managed under the supervision of opioid licensed facility in inpatient settings. Opioid dependence due to chronic pain and subsequent addiction in US has increased enormously in the last two decades and has led to an emergent need of a flexible treatment method that has minimal side effects, is cost effective and can be prescribed in office-based settings. In 2002, FDA approved Buprenorphine, a partial opioid agonist, which meets the above-mentioned criteria (1). To demonstrate that Buprenorphine is a drug of choice for opioid addiction, I searched three relevant databases, PubMed, PsycINFO and Web of Knowledge. Based on inclusion and exclusion criteria, I narrowed my search from 149 to 35 articles, then selected 3 most relevant articles and validated them via number of times these articles were used as a reference (time cited) and retrieved 25 similar articles that are present in my reference list. These 25 articles validated that Buprenorphine is efficacious, easily accessible, has less side effects and can be used in pregnancy, HIV and neonate when compared to Methadone.

### **Background**

This research is to draw a comparison between Buprenorphine and Methadone in terms of its use in an office based setting, efficacy, compliance, and side effects; and to demonstrate that Buprenorphine or Methadone is a preferred treatment in opioid dependence patients suffering with HIV, pregnant woman and in neonate abstinence syndrome.

According to National Survey on Drug Use and Health in 2013, the number of people (681,000 individuals) with opioid abuse disorder in 2013 was higher than the numbers in 2002 to 2008 (ranging from 314,000 to 455,000 individuals) (A). In 1974, FDA had approved the treatment for opioid abuse with methadone maintenance therapy (MMT) along with rehabilitation but also imposed a number of conditions for its use related to eligibility, dosages and restrictions of methadone to licensed specialty clinics and pharmacies thus inhibiting MMT by individual physicians (1). During the following years several RCTs were completed and after consultation with FDA, “Drug Addiction Treatment Act 2000” allowed Buprenorphine as office-based treatment for maintenance or detox treatment. Ability to get prescription from office-based settings for up to 30 days is an advantage to the patients who do not want services for a narcotic treatment program and do not wish to attend clinic daily to obtain medication (A). Besides being easily available through office-based setting, Buprenorphine also has less adverse consequences including minimal effect on respiratory depression and cardiovascular responses (2) (3). It has a high first pass metabolism and can be used by individuals with hepatic and renal impairment whereas methadone is metabolized by hepatic P450 glucurination (4). The Maternal Opioid Treatment: Human Experimental Research (MOTHER) project, an eight-site randomized, double-blind clinical trial showed that its use in pregnancy is associated with less severe Neonatal Abstinence Syndrome than Methadone (5). Neonates who were born to mothers in a Buprenorphine group require treatment later than methadone exposed patients.(6) Another RCT showed that Buprenorphine does not increase transaminases and can be used in liver diseases including Hepatitis B, C and HIV (9).

## **Method**

To compare that Buprenorphine is a better drug than Methadone, I searched three relevant databases, PubMed, Web of Knowledge/ Web of Science and PsycINFO. For PubMed, I opened the mesh database at <http://www.ncbi.nlm.nih.gov/mesh?otool=unmlib> and entered Buprenorphine in the search bar, selected “Restrict to Mesh Major Topic” and added it to search builder. Then I added “Methadone” in search bar but did not restrict to Mesh Major. "Buprenorphine"[Majr] and Methadone [Mesh]" is the

term that gave me 456 articles. I limited my search to 68 by selecting criteria mentioned in Table A and then exported 19 articles to Endnote.

The second database that I used is Web Knowledge/ Web of Science database <http://hslic.unm.edu>. In Basic three Search bars I added Buprenorphine, Methadone and opioid abuse with a Boolean term “AND”. Used” Topic “ for all three search bars and obtained 705 articles. I tapered them to 42 articles by criteria mentioned in the Table A. than selected 10 relevant articles and exported to Endnote.

The last database that I used was PsycINFO through <http://hslic.unm.edu> where I added Buprenorphine, Methadone and opioid abuse in the search bars with ‘AND’ as a Boolean term and with the criteria mentioned in Table A. I retrieved 39 articles, reduced it to 6, and exported to Endnote.

TABLE “A”

Pub Med	Search (" <b>Buprenorphine</b> "[Majr]) AND " <b>Methadone</b> "[Mesh] Filters: <b>Clinical Trial; published in the last 10 years; Humans; English; Adult: 19-44 years</b>	68	↔ 19
Web of knowledge	<b>TOPIC:</b> (buprenorphine) AND <b>TOPIC:</b> (methadone) AND <b>TOPIC:</b> (opioid abuse) <b>Refined by: RESEARCH AREAS:</b> ( SUBSTANCE ABUSE ) AND <b>COUNTRIES/TERRITORIES:</b> ( USA ) AND <b>SOURCE TITLES:</b> ( JOURNAL OF SUBSTANCE ABUSE TREATMENT OR ADDICTION) AND <b>PUBLICATION YEARS:</b> ( 2014 OR 2010 OR 2007 OR 2015 OR 2013 OR 2011 OR 2008 OR 2005OR 2012 OR 2009 OR 2006 ) AND <b>LANGUAGES:</b> ( ENGLISH ) AND <b>DOCUMENT TYPES:</b> ( ARTICLE ) <i>Timespan=2005-2015 Search language=Auto</i>	42	↔ 10
PsychINFO	<b>TX BUPRENORPHINE AND TX METHADONE AND TX OPIOID ABUSE</b> Limiters - <b>Publication Year: 2005-2015</b> Search modes - <b>Boolean/Phrase</b>	39	↔ 6

Out of 149 articles found in 3 databases, I selected 35 articles based on the following inclusion and exclusion criteria. Out of 3 databases, I preferred PubMed due to extensive numbers of articles in all aspects of the search topic.

**Inclusion Criteria:**

Articles with detailed comparison between Buprenorphine and Methadone based on side effects, availability and results showing abstinence from opioids abuse, Buprenorphine is a drug of choice in office based setting and why its need was so essential and use of Buprenorphine in HIV, Pregnancy and Neonates abstinence syndrome.

Exclusion Criteria:

Articles covering the broad spectrum of opioid rehabilitation, comparing different types of treatment options, Opioids and sexual, physical and mental abuse, random surveys, counselor’s awareness, pharmacokinetics, pharmacodynamics of Buprenorphine and Methadone.

**Results**

To validate my search query that Buprenorphine is a preferred treatment of choice in term of easy accessibility, less side effects, use in HIV, pregnancy and neonates abstinence syndrome, I consulted Web of Knowledge, selected 3 most relevant articles to my search query with criteria of Buprenorphine: Methadone, Buprenorphine: HIV treatment and Buprenorphine: Neonatal Abstinence Syndrome, and observed number of times, these articles were used as references (time cited). I then generated a list of 25 articles that were mutually common in my reference list and time cited references of these 3 articles. This crosslinking validated 71% of my reference list that Buprenorphine is efficacious, easy accessible, has less side effects and used efficiently in pregnancy, HIV and neonatal withdrawal syndrome. See the following Table “B”.

Criteria for validation of Search topics	Articles which validate the research topics	Times Cited	Cited Articles present in My Reference list
Buprenorphine comparison with Methadone	Jaffe JH, O’Keeffe C. From morphine clinics to buprenorphine: regulating opioid agonist treatment of addiction in the United States. (1)	53	6 / 32 Appendix A (11-16)
Buprenorphine is a drug of choice in HIV-Opioid patient	Sullivan, etc. Buprenorphine/naloxone treatment in primary care is associated with decreased human immunodeficiency virus risk behaviors. (17)	40	9/32 Appendix B (18-24)(5) (6)
Buprenorphine and Neonatal Abstinence Syndrome and pregnancy	Schindler, S. D., Eder, H., Ortner, R., Rohrmeister, K., Langer, M., & Fischer, G. (2003). Neonatal outcome following buprenorphine maintenance during conception and throughout pregnancy. Addiction, (26)	56	8/32 Appendix C (25-32)

## **Discussion.**

While developing my search strategy and skills, I learned about the significance of applying the right Mesh term, Boolean term and Keywords. In past, I used “OR” and “VS” as a Boolean term while comparing between two drugs which restricted my search and I overlooked some of the most relevant articles. Plus, in order to concise and be pertinent to search topic, I narrowed down my search on the basis of inclusion and exclusion criteria; then validating my search results by comparing articles present in my reference list to 3 most relevant articles citation list, has built my search on scientific knowledge. Also I believe, that the strength of my search is (a) choosing three enormous databases including PsycINFO, as addiction specialty comes under the umbrella of Psychiatry, (b) Buprenorphine, is a new drug and by restricting my search to last 10 years helped me to draw a relevant comparison between both drugs (c) As Buprenorphine is a decade old drug so I was able to capture all the relevant data, efficacy and its uses in HIV, pregnancy and neonatal abstinence syndrome in online data. I came across the weaknesses of search strategy when I was struggling to find article on Buprenorphine and office base settings. I only retrieved 2 articles in Mesh Databases which than diverted my search to two other databases. Although it is a good strategy to use multiple databases, it can be hard to evaluate hundreds of articles in a limited period of time. Overall, based on pertinent data, I retrieved 71 % of relevant articles in my reference list when comparing it with 3 most relevant articles citations thus validating my query that Buprenorphine is better than methadone due to minimal side effects, decreased relapses, withdrawal, dependence, less severe neonatal abstinence syndrome and a better outcome in pregnancy and HIV patients.

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## **Appendix (A)**

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