Annotated Bibliography for Master of Public Health Research on the Opioid Overdose and Abuse Epidemic

Spring 2016

Research completed by and compiled by

Graduate Assistants Madison Poiry, BA and Karishma Agarwal, MBBS

Madison100@live.missouristate.edu

Agarwal1510@live.missouristate.edu

1) Anderson, P. Survey: doctors, NPs, patients concerned about opioid dangers. Medscape; December 30, 2015. Accessed at http://www.medscape.com/viewarticle/856589

This is a survey that was conducted by Medscape called the Medscape Opioid Use and Addiction Survey. It was completed by 1,513 United States clinicians 832 were physicians, and 491 were nurse practitioners. The majority responded that they were very concerned (74%) and somewhat concerned (24%) about opioid abuse and misuse. The respondents replied that 91% explain how to take opioids after prescribing them and 93% explained side effects but only 55% discussed safe storage and disposal. This is a concern due to accidental ingestion of opioid or diversion of unused pills. These respondents reported that 88% prescribe opioid drugs to their patients. Of the physicians that responded, 69% reported that they are prescribing fewer opioids. Physicians also stated that they prescribe alternatives to opioids for pain management such as over the counter pain medications, topical analgesics, antidepressants or a nerve block. Respondents reported that the best options for preventing opioid abuse is to increase prescription monitoring programs, patient education and physician education. Dr. Bill McCarberg, a primary care physician and president of the American Academy of Pain Medicine stated that the survey does not take into account the pressure that primary physicians are under to treat pain in their patients. They often do not have ample time to discuss pain and options with patients, therefore prescriptions become a fall back. They might also report that only opioids help and the doctor feel like there is no other option than to prescribe it. Another issue that was brought up by Dr. Daniel Carr, AAPM president elect is expectations of pain that patients have. Patients want to be at a "0" on the pain scale when that just might not be realistic for their condition.

2) Arribas-Ibar, E., Sánchez-Niubò, A., Majó, X., Domingo-Salvany, A., & Brugal, M. (2014). Coverage of overdose prevention programs for opiate users and injectors: a cross-sectional study. *Harm Reduction Journal*, 11(1), 33. doi:10.1186/1477-7517-11-33

The article lays emphasis on the importance of Overdose prevention program (OPP), and its effectiveness. Globally, over 27 million people are affected by some kinds of substance use (0.6%) among which close to a 1.3 million were active opiate users, in Europe alone. Further, heroine has been classified as the second most harmful psychoactive drug.

A study conducted in Catalonia, Spain, including 513 drug users, consisting 312 opiate (i.e. heroine/ methadone) users and injectors was conducted in 2010. Of this 79.2% were male, with average age being 39.7 years. Only 24% had high school or university degree, close to a 56.3% were unemployed, 57.3% had a prison history, and close to 26.2% had some permanent disability or received a pension. Various factors related to risk of heroin overdose, fatal or non-fatal, were identified: parenteral route of administration, poly-drug use, especially with CNS depressors, using alone and after a period of abstinence.

OPP is considered an important support tool which aims at reducing overdose deaths or health consequences. Studies indicate that after attending one of the OPPs, a vast majority of participants are ready to cope with an overdose. The process consists of explaining risks and consequences of opiate use, teaching participants to recognize the signs of overdose, deal with an overdose situation step-by-step, performing CPR and naloxone administration. One study

indicated that 96% of drug users who were trained to identify overdose and administer naloxone treatment reported positive outcomes, such as avoiding death, coma and brain damage. Death from overdose usually occurs within 1-3 hours of heroin injection. Thus, there is time to act in order to avoid the poisoning from being fatal. Participants of the OPP showed certain characteristics too, being a foreigner, being in prison, starting consumption at age 12 years or under.

3) Bawor, M., Dennis, B. B., Varenbut, M., Daiter, J., Marsh, D. C., Plater, C., Samaan, Z. (2015). Sex differences in substance use, health, and social functioning among opioid users receiving methadone treatment: a multicenter cohort study. *Biology of Sex Differences*, 6(1). doi:10.1186/s13293-015-0038-6

Based on a study of 492 participants, receiving Methadone Maintenance Therapy (MMT) in Canada, this article elaborates on the differences founded on gender, social functioning domains and other factors. Canada ranks first in consumption of opioid analgesic, annually. The study results have been divided to examine one's behaviors. While women were younger than men (36.9 years vs. 39.5) and receiving a lower methadone dose (73.3 mg vs. 81.3mg) their rates of completing high school education was higher, 24.6% males and 32% females.

When asked about substance use behaviors, women are more likely to use benzodiazepines (44.1%) while men abused cocaine more (36.5%). Current smoking was prevalent in majority of the sample (84.1%), 80% in males vs. 88.8% in females; and cannabis and alcohol were the most commonly reports substance of use within the past month. Urine toxicology was highest for opioids (48.5%), followed by benzodiazepines (39.6%) and cocaine (34.7%).

Health status demonstrates over a third of sample reporting chronic pain and a quarter reporting hepatitis C (24.7%). Close to a 43% participants, admit to having unprotected sex. These are important screening questions that tell us about health behaviors of an individual, thus their potential for developing dependence.

Social functioning is another important aspect that helps screen potential future dependence. The study reported current employment rate as low as 35.6% (27.1 for women vs. 42.9% in men) with median number of days worked in the past month being 0 for women and 8 for men. Less than half of participants were married (31.8%) but a majority reported having children. Women were less likely to report current employment as mentioned above, but as many as 73.2% reported having children. The study therefore, reveals sex differences and strengthens our understanding of dependence which can be used for promoting preventive strategies and treatment better.

4) Brown, R.L. & Rounds L.A. Conjoint screening questionnaires for alcohol and other drug abuse: Criterion validity in a primary care practice. Wis Med J 1995; 94:135-140. Accessed on 2-12-16 at <a href="http://lib.adai.washington.edu/dbtwwpd/exec/dbtwpub.dll?BU=http%3A//lib.adai.washington.edu/instrumentsearch.htm&TN=Instruments&CS=0&QY=find%20(A)

ccessNo%20ct%20321)&RF=Full&DF=Full&MR=&NP=3&RL=0&DL=0&XC =&ID=&AC= QBE_QUERY

This screening was developed by Richard Brown and Laura Saunders to adapt the CAGE screening to include drugs. When this screening was studied for effectiveness in clinic settings it was found to have a sensitivity of 79 percent and a specificity of 77 percent. If the respondent answers "yes" to any questions then the screening is positive. There can be confounders to this screening such as language barrier and the honest reporting due to stigma of drug use. It also is limited in that it doesn't distinguish between active and inactive drug problems.

5) CDC. 2015 Jul 10. Vital signs: demographic and substance use trends among heroin uses-United States, 2002-2013. *Morbidity and Mortality Weekly Report (MMWR)*, 64(26) 719-725.

This report includes statistical findings regarding the increase in death rates from 2002-2013. This report states that increases in heroin overdose rates were associated with increased death from prescription opioids. Many heroin uses also have a history of using prescription opioids for non-medical uses. The rates of heroin initiation are highest among non-Hispanic whites, aged 18-25, with income less than \$20,000 a year. These rates are also higher in the Northeast part of America. But even with those specifics statistics, increases in heroin initiation were seen across all demographics. It is commonly reported by heroin users that they use at least one other drug in addition to heroin (96%) and 61% report using at least three different drugs. It the past it was mostly marijuana, cocaine and alcohol, but by 2011-2013 the most commonly reported abused drug by heroin users was prescription pain relievers.

6) CDC. 2016 Jan 1. Increases in Drug and Opioid Overdose Deaths- United States, 2000-2014. *Morbidity and Mortality Weekly Report (MMWR)*, 64(26) 719-725.

This report reviews the mortality rates for opioid overdose deaths. Opioid drugs are morphine, oxycodone, hydrocodone, heroin, methadone, fentanyl and tramadol. It is reported that 2014 had more drug related deaths than any other year on record and of this 61% were caused by opioids. This amount actually surpassed deaths from motor vehicle accidents. Heroin overdoses have also been increasing which has been shown to be closely related to opioid pain killer misuse and dependence. There are regions in the United States that struggle with this epidemic more than others, although this issue is present in every state. The highest death rates are in these five states: West Virginia (35.5 deaths per 100,000), New Mexico (27.3 per 100,000), New Hampshire (26.2 per 100,000), Kentucky (24.7 per 100,000) and Ohio (24.6 per 100,000). During 2014, the total amount of drug related deaths were 47,055 of these 28,647 were due to opioid overdose (this includes heroin). Heroin is shown to be closely linked to opioid pain reliever abuse. To prevent these deaths, steps must be made to make prescribing prescription opioids safer. The rates of prescribing these medications has risen in recent years. To prevent people who are already taking prescriptions opioids from overdosing and other harms, safeguards need to be put in place such as expanding access to naloxone (antidote for opioid overdoses), and expand access to addiction treatment and behavioral therapies. This report also shows detailed demographics of overdoses and the states increase or decrease in overdose from 2013-2014.

7) Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Unintentional Injury Prevention. (January 28, 2016). Injury prevention and control: prescription drug overdose. Accessed at http://www.cdc.gov/drugoverdose/index.html

This source shows that currently the daily death toll for opioid overdose is 44 people per day. This source provides information on alternative sources of pain management to talk to one's physician about. This site also reports that people who abuse prescription painkillers are 40% more likely to start using heroin. This also provides links to resources to review each state's prescribing standards and links to information about Prescription Drug Monitoring Programs.

8) Cicero, T. J., Ellis, M. S., & Harney, J. (2015). Shifting patterns of prescription opioid and heroin abuse in the United States. *New England Journal of Medicine*, *373*(18), 1789-1790. doi:10.1056/nejmc1505541

The findings in this study suggest a decline in prescription opioid use, with a concurrent increase in heroine abuse. 267 patients were followed over 6 years, via an online interview survey. Rates of exclusive prescription opioid abuse remained stable at 70% for the first two years, 2008-2010, but then declined steadily to become less than 50% in 2014, at an annual reduction of 6.1%. Simultaneously, there was an average annual increase of 10.3% in the parallel use of both heroine and prescription opioids. This switch was cited owing to practical factors, such as accessibility and cost.

9) Clark, R. E., Baxter, J. D., Aweh, G., O'Connell, E., Fisher, W. H., & Barton, B. A. (2015). Risk factors for relapse and higher costs among Medicaid members with opioid dependence or abuse: opioid agonists, comorbidities, and treatment history. *Journal of Substance Abuse Treatment*, 57, 75-80. doi:10.1016/j.jsat.2015.05.001

The author discusses effectiveness and costs related to various opioid addiction therapies. The treatment of opioid addiction with methadone or buprenorphine has been found to be more effective and less costly than most behavioral health treatment without Opioid Agonist Therapy (OAT). Several studies have suggested that people who remain in treatment for longer periods have better treatment outcomes.

The total healthcare expenditure during treatment episodes (a period of treatment lasting over one month, because methadone and buprenorphine are sometimes used for detoxification without an intention for maintenance treatment). A total of 56,278 individuals who received 104,840 episodes of treatment between years 2004-2010 were identified. The average Medicaid expenditure per person per month during treatment episode was found to be \$1169 for males and \$1079 for females. The number of relapses, including detoxification, ER visits and hospitalizations with primary diagnosis of a drug or alcohol disorder was 5.6 for males vs. 3.7 for females.

Having a co-occurring mental health illness, alcohol and other drug disorders collectively increase the risk of relapse by 80% and add \$786 per month to average per-person cost of treatment. Methadone and buprenorphine treatment episodes were associated with \$223 to \$153 lower total

healthcare expenditures per month than other non-OAT behavioral therapy, most likely due to their more effective reduction of relapse events.

In conclusion, OAT is significantly more effective in reducing relapses and less costly than other forms of behavior health treatment. Also, co-occurring conditions play a strong role in determining the cost and course of treatment. Previous episodes of treatment have also shown a slightly lower healthcare cost.

10) Cobaugh, D. J., Gainor, C., Gaston, C. L., Kwong, T. C., Magnani, B., McPherson, M. L., Krenzelok, E. P. (2014). The opioid abuse and misuse epidemic: Implications for pharmacists in hospitals and health systems. *American Journal of Health-System Pharmacy*, 71(18), 1539-1554. doi:10.2146/ajhp140157

This article outlines the alarming rise in the number of emergency department visits associated with use of opioids. The most common symptoms and clinical signs to recognize overdose have been listed. Various drug monitoring programs have been implemented in an attempt to track patterns of improper sales and use of opioids. Pharmacies are expected to follow certain protocols for proper distribution, dispersion and disposal of opioids.

11) Compton, P., Darakjian, J., & Miotto, K. (1998). Screening for addiction in patients with chronic pain and "problematic" substance use. *Journal of Pain and Symptom Management*, 16(6), 355-363. doi:10.1016/s0885-3924(98)00110-9

The author states definitions (by ASAM) of 'addictive disease' and compares it with 'pseudo-addiction' and 'therapeutic dependence'. Comparisons of lifetime prevalence rates of addictive disorder in the chronic pain patient vs general population has been made. The author conducted a study on 52 patients from a multidisciplinary pain clinic, based on a 'Prescription drug use questionnaire' to access their addiction status. No clear discriminating line between the addicts and non-addicts could be defined and the sample size was considerably small. However, the questionnaire that was developed, could be used as a helpful tool to screen cases at initial stages or by family members.

Studies estimate that between 3-19% of chronic pain patients suffer an addictive disorder. Compton defines addiction as "a persistent pattern of dysfunctional opioid use that may involve any of the following: adverse consequences associated with the use of opioids, loss of control over its use, and preoccupation with obtaining opioids despite the presence of adequate analgesia." Certain addictive behaviors to watch for have been listed, having more than one medicine provider, increasing analgesic use frequency or dose, calling in early for prescription refills or exhibiting a pattern of losing prescriptions.

12) Davis, C., Webb, D., & Burris, S. (2013). Changing law from barrier to facilitator of opioid overdose prevention. *Journal Of Law, Medicine & Ethics*, 4133-36. doi:10.1111/jlme.12035

Due to the epidemic proportions of opioid drug overdose deaths (16,000 per year), new strategies in prevention are needed. One such strategy that proves effective is naloxone or Narcan, in preventing deaths from overdose. The way that an opioid overdose kills a person is by slowly depressing respiratory function. When naloxone is administered it stops the opioids from affecting the brain receptors and thus stops the depressing effect. It is an easy to use medication and ordinary people could be trained to administer it. There is not a potential risk of abuse for naloxone yet when people need it, they cannot access it. The current state prescribing laws do not allow third-party prescription of naloxone to a person that could administer it to a person who has overdosed. When a suspected overdose has taken place, people are left to call 911 which is a concern because some people hesitate when drugs are involved for fear of criminal prosecution. This could lead to more deaths from overdose. Some states have amended their laws so that non-medical professionals can administer naloxone, and other states are amending the Good Samaritan laws to include administration of naloxone so people acting in good faith are not liable to legal repercussions.

13) Department of Health and Human Services, Behavioral Health Coordinating Committee. (September 2013). Addressing Prescription Drug Abuse in the United States. Washington, D.C.

This report outlines the epidemiological factors that propel the opioid epidemic. It includes demographics of people hospitalized for opioid abuse treatment and overdose. It is estimated that 72 billion dollars is spent annually on medical costs incurred by opioid drug use. The amount of money lost in productivity, legal costs, and substance abuse treatment is \$53-56 billion. This is comparable to the cost of other diseases such as HIV or asthma. This is a pressing health behavior to address and work to prevent due to the societal ramifications, costs in every facet of the medical and governmental infrastructure, and to the people personally affected.

14) Dowell, D., Haegerich, T.M., & Chou, R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016; 65: 1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1

The CDC released recommended prescribing guidelines for physicians in March 2016, the following is a summary of the recommendation. The CDC suggested that when possible, use non-pharmacological and non-opioid therapy for chronic pain. Prescribe only when benefits outweigh risks. Before starting therapy, treatment goals must be established. Continue only if meaningful improvement in pain and function are seen, consider how to discontinue if risks develop. All risks and benefits should be discussed with patient before starting therapy. Begin with prescribing immediate-release opioids. Begin with prescribing lowest effective dosage, use caution when increasing dose. For acute pain, prescribe the lowest effective dose of immediate-release opioids. Evaluate benefits and harms within 4 weeks of starting therapy. For continued therapy, evaluate benefits and harms with patient every three months. If harms outweigh benefits, taper dose or switch to alternative. Evaluate risk factors, incorporate strategies to mitigate these in the management plan, particularly with high dosages and previous history of abuse. Patient's history should be reviewed to determine whether he is receiving any opioid that put him at high risk for overdose, using Prescription Drug Monitoring Program data. For chronic pain, urine drug testing must be done before starting therapy, then annually to access for

prescribed or illicit drugs. Avoid concurrent use of opioid pain medication with benzodiazepines. For opioid use disorder, consider buprenorphine or methadone with behavioral therapy.

15) Edlund, M. J., Steffick, D., Hudson, T., Harris, K. M., & Sullivan, M. (2007). Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. *Pain*, *129*(3), 355-362. doi:10.1016/j.pain.2007.02.014

Risk Factors associated with opioid use have been stated here. Groups of possible risk factors have been taken into account: painful physical health, non-opioid substance abuse, sociodemographic factors and mental health disorders. Prevalence of mental health disorder was as high as 45.3% among users of opioids for chronic non-cancer pain.

16) Elander J, Duarte J, Maratos FA, Gilbert P. (2014 Apr 15). Predictors of painkiller dependence among people with pain in the general population. *Pain Medicine*. (4):613-24. doi: 10.1111/pme.12263.

This study used an online questionnaire to determine multiple measurements among the 112 participants from the general population in the United Kingdom. These participants were over 18 years old and had pain in the past month and used either OTC painkillers or prescription painkillers. The questionnaire was designed to measure pain frequency and intensity, use of OTC or prescription painkillers, risk of substance abuse, depression, anxiety, stress, alexthymia, pain catastrophizing, pain anxiety, pain self-efficacy, pain acceptance, mindfulness, self-compassion, and painkiller dependence (Leeds Dependence Questionnaire). Their study showed association between painkiller dependence and the predictors of prescription painkiller use, risk of substance abuse score, and pain acceptance.

17) Evans, J. L., Tsui, J. I., Hahn, J. A., Davidson, P. J., Lum, P. J., & Page, K. (2012). Mortality among young injection drug users in San Francisco: a 10-year follow-up of the UFO study. *American Journal of Epidemiology*, 175(4), 302-308. doi:10.1093/aje/kwr318

This study examined associations among mortality and risk characteristics among young injection users, between 1997 and 2007. A total of 644 injection users, <30 years old were enrolled in the study. 38 deaths over 4617 person-years of follow up, yielded a mortality rate of 9.1 per 1,000 PYs. This mortality rate was 10 times that of the general population. The major causes were overdose, self-inflicted injury, trauma/accidents, injection drug user-related medical conditions; being the highest in those reported to injecting heroin in the past month.

18) Felicilda-Reynaldo, R. D. (2014). Recognizing signs of prescription drug abuse and addiction, part I. *MEDSURG Nursing*, 23(6), 391-396.

Drug abuse has become an epidemic problem in the Unites States among all parts of society and can negatively affect relationships, employment, health, education, and wellness. Substance abuse may start as a voluntary act but as the chemicals disrupt the central nervous system,

abstaining from the drug becomes a challenge. Overdose of opioids can cause respiratory arrest and coma. The Substance Abuse and Mental Health Services Administration (SAMHSA) has stated that more emergency room visits for overdose come from prescription pills than illicit drugs. It has been suggested by this author that screening for substance abuse should be done by all levels of the medical profession since SAMHSA has stated that there is a "no wrong door policy" in regards to referral to treatment for substance abuse. The SBIRT Program is beneficial for hospital staff when talking to patients to identify early signs of substance abuse. A person overdoses on opioids when they take more than they can tolerate, take the opioid through an alternative route (snorting or injecting), or taking it with a drug that interacts with the opioid (sedatives, alcohol or antidepressants). Signs of intoxication from opioids include inappropriate behaviors, euphoria followed by apathy, agitation, impaired judgment or dysphoria. Signs of opioid overdose include fatigue, decreased awareness, abnormally slow breathing, and constricted pupils to the size of a pinpoint.

19) Fisher, F. (2004). Interpretation of "aberrant" drug-related behaviors. *Journal of American Physicians and Surgeons*, Vol. 9(1), 25-28.

When physicians are treating patients with opioids, they look for warning signs of the patient becoming addicted or displaying aberrant drug-related behaviors. This article proposes that even though some doctors interpret these signs as signaling addiction, they should first look to see if the patient actually has undertreated pain that is leading them to display these behaviors. Because there is not a completely accurate test for addictions, physicians must rely on observing behaviors to determine if they believe a patients is addicted. This author states that is a person is displaying signs such as: borrowing medicine from another individual, getting prescriptions from a non-medical source, increasing their dosage without physician approval, complaining aggressively that they need higher doses, hoarding pills even when symptoms are not present, requesting specific drugs from the physician or acquiring similar drugs from other medical sources, this could be symptomatic of undertreated pain not just addiction. Other behaviors that the author states are warning signs of addiction but could possible also be an issue of undertreated pain are: forging a prescription, stealing medications from other patients, or reporting lost prescriptions. The author states that if a physician suspects that a patient is displaying signs of addiction they should probe more into the patient's habits to see if it is the opioids that they are addicted to or a concurrent substance. This is so that the patient isn't denied pain relief or treatment if they need treatment for an addiction. The behaviors that this author states are suggestive of opioid addiction are: converting oral medications into an injectable form and using them intravenously, using concurrent illicit drugs, or selling (diverting) prescription drugs.

20) Foddy, B. & Savulescu, J. (2010). Relating addiction to disease, disability, autonomy, and the good life. *Philosophy, Psychiatry, & Psychology*, 17(1), 35-42. doi:10.1353/ppp.0.0284

This article defines addiction as a strong appetite. The author talks about how autonomy plays a role in addiction and how that eventually makes us feel conflicted and doomed. This could possibly explain the association between depression and addiction? (Though not clearly defined).

There is a terse discussion on the pathophysiology suggesting a dysfunction of the frontal lobe that normally allow us to learn behavior.

21) Fogger, S. & McGuinness, T. M. (2015). Adolescents at risk: pain pills to heroin: part II. *J Psychosoc Nurs Ment Health Serv*, *53*(2), 27-30. doi: 10.3928/02793695-20150106-01

This article states that more adolescents on prescription opioids are switching to heroin, it is more readily available and suggestively cheaper. But the risk of overdose and death increases with heroin because of higher potency, thus higher risk of overdose and deaths. The picture of an addict in the 1980s vs the current time has been discussed. The more commonly affected are: Caucasians (90%) in their early 20s (75%). The author briefly describes the appearance of Columbian and Mexican heroin and their routes of administration. Data suggests a 3% rise in heroin overdose hospitalizations for every \$100 drop in the price of one gram of pure heroin.

Signs of toxic overdose (respiratory suppression and cerebral anoxia) have been discussed. Features of withdrawal, methadone maintenance and its long term consequences have been listed. Contrary to the traditional method of total abstinence, Opioid Replacement Therapy (ORT) using methadone and buprenorphine has been discussed. Information on how naloxone should be prescribed and in what doses.

22) Fox, A. D., Sohler, N. L., Starrels, J. L., Ning, Y., Giovanniello, A., & Cunningham, C. O. (2012). Pain is not associated with worse office-based Buprenorphine treatment outcomes. *Substance Abuse*, 33(4), 361-365. doi:10.1080/08897077.2011.638734

This article discusses the specific issue of pain in people seeking opioid addiction treatment. This article describes a study where 82 patients entering addiction treatment were assessed for pain. Of these patients 60% reported pain and 38% reported persistent pain. The patients then started a buprenorphine treatment plan and followed up with the researchers at 1, 3, and 6 months of treatment. They were assessed for pain during each follow up. At 6 months, 56% of the participants were still utilizing the treatment, and after multivariate analysis, the researchers found no association between pain and whether a patient continues treatment. The researchers suggest that regardless of levels of pain, an opioid-dependent patient can have success with buprenorphine as a treatment for addiction.

23) Gardner-Nix, J. (2003). Principles of opioid use in chronic non cancer patients. Canadian Medical Association Journal, 169 (1), 38-43. http://www.cmaj.ca/content/169/1/38.full

The WHO indicates the use of opioids to provide sufficient pain control when other measures such as acetaminophen, acetylsalicylic acid, NSAIDs have failed. The author emphasizes that between 3-17% of people are potential addicts, and usually have a family history or personal history of addiction. The CAGE-AID and Screening Instrument for Substance Abuse potential (SISAP) questionnaire have been used for screening alcohol dependence and may be used to screen patients at high risk of addiction.

24) Green, T. C., Dauria, E. F., Bratberg, J., Davis, C. S., & Walley, A. Y. (2015). Orienting patients to greater opioid safety: models of community pharmacy-based naloxone. *Harm Reduction Journal*, 12(1), 1-9. doi:10.1186/s12954-015-0058-x

This article reviews the potential systems that could be used to increase the access to Naloxone for people who are using opioids and people who could be "bystanders" to person who has overdosed (a friend or family member). The argument made in this article is that pharmacists are knowledgeable and have sufficient training to distribute Naloxone rescue kits to the public without a prescription, but the current laws do not allow this and the FDA alone has the power to change that. There are community based programs called overdose education and naloxone distribution (OEND) and as of June 2014 there were 644 programs in the US and the people who participate in them report that as much as 26,463 overdose deaths were prevented. These programs are not accessible to everyone however and with the pharmacy being integrated into most stores and street corners in America, it would be better for people to access naloxone rescue kits there. It is also important to have these kits at a pharmacy because pharmacists are trusted in the community and are underutilized when it comes to the preventions in public health.

25) Harvard Mental Health Letter. January 2011. Painkillers fuel growth in drug addiction. Harvard Health Publications. Accessed from www.health.harvard.edu

Opioid drugs are used to treat cancer pain, severe acute pain and chronic pain. These are well established reasons to prescribe these types of medications, but it is still controversial to use these medications for things like migraines, arthritis or back pain. The way that opioid medications work is by causing euphoria in the brain receptors, the same way that heroin works. This causes an increase in the risk of addiction and dependence in patients being treated with long term opioid therapy. The amount of prescription opioids has increased ten times in the past two decades. As a result, the amount of people with addictions to painkillers has also increased.

Opioid addiction is more common than any other prescription drugs. The people who are at risk for developing addiction are people using them for nonmedical purposes. People with chronic pain are also at risk because they are more likely to be prescribed long term opioid painkillers. This however is not the only risk factors. Other risk factors include current or past substance use disorder and age (most commonly teenaged). The treatment for opioid addiction is very difficult because of the withdrawal symptoms which severely weakens and sickens the person. It's also difficult to abstain from drug use after detoxification because of cravings. It is important for patients to attend counseling while recovering. To assist with detoxification and maintaining sobriety from opioids requires medical treatment and maintenance therapy. The medications that are used for detoxification are Methadone, buprenorphine and naltrexone.

26) Hill, K. R., Rice, L. S., Connery, H. S., & Weiss, R. D. (2013). Diagnosing and treating opioid dependence. *Clinician Reviews*, 23(3), 31-39.

This article discusses the potential screenings to use for patients being treated with opioids and the treatment options for people with dependence to opioids. Some patients can take opioids

without experiencing dependence, but some patients can progress from treatment to misuse to dependence. These patients are usually from a vulnerable group such a people with mental illness or previous substance abuse or increased sensitivity to pain. Screening tools such as the CAGE-Adapted to Include Drugs and the Drug Abuse Screening Test could be used to try to predict which patients are at risk of becoming addicted to opioids, however some research suggests that the screenings are not more effective than obtaining a substance abuse history from a patient. A way for doctors to continue screening after the patient has started to take opioids is by using the Screening, Brief Intervention, and Referral to Treatment (SBIRT) program. Before initiating treatment for addiction, a physician should take the following into account: assessment of pain, psychological disorders, psychosocial stressors, patient's desire for help, and desire to change. A patient can be referred to a specialist that is knowledgeable with detoxification, inpatient or outpatient treatment, and pharmacological treatments. Most patients will be treated on an outpatient approach using pharmacology and behavioral therapy. The best approach for each patient should be a decision made by the patient and physician. The most commonly prescribed medications for addiction treatment are buprenorphine, methadone or naltrexone. There are special considerations and concerns for each medication and this should be discussed with the patient to determine the best approach. Even though the research on the effectiveness of behavioral intervention compared with medication alone is conflicting, most physicians consider behavioral therapy an important process of addiction treatment. It is recommended that individual counseling or group counseling and attendance at a recovery group like Narcotics Anonymous be completed.

It is the place of the physician to properly warn patients of the effects of not taking their medication properly and to monitor the patient to ensure the medication is taken properly (by doing urine screenings, requesting random pill counts or other monitoring systems). It is also important to have a contract with the patient regarding their treatment and responsibilities. It is also necessary for the person to have a lockbox for medications in the home and to go to only one doctor and pharmacy for these medicines. It might also be appropriate for the physician to prescribe a naloxene rescue kit in case of overdose to the family. It is also critical for the patient being treated for addiction to be receiving treatment for concurrent mental disorders to improve the addiction treatment outcomes.

27) Højsted, J., Nielsen, P. R., Guldstrand, S. K., Frich, L., & Sjøgren, P. (2010). Classification and identification of opioid addiction in chronic pain patients. *European Journal of Pain*, *14*(10), 1014-1020. doi:10.1016/j.ejpain.2010.04.006

The definition of addiction, by WHO is outlined. Also, recognizing addiction in those on prescription opioids and the prevalence in various subgroups. A cross-sectional study on 253 patients, being treated at a Multidisciplinary Pain Center suggested the following findings: out of the 211 patients taking potentially addictive drugs; 28% were classified as addicts, 30.9% had associated anxiety and 15.7% had depression disorders. Median daily opioid dose was 90 mg (0-840 mg). The author suggests that the ICD-10 criteria may not be appropriate in chronic pain patients, therefore contrasts it with his own Portenoy's criteria.

28) Johns Hopkins Medicine. CAGE Substance Abuse Screening Tool. Accessed on February 12, 2016 from http://www.hopkinsmedicine.org/johns_hopkins_healthcare/downloads/CAGE%2 0Substance%20Screening%20Tool.pdf

This screening tool is to see if substance abuse is a concern and should be addressed in a person using a potentially addictive substance. This was adapted from the CAGE assessment by Ewing, 1984 which was initially meant for alcohol abuse.

29) Kahan, M., Srivastava, A., Wilson, L., Gourlay, D., & Midmer, D. (2006). Misuse of and dependence on opioids. Study of chronic pain patients, 52:1081-1087.

The author describes the four Cs of addiction: loss of Control over use, continued use despite harmful Consequences, compulsion to use, and Craving. Dependence involves two related phenomena, tolerance (need to take more drug in order to achieve the same effect) and withdrawal. The symptoms of withdrawal have been divided into physical, psychological, and objective signs. The potential of abuse has been found to be highest with oxycodone. Various risk factors include youth, current or past history of abuse, concurrent psychiatric disorders; childhood history of sexual abuse.

Certain high risk behaviors such as injecting or crushing tablets, buying off of the streets, reluctance to use other methods of pain management in chronic pain patients' have been found to be more predictive of dependence. Careful observation is essential, one study showed that 21% pf CPPs without any evidence of drug-seeking-behavior had unauthorized drugs in their urine. Finally, the authors have suggested several methods of treatment and their contraindications.

30) Katz, N. P., Adams, E. H., Chilcoat, H., Colucci, R. D., Comer, S. D., Goliber, P., Weiss, R. (2007). Challenges in the development of prescription opioid abuse-deterrent formulations. *The Clinical Journal of Pain*, 23(8), 648-660. doi:10.1097/ajp.0b013e318125c5e8

The author tries to explain his outlook regarding the advertisement and popularity of opioid and opioid like substances. Various risk factors for addiction have been identified, including, younger age, past history of substance abuse or poly-substance abuse, and poor family support. The prevalence of positive urine toxicology, suggestive of concurrent substance abuse was found to be between 30-40%, based on a few studies on patients on prescription opioids. A brief description of the type of prescription opioid abusers has the also been given drawn.

A ranking of Drug-taking behaviors, and their interpretation to perceive the level of severity suggests that selling prescription drugs, forging prescriptions and altering route of administration, are the conducts most likely to result into addiction. The impacts addiction have, demands a need for abuse-limiting opioid products.

31) Manchikanti, L., Fellows, B., Ailinani, H., & Pampati, V. (2010). Therapeutic use, abuse, and nonmedical use of opioids: a ten year perspective. *Pain Physician* 2010; 13:401-435.

This article outlines concerns of the growing misuse and abuse of opioids and the efficacy of treatment of opioids. This article also reports the physiological effects of opioid therapy being hyperalgesia (hyper sensitivity to pain), hypogonadism, GI distribution, sexual dysfunction, respiratory depression, delayed gastric emptying, muscle rigidity, sleep disturbance, increased body temperature, diminished psychomotor performance, risk of overdose, and death. Another concern of opioid therapy is the risk of drug interaction with other pharmaceuticals. Diversion of drugs is a major concern because 55.9% of people using opioids for nonmedical reasons reported obtaining them for free from a friend or family member. Of this group, 8.9% said they bought pills from a friend or relative and yet another 5.4% stated that they took the pills without asking. Another 18% who used opioids for nonmedical purposes reported getting their medications from a doctor.

Opioids work by blocking pain receptors in the brain and spinal cord and have been shown to be successful in short term pain management for chronic non cancer pain, but it is not established whether long term use is effective. Some advocate groups and physicians believe that unlimited prescribing power of opioids is necessary in addressing chronic pain in patients and this has led to an increase in prescribing in America. This could be a cause for why there are high numbers of addicted patients and overdose deaths which is a strain on the healthcare system and financial cost to the public with costs reaching 300 billion.

It is difficult to treat people with addiction to opioids because of the comorbidities that add to the complexness of treating chronic pain such as physical and psychological conditions. There is a close relationship between mental illness and opioid abuse. Opioid use has also been linked to increased disability among users, increased medical costs, subsequent surgeries and continued opioid use. Epidemiological studies show less positive outcomes for functioning and quality of life with long term opioid use when compared to chronic pain patients that don't use opioids. Studies also show a range of 18-41% of patients using opioids start to abuse the drugs. The risk of overdose death appears to be higher in men and people middle aged.

There is also a major concern of diversion of drugs to people who are not prescribed them originally. There is also evidence that there are illegal sales of prescriptions by some physicians, patients, and pharmacists. There is also risk of forgery, theft and robbery associated with opioid drugs. This is a concern because prescription opioids appear to be a gateway to heroin use, but the public sees these pills as less stigmatizing and less dangerous than other illicit drugs. Diversion is one of the biggest concerns and needs to be discouraged and prevented.

32) Maremmani, A. G., Rovai, L., Rugani, F., Bacciardi, S., Massimetti, E., Gazzarrini, D., Maremmani, I. (2015). Chronology of illness in dual diagnosis heroin addicts: the role of mood disorders. *Journal of Affective Disorders*, *179*, 156-160. doi:10.1016/j.jad.2015.03.046

This article talks about co-morbid mental health issues being an important factor for heroin addiction, since individuals with psychiatric illness tend to use heroin alleviate their symptoms. The author states the three stages of opioid addiction. Also, heroin addicts with co-morbid psychiatric or mood disorders, were apparently found to have higher prevalence of failed treatment for heroin addiction.

33) Mars, S. G., Bourgois, P., Karandinos, G., Montero, F., & Ciccarone, D. (2014). "Every 'Never' I Ever Said Came True": transitions from opioid pills to heroin injecting. *International Journal of Drug Policy*, 25(2), 257-266. doi:10.1016/j.drugpo.2013.10.004

This article focuses on the patterns of opioid use in terms of administration routes. Philadelphia and San Francisco were selected for in-depth study between 2010 and 2012. The two different patterns noticed were:

- (a) Prescription pill (Percocet- oxycodone & acetaminophen) opioid users, usually white, who transitioned to injecting heroin.
- (b) Young pill users who switched to heroin, usually by nasal inhalation (sniffing) or smoking at first, followed by injecting.
- (c) Older users, more likely graduated to injecting heroin from non-opiate drugs like cannabis, methamphetamine and cocaine.

However, opioid initiates typically reports transferring to heroin for reasons of cost and ease-of access, after becoming physically and emotionally dependent on opioid pills. This is in part due to a 500% increase in opiate pill prescription from 1997-2005.

34) Nelson L, Juurlink D, & Perrone J. Addressing the opioid epidemic. *JAMA*. 2105; 314(14): 1453-1454. Doi:10.1001/jama.2015.12397.

This editorial discusses the current challenges facing the medical community regarding opioid overdose and abuse. It states that opioids are the second largest cause of poisoning that is treated in emergency departments, the first is alcohol. This editorial states that the opioid overdoses are commonly people who are taking them other than the way their physician described. This trend has been on the rise and reached 16,235 deaths in 2013 that were attributable to opioids. Most opioid prescriptions come from a legitimate source such as a prescribing physician. An estimated 53% people using a prescribed opioid for non-medical reasons reported obtaining it from a friend or relative. This editorial also states that 10% of patients that are prescribed opioid will have chronic use of opioid painkillers. Of this percentage, 25% will become nonmedical users of opioids and 10% will develop addiction-like traits. Another concern with chronic opioid use is that dependence, addiction and dose escalation make it very difficult to discontinue opioids. Many patients will experience withdrawal effects. This editorial also confirms that some chronic opioid users will end up doing heroin because it is cheaper and can be attained easier in some areas. The author's suggestion to address this epidemic is to reduce the amount of first time opioid users, invest more funds into developing safe prescribing practices, increase drug monitoring programs and bystander Naloxone for emergency treatment of overdoses.

35) Park, T. W., & Friedmann, P. D. (2014). Medications for addiction treatment: an opportunity for prescribing clinicians to facilitate remission from alcohol and opioid use disorders. *Rhode Island Medical Journal*, 97(10), 20-24.

This article discusses the treatment of addiction with medication. The authors report that addiction treatment with medication is effective yet underutilized. They are cost effective and can be utilized on an outpatient basis. The medications that work with addressing opioid (that are FDA approved) are Methadone, Buprenorphine, and Naltrexone Depot Injection. These medications work in different ways, Methadone is a full opioid agonist and is effective in retaining patients in addiction treatment and lowering opioid use. The only issue with Methadone is that it does have a risk of abuse and can only be legally prescribed by licensed opioid treatment programs which require treatment counseling and supervised dose taking for the first 9 months. With consistent compliance, the patient may be allowed to take weekly doses home. Buprenorphine is a partial opioid agonist which can be used in office-based settings. Buprenorphine is usually dosed with naloxone it discourage intravenous use of the drug. Buprenorphine blocks the euphoric effects of opioids, reduces cravings, and prevents the negative feelings of withdrawal. It also reduces the risk of respiratory depression. Patients must be completely off of opioids for 12-24 hours before starting the dose. In clinical trials, Buprenorphine is as effective as Methadone. Naltrexone depot injection blocks the opioid receptors in the brain, it is a long acting medication that blocks all opiate effects in the brain. It can be distributed in monthly shots to improve adherence to medication and patients must not be used for 7-10 days before starting the medication. Naltrexone can be taken orally also. It improves treatment retention in patients seeking addiction treatment for opioids and abstinence. Evidence reviewed in this study shows that office-based treatment and medication is as effective as longer interventions with counseling.

36) Paulozzi, L. J., Strickler, G. K., Kreiner, P. W., & Koris, C. M. (2015). Controlled substance prescribing patterns — prescription behavior surveillance system, eight states, 2013. *MMWR. Surveillance Summaries*, 64(No. SS-9), 1-14. doi:10.15585/mmwr.ss6409a1

The author states that the leading cause of injury death is drug overdose. The rate has doubled from 6 per 100,000 to 13.8 from 1999-2013. The Prescription Behavior surveillance system (PBSS) funded by the CDC and FDA, collected data on eight states and concluded that opioids have a two fold increase in prescription rate compared to other drugs. These were higher in females, peaked in either 45-54 years or the 55-64 age group. The rates are higher in women owing to a higher self-reported prevalence of certain kinds of pain.

37) Sarasa-Renedo, A., Espelt, A., Folch, C., Vecino, C., Majó, X., Castellano, Y., Brugal, M. T. (2014). Overdose prevention in injecting opioid users: The role of substance abuse treatment and training programs. *Gaceta Sanitaria*, 28(2), 146-154. doi:10.1016/j.gaceta.2013.10.012

This study on risk factors and knowledge about the risk factors of opioid addiction was conducted in Spain, Europe. The most common risk factors known are multiple drug use, amounts, taking purer forms, health causes like chronic pain problem, injecting the drug and associated psychological problems. This study also aimed to access the 'knowledge addicts have about drug overdose' and appropriate actions. It examine the actions an addict was most likely to take if witnessing an overdose. The answers included certain adequate activities like calling emergency services, keeping the overdosed person awake, giving naloxone, or facilitating breathing. Some of the poor responses were giving the person a shower, abandoning the person or laughing at him/her.

The factors associated with limited knowledge about overdose prevention were having a low educational level, never having attended drug dependency treatment, and never having suffered an overdose. Close to 40% respondents reported inadequate actions in case of witnessing an overdose. In closure, the author identifies that opioid overdose accounts for over 6500 preventable deaths in Europe, every year. Various overdose prevention programs may not have had a significant impact in reducing limited knowledge about overdose prevention. It is thus cardinal to continue developing extensive prevention programs, especially designed to address idiomatic, educational and cultural differences, in order to improve knowledge about overdose prevention and reduce potentially harmful beliefs persisting in the community.

38) Savage, S. R., Joranson, D. E., Covington, E. C., Schnoll, S. H., Heit, H. A., & Gilson, A. M. (2003). Definitions related to the medical use of opioids: evolution towards universal agreement. *Journal of Pain and Symptom Management*, 26(1), 655-667. doi:10.1016/s0885-3924(03)00219-7.

The definition of addiction is explored, and the evolution of various related definitions, including but not limited to, Physical dependence and tolerance; also how to differentiate between them. It briefly explains 'neurobiological predisposition' to be important in the progression of addiction, along with social and psychological factors. There is a succinct recognition on how to screen addicts, their actions and symptoms to watch out for; also how to distinguish it from pseudo-addiction.

39) Sehgal, N., Manchikanti, L., & Smith, H. Prescription opioid abuse in chronic pain: a review of opioid abuse predictors and strategies to curb opioid abuse. *Pain Physician* 2012; 15, ES67-ES92.

There is not a completely accurate test or screening that can predict whether or not a patient will abuse opioids therefore increased monitoring by a medical professional is needed for a patient that is being treated for chronic non cancer pain. There are however certain risk factors that could predict a higher risk for opioid abuse in patients, and these need to be taken into account when a physician is treating the patient. Patients with mental health disorders, previous substance use disorders, and certain demographics such as gender, age and ethnicity are at a higher risk for developing prescription drug abuse. This study found that patients with depression and anxiety disorders, psychosocial stressors and psychological problems are at a higher risk for opioid misuse. Some demographics that seems correlated to opioid misuse include being young, white and male. One reason that the authors gave for this was that white patients are more often treated

with opioid analgesics in emergency room and by primary care physicians compared to other races. Other predictors such as age of first alcohol or drug use are also important for doctors to ascertain because there is a correlation between very early alcohol or illicit drug use and opioid abuse. This study also looked at other factors too such as back pain being a condition that is often present in patients that misuse opioids and patients with multiple pain complaints. This study detailed screening tools that doctors can use to see if chronic opioid therapy would be a therapeutic option for patients and also recommended that increased office appointments and monitoring is needed. Potentially using urine analysis to monitor for additional illicit drug use, or opioid use that is not prescribed to the person can also catch opioid misuse. The study also recommends that people safeguard these prescriptions and not share or give them to someone else and to dispose of them immediately when they are no longer needed. There was also a recommendation for physicians to talk about the potentially harmful ramifications of seeing multiple doctors for pain treatment or "shopping for doctors" to get more pain medications.

40) Sharpe Potter, J., & Marino, E. N. (2013). How to avoid opioid misuse. *Journal of Family Practice*, S2-S7.

This article discusses screening tools that can be used before treatment with opioid analgesics, such as the Screener and Opioid Assessment for Patients with Pain (SOAPP). Using screening tools before treatment is recommended by the American Pain Society (APS) and the American Academy of Pain Medicine (AAPM). It is also important to get a very detailed history from the patient. Even if the person appears to be high risk, it is the clinical judgment of the physician on how to treat the pain. The suggested method is to agree with the patient on an evaluation period in which the patient will take opioid analgesics for 30 days and then report back with the results. If the patient improves in pain level, functioning and an improved quality of life the physician can determine if this is successful enough to continue treatment with opioids. If the opioids do not improve the patient's condition then the physician can discontinue the use of the medication and try alternative approaches or continue medication and refer to a pain specialist. In addition to screening this article also recommends prescription monitoring programs to reduce doctor shopping and opioid misuse. Another recommendation is for urine drug screens to see if there is concurrent use of illicit substances. This article also discusses the definitions for different opioid use terminology such as: misuse, abuse, dependence and aberrant drug related behavior.

41) Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. (July 17, 2014). The TEDS Report: Age of Substance Use Initiation among Treatment Admissions Aged 18 to 30. Rockville, MD.

This report gives the statistical information in graphs of the admissions into drug rehabilitation centers. It also list the drugs for which the admissions were being treated and the ages of the patients entering rehab. Heroin and prescription pain killers where used in the highest percentages in the age group 25 or older. The majority of admissions for drug treatment reported initiating drug or alcohol use at age 17, which is why it is vital to educate children and youth about substance abuse. Because the highest percentages of opioid abuse was in the older age group, prevention education on opioid abuse should not stop at children and teens. It seems to be an ongoing struggle at all age groups. Of the admissions in this report aged 25 or higher, 35.3

reported heroin as their primary drug and 33.2 reported primary drug use of prescription pain killers. An additional 21.4 percent reported secondary use of prescription pain killers.

42) Sullivan, M. D., Edlund, M. J., Fan, M.-Y., DeVries, A., Braden, J. B., & Martin, B. C. (2010). Risks for possible and probable opioid misuse among recipients of chronic opioid therapy in commercial and Medicaid insurance plans: the TROUP study. *Pain*, *150*(2), 332–339. http://doi.org/10.1016/j.pain.2010.05.020

This study article outlines risk factors for misuse of prescribed opioids. The authors define misuse of prescribed opioids in the way that the National Institute of Drug Abuse which is "taking a medication in a manner other than that prescribed or for a different condition that that which the medication is prescribed." The article states that misuse is dangerous because it can lead to accidental overdoses and may signify that a patient is developing opioid abuse. The associations that could cause possible or probable opioid misuse are younger age (18-30), chronic back pain, multiple pain complaints, previous substance abuse, and daily opioid dose in access of 120 mg Morphine Equivalency Dose (MED). The study suggests monitoring patients more closely if they require a dose higher than 120 mg MED. This study did not find data to suggest that gender or mental health issues were associated with increased risk of opioid misuse. This study was completed by reviewing medical records of patients that received Chronic Opioid Therapy and had either Medicaid insurance or private insurance in Arkansas.

43) Sussman, S. & Sussman, A.N. Considering the definition of addiction. *International Journal Environmental Research and Public Health* 2011; 8(10), 4025-4038. doi: 10.3390/ijerph8104025

This article discusses the definition of addiction that is being used currently. The authors break down the definition of addiction into 5 areas including: engagement in the behavior to achieve appetite effects, preoccupation with the behavior, temporary satiation, loss of control and suffering negative consequences. Engagement in the behavior to achieve appetite effects refers to substance used by people seeking reduction in pain, recreational enjoyment, heightened sensations, achieving a fantasy, or changing personal affect. Preoccupation with the behavior refers to thinking about and desiring to perform a behavior excessively. This also includes excessive time spent on planning the behavior and performing and possibly recovering from the effects. Two concepts that interact with preoccupation is tolerance and withdrawal. The concept of "satiation" has not been researched in depth but is a concept that is reported by people with addiction and researchers looking at addiction. Loss of control occurs when a person desires to stop the behavior but feels that they are unable to do so. Some people feel that they have lost their will to control the behavior or compulsions to do the behavior. They might even disregard other basic forms of self-care. They may be impulsive, signifying a lack of control and planning, but also exhibit future planning skills when trying to obtain the drug of choice. Negative consequences vary greatly in what they can be. They can be social, physical, legal or emotional. They include anything that can negatively impact the person as a result of their continued drug use.

44) Veilleux, J. C., Colvin, P. J., Anderson, J., York, C., & Heinz, A. J. (2010). A review of opioid dependence treatment: pharmacological and psychosocial interventions to treat opioid addiction. *Clinical Psychology Review*, *30*(2), 155-166. doi:10.1016/j.cpr.2009.10.006

The author talks about various treatment options available and the steps to pharmacological and psychosocial treatments. The aim of 'detoxification' is to stop opioid use altogether which is precipitated by an antagonist drug or by gradual tapering of opiate-type drugs. Following detoxification, comes the 'relapse prevention phase' which targets at long-term maintenance of an opioid-free life. This is usually achieved by antagonist drugs like naltrexone, which works by reducing opioid craving. Supplementary treatment components further reduce drop-out rates and increase naltrexone's efficacy.

Long-term maintenance is aimed at reducing intensity, frequency, and length of relapse to use non-prescribed opioids. The four commonly used drugs for this purpose are: methadone, LAAM, buprenorphine, and heroine itself. Recent studies, however, indicate that entrance into any maintenance program curbs HIV risk behaviors such as needle sharing etc. Psychological treatments are also important ways to prevent relapse and improve retention, but there isn't insufficient evidence to support their usefulness without medical management.

45) Ziegler, P. P. Addiction and the treatment of pain. *Substance Use & Misuse* 40, no. 13-14 (December 2005): 1945-1954. *Academic Search Complete*, EBSCOhost (accessed February 11, 2016).

This article reviews the prescribing methods for treating patients with pain who have a history of substance abuse. It is important for physician's to be aware of the risk of a patient relapsing when using prescription pain killers to the substance they were previously addicted to, or might become addicted to the pain killer being used. There are however safeguards that a physician can put in place to try to prevent relapse. It is best when prescribing opioid painkillers to prescribe them on a schedule instead of as needed so the decision to take more medication is not left to the patient. It is also best for another party to track the medications and dispense them to guard against dose escalation. Opioid painkillers should be discontinued and replaced with NSAIDS, ice/heat therapy, or physical therapy as soon as possible. During times of acute pain for a patient that is recovering from a substance use disorder, they should have more contact with their sponsor or support group and disclose that they are taking the medication for additional support and to prevent relapse.

For chronic pain patients, a thorough medical history and examination of medical records is needed. It is also important to include a family member or close friend in treatment to have someone who can communicate with physician if there are concerns of addiction or abuse. Periodic urine testing is also important to screen for other illicit substances or opioids that are not prescribed to the patient. It is also important to take a multidisciplinary approach to treating the pain and utilizing therapies such as acupuncture, biofeedback, neurofeedback, massage therapy, advanced physical therapy techniques, chiropractic therapy, Energy work-reiki, Yoga, meditation or hypnosis.

Warning signs that a patient may be developing an addiction to pain killers include, escalating tolerance in absence of objective signs of uncontrolled pain, requesting for early refills, reports of lost or damaged prescriptions, reports of lost or stolen pills, doctor shopping, visiting emergency departments for pain, stealing drugs or prescription pads from doctor's office, stealing drugs from relatives or friends, forging prescriptions, buying drugs online, and abusing other illicit drugs or alcohol. These signs could also be indicative of a person who has "pseudoaddiction" and is not trying to get the euphoria from medication but has uncontrolled pain.

Research Methods: Researchers used online based databases through the Missouri State University library and the World Wide Web for references. Specific websites were also accessed for reports on epidemiological data.

PubMed and Google Scholar:

Diagnostic criteria of opioid addiction, abuse; Prevention measures recognizing early signs, symptoms; differentiating addiction and abuse; opioid use

Google Scholar:

CAGE-AID; Aberrant drug related behaviors; Opioid abuse risk factors

Academic Search Complete:

Addiction definition; opioid abuse risk factors; painkiller abuse predictors; opioid addiction; opioid overdose; CAGE screening opioids; treatment for opioid addiction; opioid overdose prevention

Centers for Disease Control website: Morbidity and Mortality Weekly Report

Substance Abuse and Mental Health Services Administration website: The Treatment Episode Data Set