Epidemiology

According to the National Survey on Drug Use and Health (NSDUH) 2019 10.1 million people, 3.7% of the US population, were misusing opioids with the highest misuse age range of 18-25. Over the recent years 2016 – 2019 there has been most significant declines in age ranges of 12-17 and 18 – 25. The decline in part, is due to the changes in prescribing behaviors. However, once an individual has a use disorder after misuse or chronic use some individuals seek non-prescribed methods of obtaining opioids. The most common illicit substances are fentanyl, heroin, and buprenorphine. The fact that buprenorphine is identified as a substance that is obtained illicitly, highlights individuals are seeking to be relieved of withdrawal symptoms and that there are not enough providers available to obtain prescriptions appropriately. While there is a decrease in alcohol, opioids, and cocaine use there has been an increase in marijuana use in all age groups recently which has led to an increase in cannabis use disorder in most age groups and specifically in the age 12 – 17 group. Methamphetamine use unlike cocaine has increased or remained stable in all age groups. The highest number of users was in the twenty-six or older group at 1.7 million or 0.8% of the total US population. NSDUH 2019

The NSDUH has identified that illicit drugs, tobacco products, alcohol, marijuana, opioids, and cocaine use per population was 5.8%, 9.6%, 9.5%, 5.4%, 0.4% and 0.2% respectively. The 0.4% opioid and illicit drug use confers to 8,000 and 120,000 pregnant women. The percentages vary by regions and states. Arizona since 2017 has had over 16,500 verified non-fatal opioid overdose events and 7,500 confirmed opioid deaths.

The neonatal opioid withdrawal syndrome also referred to as neonatal abstinence syndrome has been monitored since 2017 by the Arizona Department of Health Services, ADHS has provided education opioid use disorder and management for of newborns born to mothers with opioid use disorders. AZDHS opioid dashboard

Neurobiology of addiction

Many neurobiological circuits involved and neuroadaptations that occur with addiction are defined by the three stages of the addiction cycle that drive drug-seeking behavior (Fig 1). The three cycles are Binge/Intoxication, Withdrawal/Negative affect, and Preoccupation/Anticipation. The ventral striatum/dorsal striatum are activated in the binge intoxication stage. In the withdrawal negative affect stage, the dopamine systems are compromised leading to brain stress systems being active leading to an aversive dysphoric state this enhances the preoccupation anticipation stage that will drive further seeking of drugs to reduce the dysphoric state. During this last stage, the cues from the hippocampus and basolateral amygdala converge with the frontal cortex in the drive and other components of the
frontal cortex are compromised which produce a reduction in executive function. Koob et al. 2008

PET and FDG-PET that measure glucose metabolism which is a sensitive indicator of damage in tissue demonstrate the changes that occur with chronic drug use (Fig 2). Damage to the orbital frontal cortex (OFC) results in improper inhibitory control and compulsive behavior, and damage to the myocardium will result in improper blood circulation. *Neuroimage*. 2013;64:277-283
Screening

All patients should be universally screened for substance use (alcohol, opioids, tobacco, sedatives, stimulants, and cannabis). Often this is done with a tool or questions that are not validated. All pregnant patients should be offered screening if positive brief intervention and referral to treatment. Initiating the screen with broad questions regarding parental, peers, partner, and past use can help the patient feel open to discussing current use. The 4P’s Plus is a validated tool that can also screen for domestic violence and depression. The time to administer is one minute if positive additional time would be needed for brief intervention and referral to treatment. SMFM Special Report July 2019.

At the Banner University Medicine Women’s Institute, we engage our social workers and behavioral health and addiction medicine team if a patient is positive for substance use disorder. Having co-located services of obstetrics, addiction medicine and behavioral health has is beneficial in establishing trust and organizing appointments.

Opioid Use Disorder

When a pregnant patient is referred for opioid use disorder the recommendation from ACOG, SMFM, SAMSHA and HRSA is to transition the patient from an illicit drug use to either methadone a full agonist or buprenorphine a partial agonist (Fig 3). Much research has been conducted over the last several years in obstetrics, in summary of that research, the priority of medications for opioid use disorder (MOUD) is to maintain recovery and abstinence from illicit opioid use. The best medication is the one that successfully achieves prolonged abstinence for the patient. The advantages of buprenorphine are a patient can receive from a prescriber with a DEA waiver often in a primary care office setting.

Fig 3. Illustration source: SAMSHA, 2012 National Survey on Drug use and Health, 2013

Currently there is not enough known about naltrexone as first line therapy in pregnancy. It is a reasonable consideration if the patient is stable on naltrexone and becomes pregnant. The other complicating variable is if the patient were to require surgery the naltrexone would affect optimal pain control. Seminars in Perinatology 43(2019)141-148
The available MOUD in pregnancy are listed in the following table.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism</th>
<th>Route of Administration</th>
<th>Dosage</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Full Agonist</td>
<td>Oral: Liquid, Pill or Wafer</td>
<td>Daily</td>
<td>Opioid Treatment Program (OTP)</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Partial Agonist</td>
<td>Sublingual: Pill or Film</td>
<td>Daily</td>
<td>Prescriber with waiver</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Implant</td>
<td>Every 6 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Injectable</td>
<td>Every 4 weeks</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Antagonist</td>
<td>Oral</td>
<td>Daily</td>
<td>Provider with prescribing authority</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Injectable</td>
<td>Monthly</td>
<td></td>
</tr>
</tbody>
</table>

**Induction of MOUD**

During pregnancy both inpatient and outpatient management is appropriate. With supportive medications both a traditional and micro-dosing method of induction to buprenorphine can be successful in either environment. *Clin Drug Invest* 2021;41(5):425-436
Traditional method requires that the mu receptor be vacated, or a precipitated withdrawal will occur secondary to the increase affinity that buprenorphine has at the receptor (Fig. 4).

The micro-induction method slowly saturates the mu receptors. (Fig. 5)

Conclusion
Addiction, defined by the Substance Abuse and Mental Health Services Administration (SAMSHA), American Society of Addiction Medicine (ASAM) and the National Institute on Drug Abuse (NIDA), is a primary, chronic disease of brain reward, motivation, memory, and related circuitry. It remains a complex medical and behavioral condition that will often require intense medical and behavior care. All persons should be screened for risk of substance misuse and use disorders. Screening to Brief Intervention should be complemented with referral to treatment when a substance use disorder is identified.

The physicians at Banner University Medical Center Phoenix Addiction Recovery Center (ARC) in Family Medicine and the Halle Empower and Affirmation Legacy (HEAL) in the Women’s Institute are committed to compassionately caring for individuals with substance use disorder. The Women’s Institute specifically works with pregnant and postpartum individuals with substance use disorder and perinatal mental health disorders.

Banner University Women’s Institute HEAL outpatient program: 602-521-5632
Banner Addiction Recovery Center: 602-839-4567