# California Health Benefits Review Program

## Analysis of California Assembly Bill 1288
## Medication-Assisted Treatment

A Report to the 2023–2024 California State Legislature

April 16, 2023

CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

# Key Findings

## Analysis of California Assembly Bill 1288
## Medication-Assisted Treatment

Summary to the 2023–2024 California State Legislature, April 16, 2023

CALIFORNIA HEALTH BENEFITS REVIEW PROGRAM

## AT A GLANCE

Assembly Bill (AB) 1288 would prohibit prior authorization requirements for several medications related to the treatment of opioid use disorder (OUD) and alcohol use disorder (AUD).

**Benefit Coverage:** Approximately 95.6% of commercial/CalPERS enrollees have a pharmacy benefit that would be subject to AB 1288. CHBRP estimates that 1% to 5% of these enrollees (the figure varies by medication) have a prior authorization requirement that would be prohibited by AB 1288. Postmandate, none would.

**Medical Effectiveness:** There is *limited evidence* that removal of prior authorization requirements for buprenorphine products is associated with increased prescriptions and higher treatment retention for OUD. There is *insufficient evidence* on the impact of prior authorization on methadone use for OUD. There is i*nsufficient evidence* on the impact of prior authorization on long-acting injectable naltrexone use for either OUD or AUD.

**Cost and Health Impacts[1]:** As benefit coverage would change for so few enrollees (5% or less, depending on the medication), and as few of that group both have AUD or OUD and are likely users of medication-assisted treatment, no measurable change in utilization, expenditures, or public health is expected at the state level. However, it is possible that there could be person-level effects. If some persons begin and continue treatment, there could be better health outcomes, possibly including the avoidance of a premature death.

## BILL SUMMARY

For these medications:

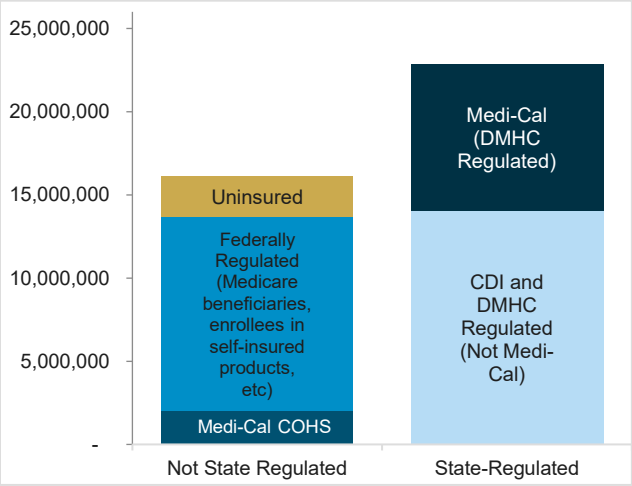
- buprenorphine products
- methadone
- long-acting injectable naltrexone

AB 1288 would not require coverage but would prohibit plans and policies regulated by the California Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI) from applying prior authorization requirements to their coverage of these prescription medications when the medications are used for detoxification or as treatment for substance use disorders (SUDs). All of these medications can be used for treatment of opioid use disorder and long-acting injectable naltrexone can be used for treatment of alcohol use disorder.

Although there are Medi-Cal beneficiaries enrolled in DMHC-regulated plans, their prescription medication benefit and benefits for some medication treatments are through centralized systems that are not subject to DMHC. Therefore, the impacts of AB 1288 would be on the health insurance of commercial/CalPERS enrollees in plans and policies regulated by DMHC or CDI.

[1] Similar cost and health impacts could be expected for the following year, though possible changes in medical science and other aspects of health make stability of impacts less certain as time goes by.

**Figure A. Health Insurance in CA**




*Source:* California Health Benefits Review Program, 2023.

# ANALYTIC APPROACH AND KEY ASSUMPTIONS

For this analysis, CHBRP has assumed that AB 1288 would not prohibit other forms of utilization management, such as formularies or step therapy, from being applicable.

# CONTEXT

The prevalence of opioid use disorder is estimated to be 1.58% among Californians aged 12 years and older. The prevalence of alcohol use disorder is estimated to be 11% among Californians aged 12 years and older.

Chronic diseases of all types often involve cycles of relapse and remission, can vary in severity, and often require ongoing professional treatment, lifestyle changes, and case management. SUDs are chronic conditions that may go into remission and are characterized by relapses requiring longitudinal, long-term care. Patients typically require long-term treatment consisting of multiple episodes of treatment or continued treatment over several years. Many patients are never able to achieve long-term recovery. Therefore, treatment goals not only focus on abstinence, but also on reducing harm from the negative consequences of substance use.

Treatments for SUD include prescription medication as well as counseling, residential facilities, and mutual help groups (e.g., Alcoholics Anonymous, Narcotics Anonymous).

There are many reasons persons with opioid use disorder and alcohol use disorder may not receive or seek treatment, including the medications addressed by AB 1288.

- Patient-level barriers may include lack of health insurance; patient-experienced stigma related to having opioid use disorder or alcohol use disorder or taking medications for these conditions; past treatment experiences and beliefs (positive or negative); readiness; logistical or financial issues; knowledge and role of medications used in treatment.
- Provider-level barriers may include general provider supply limits; some providers' unwillingness to prescribe.
- System- or policy-level barriers may include federal and/or state regulatory restrictions on the medications; for persons with health insurance, any applicable cost sharing requirements or utilization management requirements (which may include prior authorization).

# IMPACTS

## Medical Effectiveness

There is *limited evidence* that removal of prior authorization requirements for buprenorphine products is associated with increased use and higher treatment retention for opioid use disorder.

There is *insufficient evidence* on the impact of prior authorization on methadone use for opioid use disorder.

There is *insufficient evidence* on the impact of prior authorization on long-acting injectable naltrexone use for either opioid use disorder or alcohol use disorder.

For treatment of opioid use disorder, there is *clear and convincing evidence* that buprenorphine products and methadone are more effective with regard to treatment retention, reduction in use of illicit opioids, relapse, and improved health outcomes, compared to a placebo or no treatment. There is a *preponderance of evidence* that long-acting injectable naltrexone is effective with regard to treatment retention and abstinence, but not for overdose prevention, compared to a placebo or oral naltrexone.

For treatment of alcohol use disorder, there is a *preponderance of evidence* that long-acting injectable naltrexone is more effective with regard to reducing

return to drinking compared to a placebo or oral naltrexone.

## Benefit Coverage, Utilization, and Cost

### Benefit Coverage

The medications addressed by AB 1288 are most commonly covered through a pharmacy benefit.

For Medi-Cal beneficiaries in DMHC-regulated managed care plans, the pharmacy benefit is separate and is administered by the Department of Health Care Services (DHCS). Therefore, these beneficiaries have a pharmacy benefit that is not subject to DMHC regulation. Among commercial/CalPERS enrollees, 1.2% do not have a pharmacy benefit and 3.2% have a pharmacy benefit that is not regulated by DMHC or CDI. Because AB 1288 does not require coverage of the medications it addresses, baseline benefit coverage for enrollees without a pharmacy benefit or whose pharmacy benefit is not regulated by DMHC or CDI is compliant and would not change.

Approximately 95.6% of commercial/CalPERS enrollees in plans and policies regulated by DMHC or CDI have a pharmacy benefit regulated by DMHC or CDI that would be subject to AB 1288. CHBRP estimates that 1% to 5% of these enrollees (the figure varies by medication) have a prior authorization requirement that would be prohibited by AB 1288. Postmandate, none of these enrollees would have a prior authorization requirement applicable to these medications when they are on formulary.

### Utilization and Expenditures

No measurable change in utilization or expenditures at the state level is expected because benefit coverage would change for very few commercial/CalPERS enrollees (1% to 5% of depending on the medication) and few in that group would both have one of the disorders and be a likely user of one of the medications. However, it is possible that a few enrollees might increase utilization of the medications addressed by AB 1288, postmandate.

## Public Health

CHBRP projects no measurable public health impact at the population level because AB 1288 is not expected to create measurable changes in benefit coverage for or utilization at the state level. However, it is possible that AB 1288 could yield some person-level health improvements if some enrollees increase utilization of the medications the bill addresses.

## Long-Term Impacts

Because the change in benefit coverage is so limited, no state-level long-term impacts of AB 1288 on health outcomes — including premature death associated with opioid use disorder and alcohol use disorder — can be projected. However, if some enrollees increase utilization of the medications addressed by AB 1288, it is possible that there could be some reduction in premature deaths at the person level.

# A Report to the California State Legislature

# Analysis of California Assembly Bill 1288
# Medication-Assisted Treatment

April 16, 2023

**California Health Benefits Review Program**
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**www.chbrp.org**

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The California Health Benefits Review Program (CHBRP) was established in 2002. As per its authorizing statute, CHBRP provides the California Legislature with independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit-related legislation. The state funds CHBRP through an annual assessment on health plans and insurers in California.

An analytic staff based at the University of California, Berkeley, supports a task force of faculty and research staff from multiple University of California campuses to complete each CHBRP analysis. A strict conflict-of-interest policy ensures that the analyses are undertaken without bias. A certified, independent actuary helps to estimate the financial impact. Content experts with comprehensive subject-matter expertise are consulted to provide essential background and input on the analytic approach for each report.

More detailed information on CHBRP's analysis methodology, authorizing statute, as well as all CHBRP reports and other publications, are available at www.chbrp.org.

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# POLICY CONTEXT

The California Assembly Committee on Health has requested that the California Health Benefits Review Program (CHBRP)[2] conduct an evidence-based assessment of the medical, financial, and public health impacts of Assembly Bill (AB) 1288, Medication-Assisted Treatment.

For these medications:

- buprenorphine products
- methadone
- long-acting injectable naltrexone

AB 1288 would not require coverage but would prohibit plans and policies regulated by California Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI) from applying prior authorization requirements to their coverage of these prescription medications when the medications are used for detoxification or as part of treatment of substance use disorders (SUDs). All of these medications can be used for treatment of opioid use disorder and long-acting injectable naltrexone can be used for treatment of alcohol use disorder.

The full text of AB 1288 can be found in Appendix A.

## Relevant Populations

If enacted, AB 1288 would apply to the health insurance of approximately 22.8 million enrollees (58.6% of all Californians). This represents 100% of the 22.8 million Californians who will have health insurance regulated by the state that may be subject to any state health benefit mandate law, which includes health insurance regulated by DMHC and CDI. Although there are Medi-Cal beneficiaries enrolled in DMHC-regulated plans, their prescription medication benefit and benefits for some medication treatments are through centralized systems that are not subject to DMHC. Therefore, the impacts of AB 1288 would be on the health insurance of commercial/CalPERS enrollees in plans and policies regulated by DMHC or CDI.

## Analytic Approach and Key Assumptions

For this analysis, CHBRP has assumed that AB 1288 would not prohibit other forms of utilization management, such as formularies or step therapy, from being applicable.

## Interaction With Existing State and Federal Requirements

Health benefit mandates may interact and align with the following state and federal mandates or provisions.

### California Policy Landscape

#### *California law and regulations*

Prior authorization requirements are not applicable for Medi-Cal beneficiaries prescribed any of the medications listed above (DHCS, 2021).

[2] CHBRP's authorizing statute is available at www.chbrp.org/about_chbrp/faqs/index.php.

Methadone as a treatment for opioid use disorder is only available from opioid treatment programs (OTPs) (Pew Research Center, 2020). Rules governing OTPs exist at both the federal and state levels: The federal government establishes baseline requirements for OTPs, and states layer additional requirements on top of them (ASAM, 2021).

### *California Medication-Assisted Treatment Program*

In 2017, California received more than $476 million in discretionary grants from SAMHSA to aid in the opioid crisis (DHCS, 2023a). The California Department of Health Care Services (DHCS) initiated the California Medication-Assisted Treatment (MAT) Expansion Program in response to the opioid epidemic in the state and to help stop overdose deaths (DHCS, 2023a). The goals of the program are to increase access to medication-assisted treatment, reduce unmet treatment need, and reduce opioid-related overdose deaths. The program targets populations who do not have access medication including youth, people in rural areas, and American Indians and Alaska Native tribal communities (DHCS, 2023a). The program supports more than 30 projects in the state with 650 access points for treatment including more than 140,000 new Californians with opioid disorder received medication through this program (DHCS, 2023b).

### *Similar requirements in other states*

At least eighteen states (Arizona, Arkansas, Colorado, Delaware, Montana, Maine, Illinois, Massachusetts, Missouri, New Hampshire, New Jersey, New York, Oregon, Vermont, Tennessee, Virginia, Washington, and West Virginia), have laws that limit prior authorization on medications used to treat SUDs, as does the District of Columbia (LAC, 2020, NCSL, 2022).

## Federal Policy Landscape

### *Prescriber restrictions*

The Consolidated Appropriations Act, 2023, removed the federal requirement that providers submit a Notice of Intent (waiver) to prescribe buprenorphine for opioid use disorder treatment (SAMHSA, 2023b). This legislation also removed the limits on the number of patients a practitioner may treat. This allows providers with a current Drug Enforcement Administration (DEA) registration with Schedule III authority to prescribe buprenorphine for opioid use disorder treatment as allowed by scope of practice in each state. With the removal of this waiver requirement, more providers are now able to prescribe buprenorphine.

### *Affordable Care Act*

A number of Affordable Care Act (ACA) provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how AB 1288 may interact with requirements of the ACA as presently exist in federal law, including the requirement for certain health insurance to cover essential health benefits (EHBs).[3,4]

[3] The ACA requires nongrandfathered small-group and individual market health insurance — including but not limited to qualified health plans sold in Covered California — to cover 10 specified categories of EHBs. Policy and issue briefs on EHBs and other ACA impacts are available on the CHBRP website: www.chbrp.org/other_publications/index.php.

[4] Although many provisions of the ACA have been codified in California law, the ACA was established by the federal government, and therefore, CHBRP generally discusses the ACA as a federal law.

### Essential Health Benefits

In California, nongrandfathered[5] individual and small-group health insurance is generally required to cover EHBs.[6] In 2024, approximately 12.1% of all Californians will be enrolled in a plan or policy that must cover EHBs. [7]

States may require state-regulated health insurance to offer benefits that exceed EHBs.[8,9,10] Should California do so, the state could be required to defray the cost of additionally mandated benefits for enrollees in health plans or policies purchased through Covered California, the state's health insurance marketplace. However, state benefit mandates specifying provider types, cost sharing, or other details of existing benefit coverage would not meet the definition of state benefit mandates that could exceed EHBs.[11]

AB 1288 would not require coverage for a new state benefit mandate and would not appear to exceed the definition of EHBs in California.

[5] A grandfathered health plan is "a group health plan that was created – or an individual health insurance policy that was purchased – on or before March 23, 2010. Plans or policies may lose their 'grandfathered' status if they make certain significant changes that reduce benefits or increase costs to consumers." Available at: www.healthcare.gov/glossary/grandfathered-health-plan.
[6] For more detail, see CHBRP's issue brief *California State Benefit Mandates and the Affordable Care Act's Essential Health Benefits*, available at https://chbrp.org/other_publications/index.php.
[7] See CHBRP's resource *Sources of Health Insurance in California for 2024* and CHBRP's issue brief *California State Benefit Mandates and the Affordable Care Act's Essential Health Benefits*, both available at https://chbrp.org/other_publications/index.php.
[8] ACA Section 1311(d)(3).
[9] State benefit mandates enacted on or before December 31, 2011, may be included in a state's EHBs, according to the U.S. Department of Health and Human Services (HHS). Patient Protection and Affordable Care Act; Standards Related to Essential Health Benefits, Actuarial Value, and Accreditation. Final Rule. Federal Register, Vol. 78, No. 37. February 25, 2013. Available at: www.gpo.gov/fdsys/pkg/FR-2013-02-25/pdf/2013-04084.pdf.
[10] However, as laid out in the Final Rule on EHBs U.S. Department of Health and Human Services (HHS) released in February 2013, state benefit mandates enacted on or before December 31, 2011, would be included in the state's EHBs, and there would be no requirement that the state defray the costs of those state-mandated benefits. For state benefit mandates enacted after December 31, 2011, that are identified as exceeding EHBs, the state would be required to defray the cost.
[11] Essential Health Benefits. Final Rule. A state's health insurance marketplace would be responsible for determining when a state benefit mandate exceeds EHBs, and qualified health plan issuers would be responsible for calculating the cost that must be defrayed. Patient Protection and Affordable Care Act; Standards Related to Essential Health Benefits, Actuarial Value, and Accreditation. Final Rule. Federal Register, Vol. 78, No. 37. February 25, 2013. Available at: www.gpo.gov/fdsys/pkg/FR-2013-02-25/pdf/2013-04084.pdf.

# BACKGROUND ON MEDICATION-ASSISTED TREATMENT FOR SUBSTANCE USE DISORDERS

AB 1288 would prohibit state-regulated plans and policies from requiring prior authorization for buprenorphine products, methadone, or long-acting injectable naltrexone for detoxification (medically supervised withdrawal) or maintenance treatment of a substance use disorder (SUD) that is prescribed according to generally accepted national professional guidelines for the treatment of an SUD. As AB 1288 applies specifically to buprenorphine products, methadone, and long-acting injectable naltrexone — medications that are used for opioid use disorder and alcohol use disorder — this *Background* section will focus on opioid use disorder and alcohol use disorder[12], the above specific medication treatments, and prior authorization for these medications.

## Definitions of Opioid Use Disorder and Alcohol Use Disorder

### Opioid Use Disorder

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) defines opioid use disorder as "a problematic pattern of opioid use leading to clinically significant impairment or distress" and persons must meet at least two of the defined criteria within a 12-month period to receive a diagnosis (APA, 2013). Opioid use disorder applies to the class of medications or drugs that includes illegal drugs such as heroin, synthetic opioids such as fentanyl, and prescription pain medications such as oxycodone, hydrocodone, codeine, and morphine that are misused for indications other than prescribed (CDC, 2022a). Prescription opioids are used to treat moderate to severe pain, and persons who take prescription opioids can develop opioid use disorder (CDC, 2017).

### Alcohol Use Disorder

The DSM-5 characterizes alcohol use disorder as a pattern of alcohol use (e.g., wine, beer, and spirits) that results in significant impairment or distress. People meeting at least two of 11 specified criteria within a 12-month period are diagnosed with mild, moderate, or severe alcohol use disorder depending on the number of criteria met (APA, 2013).

## Prevalence of Opioid Use Disorder and Alcohol Use Disorder in California

CHBRP reports the most recent data available and cites national data when California data are unavailable. In this report, misuse[13] or dependence[14] rates are used as proxy measures when data on opioid or alcohol use disorders are unavailable.]

[12] Substance use disorder diagnosis are associated with the following: alcohol; cannabis; hallucinogens; inhalants; opioids; sedatives, hypnotics, or anxiolytics; stimulants; tobacco (nicotine); and other (or unknown) substances (CDC, 2022b). The analysis of AB 1288 will focus on opioid use disorder and alcohol use disorder.
[13] The National Institute on Drug Abuse describes the difference between drug use and drug misuse; "drug misuse is used to distinguish improper or unhealthy use from use of a mediation as prescribed or alcohol in moderation and includes repeated use of drugs to produce pleasure, alleviate stress, and/or alter or avoid reality. It also includes using prescription medications in ways other than prescribed" (NIDA, 2023).
[14] "Physical dependence can occur with regular use of any substance, even when taken as prescribed" and symptoms occur when the substance is taken away; dependence leads to cravings in order to alleviate symptoms of withdrawal (NIDA, 2023).

- *Opioid use disorder*[15] prevalence in California was 1.58% among people aged 12 years and older in 2021(SAMHSA, 2023a).
    - In the United States, among those reporting a prescription opioid use disorder, 35.2% also report alcohol use disorder[16] (NIDA, 2018).
- *Alcohol use disorder* prevalence in California was 11% among people aged 12 or older in 2021 (SAMHSA, 2023a).
    - In the United States, among those reporting alcohol use disorder, 3.9% report a concomitant prescription opioid use disorder (NIDA, 2018).

# Health Outcomes of Opioid Use Disorder and Alcohol Use Disorder

## Opioid Use Disorder

In 2017, the U.S. Surgeon General declared the opioid crisis a U.S. public health emergency due to the escalating rates of opioid overdose, and related mortality and other harms (HHS, 2018). In addition to a greater risk of mortality and premature mortality, people with opioid use disorder are at a higher risk for developing cardiac dysrhythmias; respiratory depression; impairment in daily function (Blanco et al., 2013); and contraction of infections including HIV, hepatitis (A, B, and C), tuberculosis, and endocarditis, which lead to increased use of health care services to treat those conditions (SAMHSA, 2016; Tsui et al., 2014).

### *Mortality*

The number of opioid-related overdose deaths has increased over the last decade. In 2021, 7,175 Californians died from an opioid-related overdose, which was an increase of 119% from 2019 (CDPH, 2023).

## Alcohol Use Disorder

Alcohol use disorder is the third leading cause of preventable mortality in the United States. Excessive alcohol use increases the risk of developing serious acute and chronic health problems, including but not limited to brain damage (including dementia), liver disease, heart disease, immunosuppression and infections, hypertension, cancers, depression, pancreatitis, fetal alcohol syndrome, and traumatic injuries or deaths from falls, car accidents, physical altercations, suicide, and homicide (NIAAA, 2018).

### *Mortality*

In California, an average of 19,335 people died per year due to excessive alcohol use from 2020 to 2021 (see Table 4) (Jiménez et al., 2023); 62% of deaths resulted from chronic causes (cancer, heart disease, and diseases of the liver, gallbladder, and pancreas); and almost 38% of deaths results from acute causes (injuries, violence, and motor vehicle crashes) (Jiménez et al., 2023).

# Treatment of Opioid Use Disorder and Alcohol Use Disorder

## Substance Use Disorder Relapse, Remission, and Long-term Therapy

Chronic diseases of all types often involve cycles of relapse and remission, can vary in severity, and often require ongoing professional treatment, lifestyle changes, and case management (ASAM, 2011; Goodwin

[15] "Opioid use disorder is defined as meeting the criteria for heroin or pain reliever use disorder" (SAMHSA, 2023a).
[16] Polysubstance use is the use of more than one drug, which includes when two or more are taken together or within short period of time. Polysubstance use is common (CDC, 2022c).

and Sias, 2014). SUDs are chronic conditions that may go into remission and are characterized by relapses requiring longitudinal, long-term care (Saitz et al., 2008). Patients typically require long-term treatment consisting of multiple episodes of treatment or continued treatment over several years (Dennis and Scott, 2007). Many patients are never able to achieve long-term recovery. Therefore, treatment goals not only focus on abstinence, but also on reducing harm from the negative consequences of substance abuse. It is possible for a patient who has more than one substance use disorder to be in recovery from one type of SUD, but not another. Health care professionals note that relapse and return to opioid or alcohol use is common during the recovery process for many patients, and it is important for patients to work with their provider to resume or modify the treatment plan (McCarty et al., 2018; NIDA, 2017). For many persons with opioid use disorder or alcohol use disorder, maintenance treatment plans are recommended to sustain abstinence (Schuckit, 2016).

### *Opioid use disorder*

The Substance Abuse and Mental Health Services Administration (SAMHSA) describes maintenance treatment as "providing medications to achieve and sustain clinical remission of signs and symptoms of opioid use disorder and support the individual process of recovery without a specific endpoint" (SAMHSA, 2021a). Some persons with opioid use disorder may require long-term medication treatment to ensure sustained recovery. There is evidence that relapse of opioid use disorder occurs less often for patients on medications (buprenorphine-naloxone and long-acting injectable naltrexone) for treatment (16%) compared to patients with no medication for treatment (40%) (Greiner et al., 2021).

### *Alcohol use disorder*

Some persons with alcohol use disorder experience a chronic condition with recurring treatment, abstinence, and relapse (McKay and Hiller-Sturmhöfel, 2011). Data from a nationally representative sample from 2012 to 2013 found that one third of adults with alcohol use disorder prior to the past year still had persistent alcohol use disorder, over half had remission from alcohol use disorder as classified by the DSM-5, and of the respondents that met criteria for remission, one third were indicative of recovery (Fan et al., 2019).

## Medications for Opioid Use Disorder

Treatments for SUD include prescription medication (medications for opioid use disorder or medications for alcohol use disorder), also called medication-assisted treatment [) as well as counseling, residential facilities, and mutual help groups (e.g., Alcoholics Anonymous, Narcotics Anonymous) (SAMHSA, 2023e). AB 1288 lists three FDA-approved medication options for opioid use disorder and alcohol use disorder, and the following medications will be the focus of CHBRP's review of treatments: *buprenorphine products, methadone, or long-acting injectable naltrexone* (see Table 1).

**Table 1. Comparison of FDA-Approved Medications for Opioid Use Disorder and Alcohol Use Disorder Treatment**

| Indication | Medication (Brand Name; Generic Availability) | Formulation | Use-Limiting Side Effects | Provider Administered |
|---|---|---|---|---|
| **Opioid Use Disorder Treatment** | Buprenorphine SL (no brand; generic only) | Sublingual Tablet | | No |
| | Buprenorphine (Sublocade; no generic) | Subcutaneous pre-filled syringe | Pain at injection site; Prolonged QTc interval | **Yes** |
| | Buprenorphine; Naloxone (Zubsolv; no generic) | Sublingual Tablet | | No |
| | Buprenorphine; Naloxone (no brand; generic only) | Sublingual Tablet | | No |
| | Buprenorphine; Naloxone (Suboxone; generic available) | Sublingual Film | Unpleasant taste | No |
| | Methadone (no brand; generic only) | Tablet | Only available at OTP; Prolonged QTc interval | **Yes** |
| | Methadone (no brand; generic only) | Oral Solution | Only available at OTP; Prolonged QTc interval | **Yes** |
| **Opioid Use Disorder or Alcohol Use Disorder Treatment** | Long-acting injectable naltrexone (Vivitrol; no generic) | Intramuscular | Pain at injection site | **Yes** |

*Source:* California Health Benefits Review Program, 2023; SAMHSA, 2023c; Vivitrol, 2021.
*Key:* OTP = opioid treatment program.

### *National professional guidelines for opioid use disorder treatment*

The American Society of Addiction Medicine (ASAM) provides the National Practice Guidelines for the Use of Medications in the Treatment of Addiction Involving Opioid Use (Kampman and Jarvis, 2015) and SAMHSA provides the Treatment Improvement Protocol (TIP) 63 that reviews the clinical standards of care for patients with opioid use disorder including buprenorphine, methadone, and long-acting injectable naltrexone (SAMHSA, 2021a). In 2020, the ASAM updated requirements to include that all FDA approved medication prescribed for the treatment of opioid use disorder should be available to all persons seeking treatment[17] (ASAM, 2020a).

[17] Pregnant persons seeking treatment of opioid use disorder may be prescribed buprenorphine or methadone, but not long-acting injectable naltrexone (SAMHSA, 2021a).

### Buprenorphine

Buprenorphine is prescribed for the medically supervised withdrawal and maintenance phases of opioid use disorder treatment (SAMHSA, 2021a). Buprenorphine and buprenorphine/naloxone are FDA-approved in various formulations (Table 1) (SAMHSA, 2021a).

Buprenorphine for opioid use disorder can be prescribed by any healthcare provider who has a current Drug Enforcement Administration (DEA) registration with Schedule III authority to prescribe (such as acetaminophen with codeine) so it can be prescribed by primary care physicians, emergency room physicians, pediatricians, etc., beginning January 1, 2023; additional training requirements[18] will be needed by June 27, 2023 for all providers applying for the first time or renewing the DEA registration, but the registration of Notice of Intent ("x-waiver") is no longer required to prescribe buprenorphine for opioid use disorder (SAMHSA, 2023b).

### Methadone

Methadone is prescribed for the medically supervised withdrawal and maintenance phases of opioid use disorder treatment (SAMHSA, 2021a). Methadone for opioid use disorder treatment can only be dispensed by federally certified and accredited opioid treatment programs (OTP, "methadone clinic"). Patients must go to the OTP each day to take their methadone dose. Some persons may be able to receive take-home doses of methadone if they have meet treatment goals as defined by the Federal and state OTP regulations.

Federal policies require persons younger than aged 18 years to demonstrate two prior opioid use disorder treatment attempts without medication before methadone can be initiated, and when adolescents meet these requirements, it is rare for methadone clinics to allow access (SAHM, 2021).

### Long-acting injectable naltrexone

Naltrexone is prescribed for the prevention of relapse from opioid misuse and after medically supervised withdrawal phases of opioid use disorder treatment (SAMHSA, 2021a). Before initiating long-acting injectable naltrexone, persons with opioid use disorder must adequately complete opioid withdrawal (Kampman and Jarvis, 2015; SAHMSA, 2021a). There are no regulations for healthcare professionals to prescribe naltrexone for opioid use disorder treatment. Long-acting injectable naltrexone is administered as deep intramuscular injection in the gluteal muscle every 4 weeks by a healthcare professional (Kampman and Jarvis, 2015; SAHMSA, 2021a).

## *National professional guidelines for alcohol use disorder treatment*

The ASAM Clinical Practice Guidelines on Alcohol Withdrawal Management (ASAM, 2020b) provides clinicians with recommendations for screening, treating, and managing persons with symptoms of alcohol withdrawal. *Medication for the Treatment of Alcohol Use Disorder: A Brief Guide* provides information and recommendations for clinicians in treating different phases of alcohol use disorder with medications (SAMHSA, 2015).

[18] Training requirements for the DEA registration for schedule II-V controlled medications include: "eight hours of training from certain organizations on opioid or substance use disorders, board certification in addiction medicine or addiction psychiatry from the American Board of Medical Specialties, American Board of Addiction Medicine, or the American Osteopathic Association, or graduation within five years and status in good standing from medical, advanced practice, nursing, or physician assistant school in the United States that included successful completion of an opioid or other substance use disorder curriculum of at least eight hours" (SAMHSA, 2023b).

### Long-acting injectable naltrexone

Naltrexone is prescribed for alcohol dependence treatment and helps reduce alcohol consumption. It is most effective when prescribed for persons who discontinue drinking before treatment initiation (SAHMSA, 2015). Long-acting injectable naltrexone is typically not prescribed during the acute phase of alcohol treatment and cannot be administered to someone with opioids in their system. Long-acting injectable naltrexone for alcohol use disorder treatment is prescribed and administered as deep intramuscular injection in the gluteal muscle every 4 weeks by a healthcare professional (SAMHSA, 2015).

## Opioid Use Disorder and Alcohol Use Disorder Treatment Utilization

Many persons with opioid use disorder and alcohol use disorder do not receive treatment, and programs that offer medications for treatment remain underused and underfunded (AJMC, 2020). Among adult and adolescent commercial HMO and PPO health plan members in California who received a new diagnosis for alcohol dependence or drug dependence, 38% had an initial treatment visit in 2019 (CHCF, 2022). 13% of the newly diagnosed who received an initial treatment visit received ongoing care (at least two follow-up visits within 30 days of initial treatment) (CHCF, 2022). Almost two-thirds of commercially insured persons in California with drug dependence or alcohol dependence do not initiate treatment.

### Opioid Use Disorder

Clemans-Cope et al. (2018) estimated that about 20% of Californians with opioid use disorder will seek medications for treatment based on study findings from a U.S. study (Wu et al., 2016). The number of people in California who are prescribed medications for opioid use disorder has increased from 35,231 in 2015 to 38,892 in 2019 for methadone, and 2,922 in 2015 to 9,143 in 2019 for buprenorphine (SAMHSA, 2020).

In a 2019 national dataset from the National Survey on Drug Use and Health (NSDUH) (persons aged 12 years and older), 28% of persons diagnosed with opioid use disorder received medications for treatment, 15% received treatment with no medications, and 58% received no treatment (Mauro et al., 2022). Among the persons who received treatment with medications, 35% had public insurance, 21% had private insurance, and 17% had no insurance (Mauro et al., 2022).

### Alcohol Use Disorder

Generally, alcohol use disorder is treated in specialty facilities or through mutual-help organizations such as Alcoholics Anonymous; it is treated less commonly through primary care or with medication (Jonas et al., 2014). In 2017, 5.4% of Californians aged 12 years and older reported needing but not receiving alcohol use disorder treatment (and 9.9% among those aged 18–25 years) (SAMHSA, 2017). Nationally, 1.6% of adults with alcohol use disorder used medications for treatment in 2019, and 4.6% of adults who had alcohol use disorder received any treatment in 2021 (Han et al., 2021; NIAAA, 2023).

## Barriers to Opioid Use Disorder and Alcohol Use Disorder Treatment Utilization

There are many reasons persons with opioid use disorder and alcohol use disorder do not receive or seek treatment. Barriers and delays to accessing treatment for opioid use disorder and alcohol use disorder include:

- System- or policy-level: insurance prior authorization, formulary restrictions, and regulatory requirements;
- Provider-level: provider supply and provider willingness to prescribe; and

- Patient-level: patient stigma related to having opioid use disorder or alcohol use disorder or taking medications for these conditions; past treatment experiences and beliefs (positive or negative and readiness); logistical or financial; knowledge and role of medications used in treatment (Mackey et al., 2020; Saini et al., 2022).

## System- or Policy- Level Barriers

### *Prior authorization*

Prior authorization is a utilization and price control management tool that requires prescribers or their staff to submit documentation of medical need to the health plan for approval of coverage prior to insurance coverage for the medication. Prior authorization may be required at the initiation of new medication and can be required when patients switch between medications or different formulations. Prior authorization requirements for medications prescribed for opioid use disorder and alcohol use disorder can delay care and increase the time it takes a person to begin treatment for several days (60% wait at least 1 business day and 26% wait at least 3 business days [AMA, 2017]). A delay in beginning medication treatment can mean a prolonged period that the patient experiences withdrawal, the person loses readiness to begin treatment, and periods of forced abstinence and return to use [AMA, 2022; Latronica, 2021]). Qualitative and survey data shows that among prescribers of buprenorphine, a common barrier to prescribing buprenorphine is insurance prior authorization requirements (Andraka-Christou et al., 2022; Haffajee et al., 2020; Marino et al., 2019.)

Prior authorization requirements can also limit the use of specific medication formulations that might be preferred by some patients due to side effect profiles or effectiveness (Latronica, 2021). In 2021, 17.5% of commercial formularies required prior authorization for extended-release buprenorphine injection compared to 5.4% that required prior authorization for immediate release buprenorphine products (Nguyen et al., 2022a).

### *Insurance formulary restrictions*

In addition to prior authorization, insurance coverage limitations for medication for opioid use disorder and medication for alcohol use disorder through formularies (only certain or no medications covered) and step therapy (“fail first”) requirements can cause delays in beginning treatment and loss of motivation to begin treatment for some patients (Andraka-Christou and Capone, 2018; Latronica, 2021). When medications or certain formulations of medications are not included on formularies, the patient will have a period of waiting when providers will need to find a different appropriate formulation covered under the plan and policy, and if prior authorization or step therapy is required, additional delay in care will occur (Andraka-Christou and Capone, 2018).

Long-acting injectable naltrexone is not always included on plan formularies and patients would have to pay out-of-pocket or have prior authorization requirements that other medications for opioid use disorder or alcohol use disorder do not require (Alanis-Hirsch et al., 2016).

### *Federal restrictions on prescribing and dispensing buprenorphine and methadone*

As discussed in the *Policy Context* section, the Consolidated Appropriations Act, 2023, removed the federal requirement that limited the prescription of buprenorphine for opioid use disorder (SAMHSA, 2023b). Now any healthcare professional who has a DEA registration for Schedule III controlled medications (such as acetaminophen with codeine) can prescribe buprenorphine.

Pharmacies must comply with federal and state dispensing regulations for buprenorphine as a Schedule III controlled substance and is monitored by the Suspicious Orders Report System (Qato et al., 2020). As a result of these regulations and risk of liability for opioid diversion, suppliers, pharmacies, and pharmacists may restrict supply and dispensing of buprenorphine at pharmacies. The barriers related to dispensing regulations include delayed or suspended buprenorphine shipments to pharmacies,

buprenorphine not stocked in pharmacy inventories, and buprenorphine prescriptions declined and not filled (Qato et al., 2020).

Policies in the United States limit adolescents' access to medications for opioid use disorder. Federal policies require persons younger than aged 18 years to demonstrate two prior opioid use disorder treatment attempts without medication before methadone can be initiated; when adolescents meet these requirements, it is rare for methadone clinics to allow access (Hadland et al., 2018.; SAHM, 2021).

As discussed above, due to the federal restrictions, CHBRP assumes AB 1288 would not change administration, payment, or barriers to methadone treatment.

## Provider-Level Barriers

### *Provider supply and location*

Provider supply, including geographic access to existing providers as well as the number of appropriate providers per capita and provider attitudes are barriers to treatment (Sharma et al., 2017). In California, there are providers available to prescribe medications for opioid use disorder treatment in almost every county, but most counties (around 30[19]) have fewer providers per capita then the national average of 9.7 prescribing providers per 100,000 residents (Haffajee et al., 2019). In 2020, there were 24 counties in California that did not have an opioid treatment program to provide methadone treatment (CHCF, 2022).

Patients may face supply issues or geographical barriers to accessing long-acting injectable naltrexone or subcutaneous buprenorphine (Sublocade), as it needs to be injected in a medical office (clinic) rather than dispensed at a pharmacy. The medical office (clinic) would need to order and store the medication, have staff available for the injection, and the patient would need to make an appointment and travel to the medical office (Sharma et al., 2017).

Federal law restricts methadone treatment (for opioid use disorder) to federally certified opioid treatment programs (OTPs, "methadone clinics"). There are limited OTPs in California, in limited locations (such as urban settings), and limited patient appointments. According to the SAMHSA Opioid Treatment Program Directory, there are 168 OTPs in California (SAMHSA, 2023d).

Typically, alcohol use disorder treatment occurs in specialty care settings such as rehabilitation facilities, mental health centers, and non–health care settings such as peer support groups. Barriers to initiating treatment for persons with alcohol use disorder include accessibility to these facilities and the referrals needed (Mintz et al., 2021).

In addition to removal of the Notice of Intent (waiver), the Consolidated Appropriations Act, 2023, also removed the limits on the number of patients a practitioner may treat (SAMHSA, 2023b). With the removal of this waiver for buprenorphine, more providers will be able to prescribe without limits on number of patients to treat and may result in increased patient access to buprenorphine. However, as this change occurred in the last 3 months, no updated data on prescribing patterns is available.

### *Provider willingness*

Provider willingness to treat opioid use disorder and alcohol use disorder can also be limited; not all providers are comfortable prescribing medications to treat these conditions due to a lack of clinical knowledge and SUD education in medical school and residency, lack of office space and support resources, time pressure, prior authorization requirements, financial sustainability, concern of diversion, and personal beliefs or stigma against treating opioid use disorder and alcohol use disorder (Andraka-

[19] In 2017, there were about 40 counties with low extended-release naltrexone provider rate and about 30 counties with low buprenorphine provider rate and low OTP rate (Haffajee et al., 2019).

Christou and Capone, 2018; Dhanani et al., 2022; Garrett and Young, 2022; Haffajee et al., 2020; Marino et al., 2019; McNeely et al., 2018; Mintz et al., 2021; SAMHSA, 2015; Williams et al, 2018).

Although most pharmacists are willing to dispense buprenorphine, there are often barriers and pharmacist perceived discomfort with dispensing of buprenorphine (Hill et al., 2023). Community-based pharmacists identified insurance prior authorization, ability to reach prescribers with questions, concerns about buprenorphine diversion, and DEA investigation risk as the biggest barriers to dispensing buprenorphine. Policies and perceived barriers also vary by type of pharmacy. Independent pharmacies have more restrictive policies in place than commercial pharmacies (Hill et al., 2023).

### Patient-Level Barriers

Patient-level barriers for seeking, beginning, or continuing opioid use disorder treatment include stigma, previous experience with treatment, logistical barriers, and knowledge gaps (Mackey et al., 2020). The stigma of and the ability to acknowledge their SUD may reduce their desire or ability to seek care, even more so for those who have co-occurring psychiatric conditions (Fisher et al., 2016; Jones et al., 2015; Verissimo and Grella, 2017). The stigma against medications for opioid use disorder can be due to beliefs that they are a "crutch" or the person is weak or a failure for needing them (Mackey et al., 2020). Concern for stigma or legal-related consequences of seeking treatment might defer some persons from seeking treatment (Corrigan and Nieweglowski, 2018); the Americans with Disabilities Act (ADA) prevents discrimination against persons with opioid use disorder or alcohol use disorder who are in recovery and who do not engage in illegal drug use or alcohol use while working and it includes protection during recovery when medications are prescribed for treatment (DOJ, 2022; Foreman et al. ,2000 ). It also provides protection for persons with past opioid use disorder with a "record of disability" (DOJ, 2022).

Prior experience with opioid use disorder treatment is also a barrier to initiating treatment if the previous experiences were negative. Stigma and negative treatment experiences are commonly identified by patients (Mackey et al., 2020.) Stigma is also a barrier to treatment for alcohol use disorder (Mintz et al., 2021). Additional patient-level barriers are related to logistical and financial barriers if persons do not have insurance or access to government-subsidized grants (Sharma et al., 2017) and knowledge deficits or gaps, which include where to obtain care, lack of education about medications for treatment, misconceptions of the medications, and uncertainty of what to expect with long-acting buprenorphine and naltrexone (Garett and Young, 2022; Mackey et al., 2021).

## Disparities[20] and the Role of SDOH in Opioid Use and Alcohol Use Disorder

CHBRP defines disparities as noticeable and preventable or modifiable differences between groups of people. Health insurance benefit mandates or related legislation may impact disparities. Where intersections between health insurance benefit mandates and social determinants or systemic factors exist, CHBRP describes relevant literature.

CHBRP found literature identifying disparities by race/ethnicity, gender, age, sexual orientation, and among persons with mental health disorders and persons who live in rural areas for substance use disorders and treatment rates. Taken as a whole, treatment of SUDs is inextricably linked bi-directionally with many important social determinants of health (SDOH). SDOH such as quality of a person's local built environment, proximity to crime, educational opportunities, self-efficacy, and income levels can influence a person's risk for substance use disorders (Mooney et al., 2018; Sudhinaraset et al., 2016). Conversely, SUDs can also alter a person's baseline SDOH through the consequences of the disorder, such as involvement with the criminal justice system, job loss, unstable housing or family situations, and discrimination against those with treated or untreated SUDs (Krebs et al., 2016).

[20] Several competing definitions of "health disparities" exist. CHBRP relies on the following definition: Health disparity is defined as the differences, whether unjust or not, in health status or outcomes within a population. (Wyatt et al., 2016).

Table 2 shows the prevalence of opioid use disorder and alcohol use disorder by race/ethnicity in the United States and by age in California.

**Table 2. Prevalence Rates (Percentage) of Opioid Use Disorder and Alcohol Use Disorder by Race/Ethnicity in the United States and by Age in California, 2021**

| | Opioid Use Disorder | Alcohol Use Disorder |
|---|---|---|
| **Overall rate in California (12 years old +)** | 1.6 | 11 |
| **Race/Ethnicity (a)** | | |
| Black | 2.4 | 10.1 |
| American Indian/Native Alaskan | 4.4 | 15.6 |
| Native Hawaiian/Pacific Islander | 1.5 | 14 |
| Asian | 0.7 | 6 |
| Latino | 1.9 | 10.3 |
| White | 2 | 11 |
| **Age (b)** | | |
| 12-17 | 1.2 | 3.3 |
| 18-25 | 1.5 | 15.3 |
| 26 and older | 1.6 | 11.3 |

*Source:* California Health Benefits Review Program, 2023; SAMHSA, 2023a (NSDUH data 2021); SAMHSA, 2022a

*Notes:* Rates rounded to the nearest tenth.

(a) NSDUH data for 2021 available nationally by race/ethnicity.

(b) NSDUH data for 2021 available for California by age.

Table 3 shows disparities in opioid-related overdose mortality by race/ethnicity, sex, and age in California. See the sections below for further discussion of disparities.

**Table 3. Opioid-related Overdose Mortality, Emergency Department Visit, and Hospitalization Rates in Californian per 100,000 residents by Race/Ethnicity, Sex, and Age, 2021**

| | Mortality | Emergency Department Visits | Hospitalizations |
|---|---|---|---|
| **Overall annual rate** | 18 | 54 | 12 |
| **Race/ethnicity** | | | |
| Black | 34 | 100 | 24 |
| Latino | 14 | 38 | 9 |
| American Indian/Alaskan Native | 47 | 76 | 11 |
| Asian/Pacific Islander | 4 | 7 | 2 |
| White | 27 | 88 | 19 |
| **Sex** | | | |
| Male | 27 | 78 | 16 |
| Female | 8 | 29 | 8 |
| **Age** | | | |
| 15 to 19 | 9 | 43 | 9 |
| 20 to 29 | 54 | 226 | 34 |
| 30 to 39 | 73 | 236 | 39 |
| 40 to 49 | 50 | 120 | 24 |
| 50 to 64 | 77 | 129 | 52 |
| 65 to 79 | 24 | 53 | 51 |

*Source:* California Health Benefits Review Program, 2023; CDPH, 2023.

*Note:* Rates rounded to the nearest whole number; age-adjusted rates reported except for age category (crude rates).

## Race or Ethnicity

### *Opioid use disorder*

Disparities exist for opioid use disorder prevalence, treatment, and outcomes by race/ethnicity.

In 2019, almost one third of White persons with opioid use disorder received medications for treatment compared to 20% of Black or other non-Latino multiracial groups and 15% of Latino persons (Mauro et al., 2022). Prescribing practices changed significantly for medications prescribed for opioid use disorder (buprenorphine and long-acting injectable naltrexone) after the beginning of the COVID-19 pandemic, with 30.5% decrease for buprenorphine and 10.5% decrease of long-acting injectable naltrexone across all races/ethnicities. However, Black, Latino, and Asian persons experienced greater decreases in buprenorphine prescription fills compared to White persons (Nguyen et al, 2022b).

Racial disparities in overdoses have emerged with greater increases among Black and Latino persons (Furr-Holden et al., 2021). In California, the opioid-related overdose death rate was highest among American Indian/Alaskan Native and Black persons compared to White persons and healthcare utilization for opioid-related overdoses in the emergency department and hospitalization was highest among Black persons during 2021 (see Table 3) (CDPH, 2023).

### *Alcohol use disorder*

Disparities exist for alcohol use disorder prevalence and outcomes by race/ethnicity nationally and in California.

Nationally, American Indian/Alaskan Native persons have the highest prevalence of alcohol use disorder (SAMHSA, 2021b; SAMHSA, 2022a). Latino and Black persons have relatively lower rates of alcohol use disorders than do White persons; however, ethnic and racial disparities exist for alcohol-related diseases, problems, and deaths in these groups (NIAAA, 2019). For example, Latino and Black persons have a higher risk for developing alcohol-related liver disease and subsequent cirrhosis mortality than White persons. Self-reported rates of driving under the influence (DUI) are highest among mixed race and Native Americans and Alaska Native persons (NIAAA, 2019). In California, alcohol-induced death rates during 2016 were twice as high for American Indian/Alaskan Native persons compared to all other racial/ethnic groups (CHCF, 2022).

## Sex or Gender[21]

In California, men have higher rates of both alcohol-induced deaths and opioid-related overdose deaths with rates two to three times higher compared to females (CHCF, 2022; CDPH, 2023). Men in California also have higher rates of opioid-related overdose emergency department visits and hospitalizations compared to women (see Table 3) (CDPH, 2023).

### *Opioid use disorder*

Disparities exist between women and men with opioid use disorder presentation and treatment.

Women with opioid use disorder often present to treatment with more co-occurring mental health and substance use disorders and life instability compared to men (Huhn et al., 2019; Leone et al., 2017; Vo et al., 2016). Men with opioid use disorder are more likely to present to treatment with persistent drug use and risky drug-related behavior compared to women (Huhn et al., 2019).

### *Alcohol use disorder*

Disparities exist between women and men with alcohol use disorder presentation, treatment, and outcomes.

As noted in Table 4, men have higher rates of alcohol attributable death compared to women (Jiménez et al., 2023). Women with alcohol use disorder have increased risk of developing alcohol-related heart disease, cancer, and liver disease and have higher rates of co-occurring psychiatric disorders compared to men with alcohol use disorder (Erol and Karpyak, 2015; Karpyak et al., 2016). Compared to men, women with alcohol use disorder experience alcohol cravings as a way to cope with negative emotion and stress (Peltier et al., 2019) and are more likely to have family or spouse history of alcohol use disorder (Khan et al., 2013). Women with alcohol use disorder are less likely to receive treatment compared to men (5% vs. 7%) (SAMHSA, 2015).

[21] CHBRP uses the National Institutes of Health (NIH) distinction between “sex” and “gender”: “‘Sex’ refers to biological differences between females and males, including chromosomes, sex organs, and endogenous hormonal profiles. ‘Gender’ refers to socially constructed and enacted roles and behaviors which occur in a historical and cultural context and vary across societies and over time.” (NIH, 2019).

**Table 4. Number of Alcohol Attributable Deaths for All, Acute, and Chronic Causes by Sex in California, 2020-2021**

| | All Causes | Acute Causes | Chronic Causes |
|---|---|---|---|
| Total | 19,335 | 7,322 | 12,013 |
| Males | 13,445 | 5,698 | 7,747 |
| Females | 5,890 | 1,624 | 4,266 |

*Source:* California Health Benefits Review Program, 2023; Jiménez et al., 2023.

*Note:* Chronic causes of alcohol attributable death include cancer, heart disease, and diseases affecting the liver, gallbladder, and pancreas. Acute causes of alcohol attributable death include injuries, violence, and motor vehicle crashes (Jiménez et al., 2023).

## Age

### *Opioid use disorder*

Disparities exist in opioid use disorder prevalence, treatment, and outcomes by age.

Adolescents experience disparities in access to opioid use disorder treatment compared to adults. Many adolescents do not receive treatment for opioid use disorder in the United States and when they do receive treatment, about 1 in 4 receive timely administration of buprenorphine, methadone, or naltrexone (Hadland et al., 2018). In 2019, the NSDUH found that no adolescents (aged 12-17 years) received medications for opioid use disorder (Mauro et al., 2022).

### *Alcohol use disorder*

Disparities exist in alcohol use disorder prevalence by age.

In California, young adults aged 18 to 25 years had the highest rate of alcohol use disorder compared to adults aged 26 and older (15.3% vs. 11.3%) (see Table 2) (SAMHSA, 2023a).

CHRBP was unable to find alcohol use disorder treatment or outcome rates by age.

## Sexual Orientation

Lesbian, gay, and bisexual individuals are more likely to have substance use disorders, oftentimes more severe, than heterosexuals (Krueger et al., 2020; Philbin et al., 2020).

### *Opioid use disorder*

Disparities exist in opioid use disorder prevalence and treatment for lesbian, gay, and bisexual persons.

In 2020, Lesbian, gay, and bisexual adult opioid use disorder prevalence was 2.4% (SAMHSA, 2022b). Opioid misuse (heroin, prescription opioid misuse) prevalence was 6.7% for lesbian, gay, and bisexual persons compared to 3.4% for the general population in the United States (SAMHSA, 2022b; SAMHSA, 2022c). Among lesbian, gay, and bisexual adults with opioid misuse in the past year, 11.9% also reported heavy alcohol use in the past month (SAMHSA, 2022b).

In the United States, there is limited availability of LGBTQ-specific opioid use disorder treatment programs. Of the programs or facilities that advertised medications for opioid use disorder and LGBTQ special programs for opioid use disorder treatment, 24% offered those services (Paschen-Wolff et al., 2022).

### *Alcohol use disorder*

Disparities exist in alcohol use disorder prevalence for lesbian, gay, and bisexual persons.

In 2020, lesbian, gay, or bisexual adults had high rates of alcohol use disorder compared to the general population in the United States (aged 18 to 25 years: 23.8% vs. 15.6%; aged 26 and older: 20.8% vs. 10.3%) (SAMHSA, 2022b; SAMHSA, 2022d). Among lesbian, gay, or bisexual adults with serious mental illness, 25.2% reported heavy alcohol use in the past month (SAMHSA, 2022b).

The National Institute on Drug Abuse reports a series of statistics regarding disparities in alcohol misuse/abuse according to sexual orientation (NIDA, 2017). 2013 survey data from the U.S. Census Bureau showed that more gay or lesbian adults, and bisexual adults aged 18 to 64 years reported past-year binge drinking (five or more drinks on a single occasion) than heterosexual adults (35.1%, 41.5%, and 26.0%, respectively) (Ward et al., 2014). Another analysis of LGBT people in treatment for substance use disorders found that they initiated alcohol consumption earlier than their heterosexual counterparts (McCabe et al., 2013).

## Mental Health Disorders

Dual diagnosis describes a condition of co-occurrence of substance use disorders and mental health disorders (Ludici et al., 2020). Nationally, one in four persons with serious mental illness also have a substance use disorder (NIDA, 2020). Treatment of persons with dual diagnosis is complex and often treatments have unsuccessful outcomes (Ludici et al., 2020).

### *Opioid use disorder*

Nationally, among adults with opioid use disorder, 64.3% had any mental illness and 26.9% had a serious mental illness in the past year. Among persons with opioid use disorder and any mental illness, 38.4% sought substance use disorder treatment and 54.7% sought mental health treatment services, and among those with opioid use disorder and serious mental illness, 38.2% sought substance use disorder treatment and 64.6% sought mental health disorder treatment (Jones and McCance-Katz, 2019).

### *Alcohol use disorder*

Rates of mood, anxiety, substance, and thought disorders are higher among persons with alcohol use disorder than the general population (Castillo-Carniglia et al., 2019). National data shows that the prevalence of major depressive disorder with current alcohol use disorder ranges from 4% to 22%; estimated prevalence of alcohol use disorder among persons with anxiety disorder ranges from 20% to 40%; and among persons with bipolar disorder, the prevalence of alcohol use disorder is 42% (Castillo-Carniglia et al., 2019).

## Geography

### *Opioid use disorder*

Disparities exist in opioid use disorder treatment for persons living in rural areas.

In California, there were over 500,000 persons with opioid use disorder without access to treatment in 2019 and most counties had fewer providers that could prescribe opioid use disorder medications per capita than the national averaged (Clemans-Cope et al., 2019; Haffajee et al., 2019). Access to treatment is especially challenging to persons who live in rural areas such as Northern and Central California (UCSF, 2023).

### *Alcohol use disorder*

Disparities exist in alcohol use disorder treatment access for persons living in rural areas.

Persons with alcohol use disorder living in rural areas are less likely to have access to specialty providers that prescribe medications for alcohol use disorder (Abraham and Yarbrough, 2021; Davis and O'Neill, 2022).

## Societal Impact of Substance Use Disorder in California

The presence of substance use disorder in California has direct and indirect economic and societal costs. The California Department of Public Health estimates that substance use disorder in California produces an estimated economic loss of over $230 billion annually. Illicit drugs and misuse of prescription opioids account for $18 billion and alcohol accounts for $45 billion in direct health care costs (DHCS, 2013). The remaining $155 billion accounts for indirect costs, such as lost work productivity and crime (NIDA, 2017). In 2010, California taxpayers spent $35.011 billion due to excessive alcohol use and when adjusted for inflation, $47.264 billion in 2022 (NCDAS, 2023). Please note, the societal impact discussed here is relevant to a broader population than AB 1288 impacts, which would affect the health insurance of a subset of Californians (see *Policy Context*).

# MEDICAL EFFECTIVENESS

As discussed in the *Policy Context* section, AB 1288 would prohibit state-regulated plans and policies from requiring prior authorization for buprenorphine products, methadone, or long-acting injectable naltrexone for detoxification (medically supervised withdrawal) or maintenance treatment of a substance use disorder (SUD) that is prescribed according to generally accepted national professional guidelines for the treatment of an SUD. These medications, their role in treatment for opioid use disorder and alcohol use disorder, and mode of administration are outlined in Table 5. The medical effectiveness review summarizes findings from evidence[22] on the impact of prior authorization on outcomes related to use of buprenorphine products, methadone, and long-acting injectable naltrexone and includes summaries of findings on the effectiveness and harms of these medications as well.

**Table 5. Medications Addressed by AB 1288 for Treatment of Opioid Use Disorder and Alcohol Use Disorder**

| Medication | Substance Use Disorder(s) | Role in Treatment | Mode of Administration |
|---|---|---|---|
| Buprenorphine (including buprenorphine-naloxone) | Opioid use disorder | Manage withdrawal symptoms, maintain abstinence from opioids | Tablet, film, injection (by medication provider) |
| Methadone | Opioid use disorder | Manage withdrawal symptoms, maintain abstinence from opioids | Tablet, liquid (a) |
| Naltrexone | Opioid use disorder, Alcohol use disorder | Maintain abstinence from opioids or abstinence from or reduction in alcohol consumption | Injection (by medical provider) (b) |

*Source:* California Health Benefits Review Program, 2023.

*Notes:* (a) AB 1288 would affect coverage for methadone but would not affect the dispensing of methadone because federal law restricts methadone treatment (for opioid use disorder) to federally certified opioid treatment programs (i.e., methadone clinics).

(b) Naltrexone is also available in tablet formulation, but AB 1288 is limited to long-acting injectable naltrexone only.

Additional information on SUDs treated using buprenorphine, methadone, and long-acting injectable naltrexone is included in the *Background on Medication-Assisted Treatment for Substance Use Disorders* section.

## Research Approach and Methods

Studies of buprenorphine products, methadone, and long-acting injectable naltrexone and prior authorization restrictions for these medications were identified through searches of PubMed/MEDLINE, the Cochrane Library, CINAHL, SCOPUS, Embase, and PsychInfo. The search was limited to abstracts of studies published in English. The search was limited to studies published from 2020 to present because

[22] Much of the discussion in this section is focused on reviews of available literature. However, as noted in the section on Implementing the Hierarchy of Evidence in the *Medical Effectiveness Analysis and Research Approach* document (posted at https://www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis in the absence of fully applicable to the analysis peer-reviewed literature on well-designed randomized controlled trials (RCTs), CHBRP's hierarchy of evidence allows for the inclusion of other evidence.

CHBRP had previously conducted thorough literature searches on these topics in 2020 for SB 854 (Substance Use Disorders) and in 2018 for AB 2384 (Medication-Assisted Treatment).

Although the focus of AB 1288 is on prior authorization for use of buprenorphine products, methadone, and long-acting injectable naltrexone when already covered by an insurance plan, CHRBP included a discussion on the effectiveness, comparative effectiveness, and harms of these medications as patients might be prescribed a certain medication or changed between medications due to effectiveness, relative effectiveness, or harms. CHBRP did not review new literature published since January 2020 regarding the effectiveness of buprenorphine products or methadone versus a placebo or no treatment as the previous CHBRP review for SB 854 concluded that there is *clear and convincing evidence* that these medications are more effective than a placebo or no treatment. Where available, new studies were included in the evidence summary from SB 854 for the effectiveness of long-acting injectable naltrexone and the comparative effectiveness between different medications.

This report summarizes relevant findings from these previous CHBRP reviews plus literature published from January 1, 2020, through March 6, 2023, regarding impact of prior authorization on outcomes related to use of buprenorphine products, methadone and long-acting injectable naltrexone. A more thorough summary of this evidence is available in Appendix C.

Of the 556 articles identified in the search for articles published since January 2020, 120 were reviewed for potential inclusion and a total of 17 new studies were included in the medical effectiveness review for this report. The other articles were eliminated because they did not address the medications specified by AB 1288, were of poor quality, or did not report findings from clinical research studies. A more thorough description of the methods used to conduct the medical effectiveness review is presented in Appendix B.

The conclusions below are based on the best available evidence from peer-reviewed and grey literature.[23] Unpublished studies are not reviewed because the results of such studies, if they exist, cannot be obtained within the 60-day timeframe for CHBRP reports.

## Key Questions

CHBRP's medical effectiveness review addressed the following primary key question:

1. How does health plans' use of prior authorization affect the use of buprenorphine products, methadone, and long-acting injectable naltrexone, and related patient outcomes?

Additionally, CHBRP's medical effectiveness review addressed the following supporting key questions:

2. What is the effectiveness of buprenorphine products, methadone, and long-acting injectable naltrexone used to treat opioid use disorder and alcohol use disorder compared to no treatment or a placebo?

3. What is the comparative effectiveness of buprenorphine products, methadone, and long-acting injectable naltrexone for treatment of opioid use disorder and alcohol use disorder ?

4. What are the harms of buprenorphine products, methadone, and long-acting injectable naltrexone for treatment of opioid use disorder and alcohol use disorder ?

[23] Grey literature consists of material that is not published commercially or indexed systematically in bibliographic databases. For more information on CHBRP's use of grey literature, visit https://www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis.

This report briefly summarizes relevant evidence regarding the effectiveness, comparative effectiveness and harms of these medications; a more thorough summary of this evidence is available in Appendix C.

## Methodological Considerations

The systematic reviews CHBRP cites in the Medical Effectiveness review of AB 1288 include overlapping groups of studies on these medications to treat SUD. Thus, the conclusions of these systematic reviews regarding the effectiveness of these medications are not independent of one another.

The systematic reviews included randomized controlled trials (RCTs) and observational studies. RCTs maximize ability to discern whether any differences observed between intervention and comparison groups are due to the intervention or to other factors. However, in the case of FDA-approved medications for SUDs, many of the RCTs follow subjects for less than one year, which limits ability to assess the long-term impact of receiving these medications. Most studies that have assessed long-term health impacts of treatment for opioid- and alcohol use disorders, such as mortality, liver disease, lung disease, human immunodeficiency virus (HIV), and hepatitis C, are observational studies. Findings from observational studies need to be interpreted with more caution because observational studies are less able to control for other differences between intervention and comparison groups that may affect the outcome of interest.

As there were limited studies on prior authorization requirements for these medications among commercial enrollees, this Medical Effectiveness review included studies assessing the impact of prior authorization among Medicare and Medicaid populations. Medicare and Medicaid populations can differ from commercially insured populations by health needs, comorbidities, demographics and other aspects of health insurance coverage.

## Outcomes Assessed

Studies of buprenorphine products, methadone, and long-acting injectable naltrexone for opioid use disorder have primarily examined outcomes related to opioid use and participation in treatment. Outcomes assessed include use of opioids during treatment, use of opioids at follow-up, and retention in treatment. Some studies have examined effects of opioid use disorder medications on morbidity or mortality. Studies of effects on morbidity have addressed birth outcomes for pregnant women treated for opioid use disorder and effects on the likelihood of contracting HIV and hepatitis C, two contagious diseases for which persons who inject opioids are at elevated risk. Studies of long-acting injectable naltrexone for alcohol use disorder have primarily examined outcomes related to alcohol use and participation in treatment. Outcomes assessed include drinking days, number of drinks consumed, and reducing lapse/relapse in drinking.

## Study Findings

This following section summarizes CHBRP's findings regarding the strength of evidence for the effectiveness of buprenorphine products, methadone, and long-acting injectable naltrexone for detoxification or maintenance treatment of a substance use disorder. Each section is accompanied by a corresponding figure. The title of the figure indicates the test, treatment, or service for which evidence is summarized. The statement in the box above the figure presents CHBRP's conclusion regarding the strength of evidence about the effect of a particular test, treatment, or service based on a specific relevant outcome and the number of studies on which CHBRP's conclusion is based. Definitions of CHBRP's grading scale terms is included in the box below, and more information is included in Appendix B.

The following terms are used to characterize the body of evidence regarding an outcome:

*Clear and convincing evidence* indicates that there are multiple studies of a treatment and that the large majority of studies are of high quality and consistently find that the treatment is either effective or not effective.

*Preponderance of evidence* indicates that the majority of the studies reviewed are consistent in their findings that treatment is either effective or not effective.

*Limited evidence* indicates that the studies have limited generalizability to the population of interest and/or the studies have a fatal flaw in research design or implementation.

*Inconclusive evidence* indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.

*Insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

More information is available in Appendix B.

## Effects of Prior Authorization on Use of Buprenorphine Products, Methadone, and Long-Acting Injectable Naltrexone

CHBRP's previous reviews for SB 854 and AB 2384 identified two studies that addressed the impact of utilization management (including prior authorization) on use of buprenorphine products to treat opioid use disorder or patient outcomes (Accurso and Rastegar, 2016; Clark et al., 2014). The updated literature search for AB 1288 identified an additional four studies examining the impact of prior authorization on use of medications to treat opioid use disorder or patient outcomes (Ferries et al., 2021; Keshwani et al., 2022; Mark et al., 2020; Parish et al., 2022).

### *Buprenorphine or buprenorphine-naloxone*

Accurso and Rastegar (2016) conducted a retrospective study including patients at one primary care practice associated with an academic medical center (n=297 people) on the effect of a change in insurer policy, in which a Medicaid managed care organization (which covered 55% of the patients prescribed buprenorphine for opioid use disorder during the study period) imposed a prior authorization requirement for sublingual buprenorphine dose of 16 mg/day, which led physicians in the practice to increase the daily dose for patients on higher daily doses. These patients were compared to other patients in the practice whose insurers did not require prior authorization for higher doses of buprenorphine. The rate of positive urine drug tests (defined as the presence of other opioids, nonprescribed benzodiazepines or cocaine, or the absence of prescribed buprenorphine) among patients who experienced a dose decrease rose from 27.5% to 34.2% (p=0.043). Persons in comparison groups who did not experience a change in buprenorphine dose showed no significant change in positive urine drug test rates. Moreover, all persons who were prescribed buprenorphine doses greater than 16 mg/day displayed lower rates of positive urine drug tests than groups prescribed lower doses. Retention in treatment was also highest among those prescribed greater than 16 mg/day (Accurso and Rastegar, 2016).

Clark et al. (2014) examined the effects of a change in the Massachusetts Medicaid program's prior authorization requirements for coverage of buprenorphine-naloxone (n=2,049 people). Under the policy, prior authorization was required for doses greater than 16 mg/day. After the prior authorization policy was

implemented the number of people prescribed doses of buprenorphine-naloxone greater than 24 mg/day decreased while the number prescribed lower doses per day increased. The relapse rate increased temporarily, and the increase was most pronounced among people who received baseline doses greater than 16 mg/day. The relapse rate returned to previous levels within 3 months. The authors did not report any other outcomes. A major limitation of this study is that it assessed the effects of instituting a prior authorization requirement. It does not address the impact of prohibiting prior authorization. This study also does not provide any information about the effects of other utilization management techniques.

Ferries et al. (2021), in a single group retrospective cohort study, compared Medicare Advantage enrollees with chronic opioid use who filled at least one prescription for buprenorphine products or oral naltrexone before (n=999 people) and after (n=1,222 people) the removal of prior authorization requirements by one large health insurer offering both commercial and Medicare Advantage plans. Under the prior authorization policy (effective through March 2018), prescriptions for buprenorphine products and oral naltrexone required renewal every 6 months and demonstration that the medication(s) was being used for treatment of opioid dependence. After removal of prior authorization, filled prescriptions for buprenorphine products or oral naltrexone increased by 7.8%, after adjusting for overall increases in Medicare Advantage Part D enrollment from 2017 to 2018. After adjusting for comorbidities and other demographic factors, removal of prior authorization led to a statistically significant 19% reduction in the likelihood of relapse for those who started a buprenorphine product or oral naltrexone after prior authorization was removed. Findings indicate that prior authorization led to a nonstatistically significant decrease in the frequency of ED visits in the six months following medication-assisted treatment initiation. The authors found no statistically significant differences in the rate of inpatient stays in the six months after treatment initiation, use of behavioral health services, or use of non-opioid medications for those initiating medication-assisted treatment before or after removal of prior authorization. CHBRP notes that the timing of the study was 1 to 2 years after the release of CDC opioid use guidelines for pain that encouraged caution with opioid prescriptions and might have influenced opioid use disorder diagnosis and treatment trends.

Using Medicaid data from 2013 to 2020, Keshwani et al. (2022) evaluated changes in buprenorphine use for opioid use disorder after removal of prior authorization requirements in California and Illinois compared to eight control states. After removal of prior authorization, there was a statistically significant immediate increase in buprenorphine prescriptions in Illinois (RR, 6.66; 95% CI: 4.67 to 10.47) and no statistically significant change in California (RR, 1.11; 95% CI: 0.76 to 1.61). The authors posit that these findings may be due to the existence of strict lifetime caps on opioid prescriptions and tapering dosage requirements for opioid prescriptions in Illinois prior to the removal of prior authorization, whereas California did not have any such requirements.

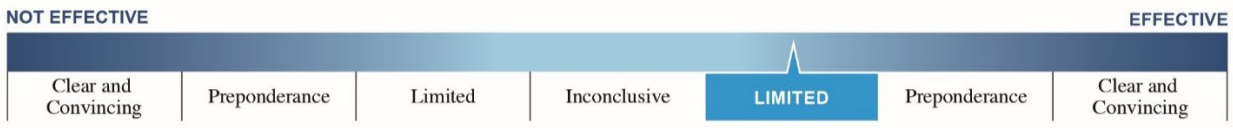
Mark et al. (2020) compared treatment initiation and health outcomes among Medicare enrollees with opioid use disorder who filled a prescription for buprenorphine-naloxone between 2012 and 2017. During this time period, the researchers compared outcomes for enrollees in Medicare Part D plans that always required prior authorization for buprenorphine-naloxone (n=775,874 people), enrollees in plans that removed prior authorization (n=113,286), enrollees in plans that never required prior authorization (n=189,461 people), and enrollees in plans that added prior authorization (n=616,919). Removal of prior authorization for buprenorphine-naloxone resulted in an increase of 1.8 new prescriptions for buprenorphine-naloxone per plan per year (95% CI: 0.8 to 2.9 new prescriptions per plan per year) and a statistically significant increase of 17.9 total prescriptions for buprenorphine-naloxone per plan per year (95% CI: 1.1 to 34.7 total prescriptions per plan per year), which is more than double the number of total prescriptions per plan per year, on average. On average, removal of prior authorization was associated with fewer all-cause inpatient admissions (- 5.7 admissions [95% CI: -12.1 to -0.3]), all-cause emergency department visits (-12.6 visits; 95% CI: -25.9 to -0.5), substance use disorder-related inpatient admissions (-2.0 admissions; 95% CI: -4.3 to -0.1), substance use disorder-related emergency department visits (-1.4 visits; 95% CI: -3.2 to -0.1), and decreases in nondrug medical expenditures (-$479.2; 95% CI: -$942.7 to -$21.1).

Parish et al. (2022) examined the quality of opioid use disorder treatment among Medicare enrollees in Part D plans requiring prior authorization for buprenorphine-naloxone and enrollees in Part D plans that

did not use prior authorization between March 2012 and July 2017. The authors assessed the relationship between prior authorization, receipt of opioid use disorder treatment aligned with best practices for initiating buprenorphine-naloxone (screening for comorbidities commonly occurring with SUD [hepatitis B, hepatitis C, liver function], weekly outpatient visits, and ongoing drug monitoring) and two quality measure of opioid prescribing (continuity of buprenorphine-naloxone use for 6 months and concurrent use of opioid medications and benzodiazepines). Compared to patients in Part D plans with prior authorization, the authors found that patients in plans with prior authorization were less likely to be screened for hepatitis B and hepatitis C, less likely to receive ongoing urine drug testing and similarly likely to remain on buprenorphine-naloxone for at least six months. Patients in plans with prior authorization were less likely to refill a prescription for benzodiazepines in the six months following opioid treatment initiation but more likely to fill a new prescription for benzodiazepines in the six months following opioid treatment initiation.

**Summary of findings regarding the effects of prior authorization requirements of buprenorphine products, methadone, and long-acting injectable naltrexone to treat opioid use disorder:** There is *limited evidence* from five retrospective studies that suggest that removal of prior authorization requirements for buprenorphine products is associated with increases in filled prescriptions for buprenorphine products, retention in treatment, and decreases in healthcare utilization (e.g., fewer all-cause and substance use disorder-related emergency department visits and inpatient admissions).

**Figure 1. The Effects of Prior Authorization Requirements of Buprenorphine Products to Treat Opioid Use Disorder**




## *Methadone and long-acting injectable naltrexone*

The medical effectiveness review did not identify any studies evaluating the impact of prior authorization on methadone or long-acting injectable naltrexone to treat opioid use disorder or alcohol use disorder.

**Summary of findings regarding the effects of prior authorization requirements of methadone, and long-acting injectable naltrexone to treat opioid use disorder or alcohol use disorder:** There is *insufficient evidence* to assess the impact of prior authorization on methadone or long-acting injectable naltrexone to treat opioid or alcohol use disorders and patient outcomes. *Insufficient evidence* is not "evidence of no effect"; it is possible that AB 1288 could impact outcomes related to prior authorization for methadone and long-acting injectable naltrexone to treat opioid use disorder or alcohol use disorder, but current evidence is insufficient to inform an estimate.

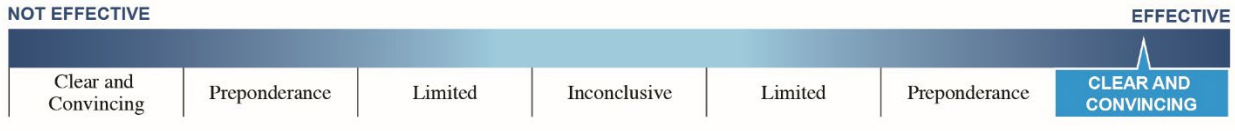
**Figure 2. The Effects of Prior Authorization Requirements of Methadone or Long-Acting Injectable Naltrexone to Treat Opioid Use Disorder or Alcohol Use Disorder**

## Effectiveness of Buprenorphine Products, Methadone and Long-Acting Injectable Naltrexone versus Placebo or No Medication

As mentioned previously, this Medical Effectiveness review did not assess new literature regarding the effectiveness of buprenorphine products and methadone versus a placebo or no treatment since CHBRP's 2020 analysis of SB 854 concluded that there is *clear and convincing evidence* that these medications are more effective than a placebo or no treatment. The study finding and conclusions in this section reflect those of SB 854. Additional details regarding included studies and findings about the effectiveness of buprenorphine products, methadone, or long-acting injectable naltrexone versus placebo or no medication are available in Appendix C.

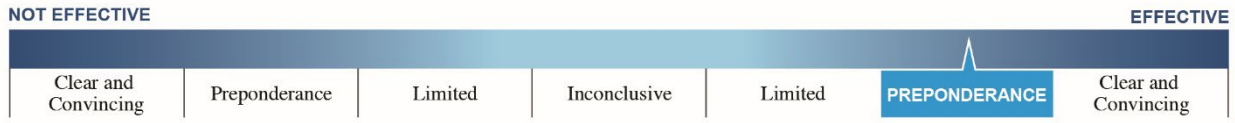
**Summary of findings regarding the effectiveness of buprenorphine and methadone for opioid use disorder:** There is *clear and convincing evidence* from 10 systematic reviews and five RCTs that buprenorphine (including buprenorphine-naloxone) and methadone are more effective than a placebo or no treatment with regard to retention in treatment for opioid use disorder, reduction in use of illicit opioids, relapse, lower likelihood of engaging in behaviors associated with elevated risk for HIV and hepatitis C, better birth outcomes, and lower mortality rates. Additional details regarding these studies and findings are available in Appendix C.

**Figure 3. The Effectiveness of Buprenorphine or Methadone for Opioid Use Disorder Versus Placebo or No Medication**



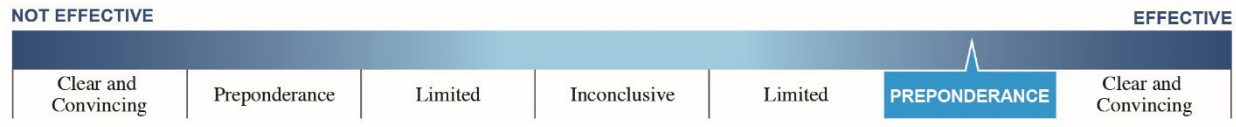

**Summary of findings regarding the effectiveness of long-acting injectable naltrexone for opioid use disorder:** There is *a preponderance of evidence* from two systematic reviews, one additional RCT, and one additional cohort study that long-acting injectable naltrexone is effective for treatment retention and abstinence, but not for overdose prevention, compared to placebo or oral naltrexone. Additional details regarding these studies and findings are available in Appendix C.

**Figure 4. The Effectiveness of Long-Acting Injectable Naltrexone for Opioid Use Disorder Versus Placebo or Oral Naltrexone**




**Summary of findings regarding the effectiveness of long-acting injectable naltrexone for alcohol use disorder:** There is a *preponderance of evidence* from three systematic reviews and one additional cohort study that long-acting injectable naltrexone is effective at reducing return to drinking compared to a placebo or oral naltrexone. Additional details regarding these studies and findings are available in Appendix C.

**Figure 5. The Effectiveness of Long-Acting Injectable Naltrexone for Alcohol Use Disorder Versus Placebo or No Medication**




## Comparative Effectiveness of Buprenorphine Products, Methadone, and Long-Acting Injectable Naltrexone

**Summary of findings regarding the comparative effectiveness of buprenorphine products versus methadone to treat opioid use disorder in a general population:** There is a *preponderance of evidence* from seven systematic reviews and four additional RCTs that the impact of methadone is similar or better than buprenorphine or buprenorphine-naloxone on retention in treatment and abstinence from opioids. Additional details regarding these studies and findings are available in Appendix C.

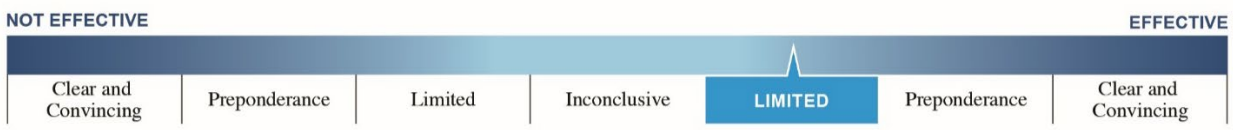
**Figure 6. Comparative Effectiveness of Buprenorphine Products vs. Methadone to Treat Opioid Use Disorder in a General Population (Similar Effectiveness or Favors Methadone)**


**Summary of findings regarding the comparative effectiveness of buprenorphine products versus methadone to treat opioid use disorder in pregnant persons:** There is a *preponderance of evidence* from six systematic reviews that buprenorphine products are associated with better newborn medical outcomes (i.e., birthweight, APGAR scores, neonatal abstinence syndrome) than methadone, but pregnant persons receiving buprenorphine products were less likely to remain in treatment compared to those receiving methadone. Additional details regarding these studies and findings are available in Appendix C.

**Figure 7. Comparative Effectiveness of Buprenorphine Products vs. Methadone to Treat Opioid Use Disorder in Pregnant Persons (Favors Buprenorphine Products)**


**Summary of findings regarding the comparative effectiveness of buprenorphine products versus long-acting injectable naltrexone to treat opioid use disorder:** There is *limited evidence* from three RCTs and two cohort study that buprenorphine or buprenorphine-naloxone is of similar effectiveness compared to long-acting injectable naltrexone on treatment retention, relapse rates or overdose. One RCT that compared long-acting injectable naltrexone to orally administered buprenorphine-naloxone found that people have more difficulty initiating treatment with long-acting injectable naltrexone and were more likely to relapse, and one cohort study found that overdose rates were higher among patients taking long-acting injectable naltrexone compared to buprenorphine. Additional details regarding these studies and findings are available in Appendix C.

**Figure 8. Comparative Effectiveness of Buprenorphine Products vs. Long-Acting Injectable Naltrexone to Treat Opioid Use Disorder — Buprenorphine vs. Long-Acting Injectable Naltrexone (Similar Effectiveness)**




## Harms Associated with Buprenorphine Products, Methadone, and Long-Acting Injectable Naltrexone

**Summary of findings regarding harms associated with buprenorphine products and methadone for opioid use disorder:** People treated with methadone and buprenorphine may experience side effects similar to those of opioids. People who receive methadone have a greater risk of opioid overdose during the first few weeks of treatment compared to prior to starting treatment and compared to those starting buprenorphine. Additional details regarding these studies and findings are available in Appendix C.

**Summary of findings regarding harms associated with long-acting injectable naltrexone for opioid or alcohol use disorder:** People treated with long-acting injectable naltrexone may experience side effects or injection site reactions. Initiating long-acting injectable naltrexone is associated with a higher risk of opioid overdose compared to initiating buprenorphine because people must abstain from opioids before initiating treatment and may be sensitive to lower doses of opioids if they relapse. Additional details regarding these studies and findings are available in Appendix C.

## Summary of Findings

Table 6 summarizes the evidence of effectiveness of prior authorization requirements on the use of buprenorphine products, methadone and long-acting injectable naltrexone to treat substance use disorders.

**Table 6. Summary of Evidence of the Impact of Prior Authorization on the Use of Buprenorphine Products, Methadone and Long-Acting Injectable Naltrexone to Treat Substance Use Disorder**

| Substance Use Disorder | Impact of Prior Authorization |
|---|---|
| **Opioid Use Disorder** | ***Limited evidence*** that removal of prior authorization requirements for buprenorphine products is associated with increased use of buprenorphine products and higher treatment retention.<br><br>***Insufficient evidence*** on the impact of prior authorization on methadone use for opioid use disorder.<br><br>***Insufficient evidence*** on the impact of prior authorization on long-acting injectable naltrexone use for opioid use disorder. |
| **Alcohol Use Disorder** | ***Insufficient evidence*** on the impact of prior authorization on long-acting injectable naltrexone use for alcohol use disorder. |

*Source:* California Health Benefits Review Program, 2023.

# BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

As discussed in the *Policy Context* section, for these medications

- buprenorphine products
- methadone
- long-acting injectable naltrexone

AB 1288 would not require coverage but would prohibit plans and policies regulated by DMHC or CDI from applying prior authorization requirements to the coverage of these prescription medications when the medications are used for detoxification (medically supervised withdrawal) or maintenance of treatment of a substance use disorder (SUD).

This section reports the potential incremental impacts of AB 1288 on estimated baseline benefit coverage, utilization, and overall cost.

For further details on the underlying data sources and methods used in this analysis, please see Appendix D.

## Baseline and Postmandate Benefit Coverage

Prescription medications are most commonly covered under an enrollee's pharmacy benefit. However, not all enrollees in a plan or policy regulated by DMHC or CDI have a pharmacy benefit regulated by DMHC or CDI. [24] For Medi-Cal beneficiaries in DMHC-regulated managed care plans, the pharmacy benefit is separate and is administered by DHCS. Therefore, these beneficiaries have a pharmacy benefit that is not subject to DMHC regulation. Among commercial/CalPERS enrollees, 1.2% do not have a pharmacy benefit and 3.2% have a pharmacy benefit that is not regulated by DMHC or CDI. Because AB 1288 does not require creation of a pharmacy benefit — only compliant benefit coverage when a pharmacy benefit is present — baseline benefit coverage for enrollees without a pharmacy benefit or whose pharmacy benefit is not regulated by DMHC or CDI is compliant and would not change.

Almost all — 95.6% — commercial/CalPERS enrollees in plans and policies regulated by DMHC or CDI do have a pharmacy benefit regulated by DMHC or CDI that covers both generic and brand-name outpatient prescription medications. These enrollees have a pharmacy benefit that would have to comply with AB 1288.

Current coverage of the medications addressed by AB 1288 was determined by a survey of the largest (by enrollment) providers of health insurance in California. Benefit coverage responses to an earlier survey[25] were verified through a new supplemental survey and review of current claims data. In addition, CalPERS was queried regarding related benefit coverage.

At baseline, as noted in Table 7, prior authorization requirements for the medications addressed by AB 1288 are uncommon for commercial/CalPERS enrollees with a pharmacy benefit regulated by DMHC or CDI.

[24] For more detail, see CHBRP's resource, *Pharmacy Benefit Coverage in State-Regulated Health Insurance*, available at http://chbrp.org/other_publications/index.php.
[25] *SB 854 Health Care Coverage: Substance Use Disorders*, available at chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.chbrp.org/sites/default/files/bill-documents/SB854/sb854-FullReport.pdf

**Table 7. AB 1288 Medication-Specific Baseline Benefit Coverage for Commercial/CalPERS Enrollees, 2024**

| Medication | % of enrollees with on-formulary medication coverage that is……Subject to prior authorization requirements |
|---|---|
| ***Opioid Use Disorder*** | |
| Buprenorphine | 5% |
| Methadone | 1% |
| Long-Acting Injectable Naltrexone | 5% |
| Combination Buprenorphine/ Naloxone | 1% |
| ***Alcohol Use Disorder*** | |
| Naltrexone – IM | 5% |

*Source: California Health Benefits Review Program, 2023.*

Postmandate, none of these enrollees would have a prior authorization requirement applicable to these medications when they are on formulary.

## Baseline and Postmandate Utilization and Expenditures

No measurable change in utilization or expenditures at the state level is expected. Benefit coverage would change for very few commercial/CalPERS enrollees (1% to 5% of depending on the medication) and few in that group (see prevalence estimates in the *Background* section) would have one of the disorders. However, it is possible that a few enrollees for whom benefit coverage would change, who have one of the disorders, might increase utilization of the medications addressed by AB 1288, postmandate.

# PUBLIC HEALTH IMPACTS

As discussed in the *Policy Context* section, AB 1288 would prohibit state-regulated plans and policies from requiring prior authorization for buprenorphine products, methadone, or long-acting injectable naltrexone for detoxification or maintenance treatment of a substance use disorder (SUD) that is prescribed according to generally accepted national professional guidelines for the treatment of an SUD.

The public health impact analysis includes estimated impacts in the short term (within 12 months of implementation) and in the long term (beyond the first 12 months postmandate). This section estimates the short-term impact[26] of AB 1288 on barriers to treatment, health outcomes, and disparities for opioid use disorder and alcohol use disorder and prohibition of prior authorization for buprenorphine products, methadone, or long-acting injectable naltrexone. See *Long-Term Impacts* for discussion of social determinants of health, premature death, and economic loss.

## Estimated Public Health Outcomes

As presented in *Medical Effectiveness*, there is *limited evidence* that removal of prior authorization for buprenorphine products is associated with increased prescriptions for treatment of opioid use disorder and *insufficient evidence* to assess the impact of prior authorization on methadone or long-acting injectable naltrexone to treat opioid or alcohol use disorders and patient outcomes.

There is *clear and convincing evidence* that buprenorphine products (including buprenorphine-naloxone) and methadone are more effective than a placebo or no treatment related to retention in treatment for opioid use disorder, reduction in use of illicit opioids, relapse, lower likelihood of engaging in behaviors associated with elevated risk for HIV and hepatitis C, better birth outcomes, and lower mortality rates.

As presented in *Benefit Coverage, Utilization, and Cost Impacts*, no measurable change in medication utilization at the state-level is expected, postmandate, because at baseline 1% to 5% (depending on the medication) of commercial/CalPERS enrollees have health insurance that includes a prior authorization requirement for buprenorphine products, methadone, or long-acting injectable naltrexone.

Because the estimated change in benefit coverage is so limited, no state-level long-term impacts of AB 1288 on health outcomes, including premature death associated with opioid use disorder and alcohol use disorder, can be projected. However, it is possible that AB 1288 could yield some person-level health improvements if some enrollees increase utilization of the medications the bill addresses.

### Impact of Barriers on Opioid Use Disorder and Alcohol Use Disorder Treatment

Barriers exist at the system/policy, provider, and patient levels which contribute to low treatment rates for patients with opioid use disorder or alcohol use disorder. As identified by providers and patients, system- or policy-level barriers such as prior authorization can be a significant barrier to treatment with medications for opioid use disorder and alcohol use disorder (Andraka-Christou et al., 2022; Haffajee et al., 2020; Marino et al., 2019). AB 1288 would prohibit use of prior authorizations for buprenorphine products, methadone, and long-acting injectable naltrexone included on state-regulated plan and policies existing formularies. At the person level, the removal of this barrier may prevent delays in initiating treatment for opioid use disorder with medications that would have been subject to prior authorization and may increase the number of patients who receive and fill prescriptions for treatment for the patient with opioid or alcohol use disorder who attempt to access treatment among the 1% to 5% of commercial/CalPERS enrollees (depending on the medication) whose insurance coverage would be impacted by AB 1288 (Mark et al., 2020; Parish et al, 2022).

[26] CHBRP defines short-term impacts as changes occurring within 12 months of bill implementation.

Independent of AB 1288, at the start of 2023, another barrier to opioid use disorder treatment was reduced with the Consolidated Appropriations Act (2023), which removed the federal requirement that providers had to submit a Notice of Intent (waiver) to prescribe buprenorphine for opioid use disorder treatment (SAMHSA, 2023b) and removed limitations on how many patients each prescriber could treat with buprenorphine. With the removal of this waiver for buprenorphine, more providers will be able to prescribe buprenorphine. This may result in increased patient access to buprenorphine, but data on any change in prescribing patterns or patient access is not yet available.

While AB 1288 would remove prior authorizations as a barrier to medications for the treatment of opioid use disorder or alcohol use disorder for 1% to 5% of commercial/CalPERS enrollees (depending on the medication), additional barriers remain as described in *Background on Substance Use Disorders* section. AB 1288 does not mandate coverage of the medications. Provider supply and willingness to prescribe could remain a barrier as could pharmacy ability and willingness to dispense, and patient interest and ability to access care due to stigma, geographic, or other barriers such as past treatment experiences, knowledge deficits, and financial barriers (Mackey et al., 2020; Saini et al., 2022).

### Potential Harms of Opioid Use Disorder and Alcohol Use Disorder Treatment Medications

When data are available, CHBRP estimates the marginal change in relevant harms associated with interventions affected by the proposed mandate. In the case of AB 1288, CHBRP does not project harms at the population level as no measurable change in utilization of medications (buprenorphine products, methadone, and long-acting injectable naltrexone) associated with harms (see *Medical Effectiveness* section) is expected.

## Impact on Disparities[27]

Disparities are differences between groups that are modifiable, and insurance benefit mandates that impose coverage parity among state-regulated plans and policies may change an existing disparity.[27] As described in the *Background on Substance Use Disorders* section, disparities in opioid use disorder and alcohol use disorder exist by race/ethnicity, sex or gender, age, sexual orientation, mental health disorders, and geography. CHBRP estimates AB 1288 would not change these disparities in the first 12 months postmandate as the public health impact is limited by an estimate of no measurable change in utilization of buprenorphine products, methadone, and long-acting injectable naltrexone for treatment of opioid use disorder and alcohol use disorder. (For a discussion of potential impacts beyond the first 12 months of implementation [including social determinants of health], see *Long-Term Impacts*.)

### Impact on Disparities in Health Outcomes for Opioid Use Disorder

As presented in the *Background on Substance Use Disorders* section, disparities occur within many demographic categories in California. Disparities in opioid overdose mortality rates, hospitalizations, and emergency department use exist among racial/ethnic groups (highest mortality among Black persons and American Indian/Alaskan native persons compared to White persons); by gender (males have two times the mortality rate of females); and by age cohorts (highest mortality among those aged 30 to 39 years and 50 to 64 years).

[27] For details about CHBRP's methodological approach to analyzing disparities, see the *Benefit Mandate Structure and Unequal Racial/Ethnic Health Impacts* document here: https://www.chbrp.org/about/analysis-methodology/public-health-impact-analysis.

The demographic composition of the commercial/CalPERS enrollees with opioid use disorder with health insurance that would be subject to this mandate is unknown, and CHBRP estimates no measurable population-level impact of AB 1288, due to the small increase in commercial/CalPERS enrollees (5% for buprenorphine, 1% for methadone, and 5% for long-acting injectable naltrexone) to no longer have prior authorization for opioid use disorder treatment medication. Therefore, AB 1288 is estimated to have no measurable impact on existing disparities in opioid-related overdose mortality and related health services use.

## Impact on Disparities in Health Outcomes for Alcohol Use Disorder

As described in the *Background on Substance Use Disorders* section, alcohol use disorder–related disparities occur within many demographic categories in California. Disparities in alcohol-induced death, hospitalization, and health outcomes exist among racial/ethnic groups (American Indian/Alaskan Native persons exhibiting the highest rates alcohol-induced death) and by gender (women have increased risk of alcohol-related heart disease, cancer, and liver disease).

The demographic composition of the commercial/CalPERS enrollees with alcohol use disorder with health insurance that would be subject to this mandate is unknown, and CHBRP estimates no measurable population-level impact of AB 1288, due to the small increase in commercial/CalPERS enrollees (5% for long-acting injectable naltrexone) to no longer have prior authorization for alcohol use disorder treatment medication. Therefore, AB 1288 is estimated to have no measurable impact on existing disparities in alcohol-induced death or illness.

# LONG-TERM IMPACTS

In this section, CHBRP estimates the long-term impact of AB 1288, which CHBRP defines as impacts occurring beyond the first 12 months after implementation. These estimates are qualitative and based on the existing evidence available in the literature. CHBRP does not provide quantitative estimates of long-term impacts because of unknown improvements in clinical care, changes in prices, implementation of other complementary or conflicting policies, and other unexpected factors.

## Long-Term Utilization and Cost Impacts

The mandate is not expected to have measurable, at the state level, impacts on utilization or cost in the years following the implementation year.

## Long-Term Public Health Impacts

Some interventions in proposed mandates provide immediate measurable impacts (e.g., maternity service coverage or acute care treatments), whereas other interventions may take years to make a measurable impact (e.g., coverage for tobacco cessation or vaccinations). When possible, CHBRP estimates the long-term effects (beyond 12 months postmandate) to the public's health that would be attributable to the mandate, including impacts on disparities, premature death, and economic loss.

In the case of AB 1288, CHBRP estimates no measurable change in utilization at a population level and no measurable public health impact in the first 12 months; therefore, there are no expected long-term public health impacts at the population level. However, for persons who recover from opioid use disorder and alcohol use disorder, there are potential long-term impacts on social determinants of health (SDOH) and premature death at a person level.

### Impacts on Disparities and the Social Determinants of Health[28]

Taken as a whole, treatment of substance use disorders (SUDs) is inextricably linked bidirectionally with many important SDOH. SDOH such as quality of built environment, proximity to crime, educational opportunities, self-efficacy, and income levels can influence a person's risk for SUDs (Mooney at al., 2018; Sudhinaraset et al., 2016). Conversely, SUDs can also alter a person's baseline SDOH, namely through the consequences of the disorder, such as involvement with the criminal justice system, job loss, unstable housing or family situations, and discrimination against those with treated or untreated SUDs (Krebs et al., 2016).

Although disparities in race/ethnicity, sex or gender, age, sexual orientation, and SDOH exist and likely contribute to increased opioid overdose–related health outcomes and mortality and alcohol-induced health outcomes and mortality, CHBRP projects no change in these disparities at a population level that would be attributable to AB 1288 due to no measurable increase in utilization after removal of prior authorization requirements for 1% to 5% commercial/CalPERS enrollees with insurance subject to AB 1288.

[28] For more information about SDOH, see CHBRP's Public Health Impact *Analysis and Research Approach* at https://www.chbrp.org/about/analysis-methodology/public-health-impact-analysis.

## Impact on Premature Death

### *Premature death*

Premature death is often defined as death occurring before the age of 75 years (NCI, 2019).[29] In California, it is estimated that there were nearly 5,300 years of potential life lost (YPLL) per 100,000 population each year between 2015 and 2017 (CDPH, 2019).[30] Overdose deaths, injuries/accidents, chronic diseases, and violence related to opioid use disorder and alcohol use disorder are contributing factors to that rate.

**Opioid use disorder:** Opioid-related mortality is considered a public health crisis, with more than 2,000 unintentional opioid deaths occurring in California in 2016 (Clemans-Cope et al., 2018; HHS, 2018). In terms of years-of-life-lost (YLL), Gomes et al. estimated the national burden of opioid deaths in 2016 represented 1 in 65 deaths (5.2 YLL/1,000 population), or about a quarter of the YLL due to cancer, the second leading cause of death in the United States. Males experience twice the rate of YLL as females (7.0 YLL/1,000 population versus 3.4 YLL/1,000 population); and the opioid-related YLL for males aged 25 to 34 years (18.1/1,000 population) represented about a quarter of all YLL in the United States in 2016 (Gomes, et al., 2018).

**Alcohol use disorder:** The CDC reported from 2011 to 2015, there were 28 YPLL per alcohol-attributable death[31] in California and 803.8 YPLL per 100,000 persons (Esser et al., 2020). In 2006 to 2010 the "average annual alcohol attributable years of life lost" was 8.23/1,000 Californians. Fifty-four alcohol conditions were included in the calculation including acute and chronic conditions such as motor vehicle accidents, cancers, and cardiovascular diseases (Gonzales et al., 2014). California males experienced triple the rate of YLL as compared with their female counterparts (1,215/100,000 versus 4.34/1,000). Black persons had the highest YLL (11.87/1,000), followed by Latino (9.15/1,000), White (8.58/1,000), Alaska Native/American Indian (6.91/1,000), and Asian persons (3.09/1,000) (Gonzales et al., 2014).

Because the change in benefit coverage is so limited, no state-level quantitative long-term impacts of AB 1288 on health outcomes, including premature death associated with opioid use disorder and alcohol use disorder, can be projected. However, it is possible that, if, at the person-level, some enrollees increase utilization of the medications addressed by AB 1288, there could be some reduction in premature deaths.

[29] For more information about CHBRP's public health methodology, see http://chbrp.com/analysis_methodology/public_health_impact_analysis.php.
[30] The overall impact of premature death due to a particular disease can be measured in years of potential life lost prior to age 75 and summed for the population (generally referred to as "YPLL") (Gardner and Sanborn, 1990).
[31] "Deaths attributable to excessive alcohol use include deaths from (1) conditions that are 100% alcohol-attributable, (2) deaths caused by acute conditions that involved binge drinking, and (3) deaths caused by chronic conditions that involved medium or high levels of average daily alcohol consumption" (Esser et al., 2020).

# APPENDIX A TEXT OF BILL ANALYZED

On February 21, 2023, the California Assembly Committee on Health requested that CHBRP analyze AB 1288 as introduced on February 16, 2023.

**ASSEMBLY BILL** **NO. 1288**

**Introduced by Assembly Member Reyes**

**February 16, 2023**

An act to add Section 1342.75 to the Health and Safety Code, and to add Section 10123.1934 to the Insurance Code, relating to health care coverage.

LEGISLATIVE COUNSEL'S DIGEST

AB 1288, as introduced, Reyes. Health care coverage: Medication-assisted treatment.

Existing law, the Knox–Keene Health Care Service Plan Act of 1975, provides for the licensure and regulation of health care service plans by the Department of Managed Health Care and makes a willful violation of the act a crime. Existing law also provides for the regulation of health insurers by the Department of Insurance. Existing law authorizes health care service plans and health insurers that cover prescription drugs to utilize reasonable medical management practices, including prior authorization and step therapy, consistent with applicable law.

This bill would prohibit a medical service plan and a health insurer from subjecting a buprenorphine product, methadone, or long-acting injectable naltrexone for detoxification or maintenance treatment of a substance use disorder that is prescribed according to generally accepted national professional guidelines for the treatment of a substance use disorder to prior authorization. Because a willful violation of these provisions by a health care service plan would be a crime, this bill would impose a state-mandated local program.

The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

Vote: majority Appropriation: no Fiscal Committee: yes Local Program: yes

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THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

**SECTION 1.** Section 1342.75 is added to the Health and Safety Code, to read:

**1342.75.** Notwithstanding any other law, a health care service plan shall not subject, a buprenorphine product, methadone, or long-acting injectable naltrexone for detoxification or maintenance treatment of a substance use disorder prescribed according to generally accepted national professional guidelines for the treatment of a substance use disorder to prior authorization.

**SEC. 2.** Section 10123.1934 is added to the Insurance Code, to read:

**10123.1934.** Notwithstanding any other law, a health insurer shall not subject a buprenorphine product, methadone, or long-acting injectable naltrexone for detoxification or maintenance treatment of a substance use disorder prescribed according to generally accepted national professional guidelines for the treatment of a substance use disorder to prior authorization.

**SEC. 3.** No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs that may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, eliminates a crime or infraction, or changes the penalty for a crime or infraction, within the meaning of Section 17556 of the Government Code, or changes the definition of a crime within the meaning of Section 6 of Article XIII B of the California Constitution.

# APPENDIX B LITERATURE REVIEW METHODS

This appendix describes methods used in the literature review conducted for this report. A discussion of CHBRP's system for medical effectiveness grading evidence, as well as lists of MeSH Terms, publication types, and keywords, follows.

Studies of buprenorphine products, methadone, and long-acting injectable naltrexone were identified through searches of PubMed/MEDLINE, the Cochrane Library, CINAHL, SCOPUS, Embase, and PsychInfo. The search was limited to abstracts of studies published in English. The search was limited to studies published from 2020 to present because CHBRP had previously conducted thorough literature searches on these topics in 2020 for SB 854 (Substance Use Disorders) and in 2018 for AB 2384 (Medication-Assisted Treatment). This report summarizes relevant findings from these previous CHBRP reviews plus literature published from January 1, 2020, through March 6, 2023, regarding the effectiveness and harms of buprenorphine products, methadone, and long-acting injectable naltrexone as well as the impact of prior authorization on outcomes related to use of these medications. As the previous CHBRP review for SB 854 concluded that there is *clear and convincing evidence* that these medications are more effective than a placebo or no treatment, CHBRP did not review new literature published since January 2020 regarding the effectiveness of buprenorphine products and methadone versus a placebo or no treatment. The literature search strategy is available upon request.

Reviewers screened the title and abstract of each citation retrieved by the literature search to determine eligibility for inclusion. The reviewers acquired the full text of articles that were deemed eligible for inclusion in the review and reapplied the initial eligibility criteria.

## Medical Effectiveness Review

Of the 556 articles identified in the search for articles published since January 2020, 120 were reviewed for potential inclusion and a total of 17 new studies were included in the medical effectiveness review for this report. The other articles were eliminated because they did not address the medications specified by AB 1288, were of poor quality, or did not report findings from clinical research studies.

## Medical Effectiveness Evidence Grading System

In making a "call" for each outcome measure, the medical effectiveness lead and the content expert consider the number of studies as well the strength of the evidence. Further information about the criteria CHBRP uses to evaluate evidence of medical effectiveness can be found in CHBRP's *Medical Effectiveness Analysis Research Approach*.[32] To grade the evidence for each outcome measured, the team uses a grading system that has the following categories:

- Research design;
- Statistical significance;
- Direction of effect;
- Size of effect; and
- Generalizability of findings.

The grading system also contains an overall conclusion that encompasses findings in these five domains. The conclusion is a statement that captures the strength and consistency of the evidence of an intervention's effect on an outcome. The following terms are used to characterize the body of evidence regarding an outcome:

[32] Available at: https://www.chbrp.org/about/analysis-methodology/medical-effectiveness-analysis.

- *Clear and convincing evidence;*
- *Preponderance of evidence;*
- *Limited evidence;*
- *Inconclusive evidence;* and
- *Insufficient evidence.*

A grade of *clear and convincing evidence* indicates that there are multiple studies of a treatment and that the large majority of studies are of high quality and consistently find that the treatment is either effective or not effective.

A grade of *preponderance of evidence* indicates that the majority of the studies reviewed are consistent in their findings that treatment is either effective or not effective.

A grade of *limited evidence* indicates that the studies had limited generalizability to the population of interest and/or the studies had a fatal flaw in research design or implementation.

A grade of *inconclusive evidence* indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.

A grade of *insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

# APPENDIX C ADDITIONAL EVIDENCE ON THE EFFECTIVENESS AND HARMS OF BUPRENORPHINE PRODUCTS, METHADONE, AND LONG-ACTING INJECTABLE NALTREXONE TO TREAT OPIOID USE DISORDER AND ALCOHOL USE DISORDER

## Effectiveness of Buprenorphine Products, Methadone, and Long-Acting Injectable Naltrexone versus Placebo or No Medication

Research has demonstrated the effectiveness of buprenorphine products, methadone, and long-acting injectable naltrexone to maintain abstinence from opioid use disorder relative to a placebo or no treatment. Most studies were conducted in adults. There is far less literature on effects in adolescents (2014).

As mentioned in the *Medical Effectiveness* section, this medical effectiveness review did not assess new literature regarding the effectiveness of buprenorphine products and methadone versus a placebo or no treatment since CHBRP's 2020 analysis of SB 854 concluded that there is *clear and convincing evidence* that these medications are more effective than a placebo or no treatment. The study finding and conclusions in this section reflect those of SB 854.

### *Buprenorphine or Buprenorphine-Naloxone Combination*

Mattick et al.'s (2014) Cochrane review of 11 RCTs (sample sizes: 40–736 people) found that persons who were given buprenorphine or buprenorphine-naloxone combination medication for maintenance treatment of opioid use disorder were more likely to be retained in treatment than people who received a placebo. The authors found that only high-dose buprenorphine ($\geq$ 16 mg) was more effective than placebo in suppressing use of illegal opioids as measured by urinalysis in the trials (Mattick et al., 2014) (3 studies; 729 people).

Two other systematic reviews also found that persons who received buprenorphine or buprenorphine-naloxone were more likely to be retained in treatment than people who received a placebo (Thomas et al., 2014; Timko et al., 2016). Thomas et al.'s (2014) systematic review included 17 RCTs, a randomized crossover study, a study using a self-administered survey, a retrospective descriptive study, and seven reviews or meta-analyses (sample sizes: 12–4,497 people). Timko et al.'s (2016) review of buprenorphine or buprenorphine-naloxone combination included 14 RCTs, four quasi-experimental design studies, and nine cohort studies (sample sizes: 70–1,269 people). Timko et al. (2016) reported that 65.7% of persons who received buprenorphine were retained in treatment at 6 months versus 30.9% of persons who received a placebo.

In a systematic review of three prospective or retrospective cohort studies (sample sizes: 1,373–11,940 people) in people with opioid use disorder, Sordo et al. (2017) found buprenorphine treatment is associated with substantial reductions in the risk for all cause and overdose mortality in people dependent on opioids relative to not receiving treatment.

One systematic review examining 16 RCTs (sample sizes: 12–653 people) found that buprenorphine and buprenorphine-naloxone combination maintenance treatments were associated with less risk of adverse events and improved maternal and fetal outcomes in pregnancy compared with not receiving treatment (Thomas et al., 2014).

Most studies of buprenorphine have examined the effectiveness of sublingual tablets or film that users must take on a daily basis. An important limitation of these forms of buprenorphine are that users may forget to take the medication every day, may misuse it, or sell it to others. Implantable and extended-

release injectable formulations of buprenorphine have been developed to provide longer-acting forms of buprenorphine treatment that are administered in a provider's office.

An RCT (sample size: 163 people) that compared persons who received four buprenorphine implants over a 6-month period (80 mg per implant) to people who received placebo implants found that people who received the buprenorphine implants were more likely to abstain from opioids and had fewer cravings for opioids (Ling et al., 2010). A subsequent RCT (sample size: 177 people) that compared buprenorphine implants to sublingual buprenorphine tablets found that people who received the implants were more likely to abstain from opioids for six months (85.7% vs. 71.9%) (Rosenthal et al., 2016).

An RCT (sample size: 504 people) that compared persons who received one of two different dosing regimens for extended-release injectable buprenorphine over a 6-month period (300 mg/300 mg injection or 300 mg/100 mg injection) to people who received a placebo found that abstinence was, on average similar in both treatment arms (41.3% in the 300 mg/300 mg arm and 42.7% in the 300 mg/100 mg arm) compared to the placebo arm (5.0%), and that treatment success (≥80% abstinence) was significantly higher in both treatment arms compared to the placebo arm (Haight et al., 2019).

### *Methadone*

As discussed in the *Benefit Coverage, Utilization, and Cost Impacts* section, AB 1288 would affect prior authorization for methadone but would not change the manner in which methadone is dispensed because federal law requires that methadone be administered only by federally certified opioid treatment programs (i.e., "methadone clinics"). For these reasons, AB 1288 is likely to have a limited impact on costs associated with methadone treatment. CHBRP decided to include methadone in its medical effectiveness review despite AB 1288's limited impact on its use because it has been used to treat opioid use disorder for many years and providers and patients may consider it as an alternative to buprenorphine.

Two systematic reviews of overlapping groups of studies have compared methadone maintenance treatment to a placebo or no treatment for opioid use disorder (Fullerton et al., 2014; Mattick et al., 2009). Fullerton (2014) included seven RCTs, two quasi-experimental studies (sample sizes: 81–319 people) and 15 reviews or meta-analyses of multiple studies. Mattick et al. (2009) assessed 11 RCTs (sample sizes: 32–382 people). Both systematic reviews concluded that methadone is more effective than a placebo or no treatment for retaining patients in treatment and reducing use of illegal opioids as measured by self-report and urine/hair analysis. Mattick et al. (2009) also found that methadone was statistically significantly more effective in the suppression of heroin use as measured by self-report and urine/hair analysis.

Fullerton et al.'s systematic review (2014) found two systematic reviews and one RCT that addressed the impact of methadone on HIV risk. The authors concluded that receipt of methadone maintenance treatment was associated with lower risk of injecting opioids and engaging in sexual behaviors that elevate a person's risk of contracting HIV. A systematic review of nine studies (with a sample that included 819 incident HIV infections over 23,608 person years of follow-up) concluded that receipt of methadone maintenance treatment reduces risk of HIV transmission (MacArthur et al., 2012).

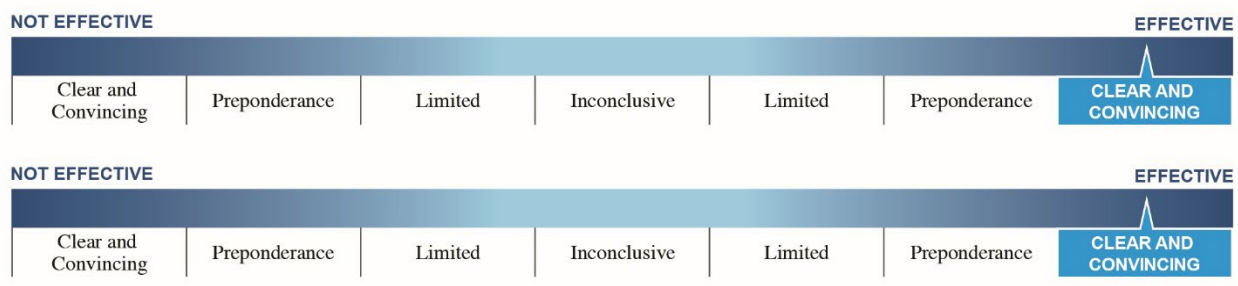
The authors of one systematic review of RCTs found no statistically significant difference in mortality between persons receiving methadone maintenance treatment and persons who received a placebo or no treatment (4 studies) (Mattick et al., 2009). In a subsequent systematic review of 18 prospective or retrospective cohort studies (sample sizes: 56–122,885 people) that had longer follow-up periods than the studies included in Mattick et al.'s (2009) systematic review, Sordo et al. (2017) found methadone maintenance treatment is associated with substantial reductions in the risk for all cause and overdose mortality in people dependent on opioids. In patients using methadone maintenance treatment there are, on average, 25 fewer deaths/1,000 person years than in patients who do not receive methadone maintenance treatment.

### *Methadone or buprenorphine*

A systematic review of 38 observational studies (sample sizes: 18–726 people) found that receipt of either methadone or buprenorphine was associated with less injection drug use, less sharing of injection equipment, less exchange of sex for drugs, and lower likelihood of having multiple sex partners among people with opioid use disorder (Gowing et al., 2011). Two cohort studies found that receipt of methadone or buprenorphine was associated with lower risk of hepatitis C among persons with opioid use disorder (Nolan et al., 2014; Tsui et al., 2014).

**Summary of findings regarding the effectiveness of buprenorphine and methadone for opioid use disorder:** There is *clear and convincing evidence* from 10 systematic reviews and five RCTs that buprenorphine (including buprenorphine-naloxone) and methadone are more effective than a placebo or no treatment with regard to retention in treatment for opioid use disorder, reduction in use of illicit opioid drugs, relapse, lower likelihood of engaging in behaviors associated with elevated risk for HIV and hepatitis C, better birth outcomes, and lower mortality rates.

**Figure 9. The Effectiveness of Buprenorphine or Methadone for Opioid Use Disorder Versus Placebo or No Medication**




### *Long-acting injectable naltrexone*

In contrast to methadone and buprenorphine, which can be administered while a person tapers off misuse of opioids, people must complete withdrawal from opioids before receiving naltrexone. Many people with opioid use disorder do not successfully initiate treatment with naltrexone because they are unable to completely abstain from using opioids for days. A long-acting intramuscular injectable formulation of naltrexone has been developed to provide a longer-acting form of the medication that does not depend on a patient taking a medication on a daily basis.

#### Opioid Use Disorder

CHBRP's 2020 analysis of SB 854 identified one systematic review (Jarvis et al., 2018) and two additional studies (Morgan et al., 2019; Sullivan et al., 2019) examining the effectiveness of long-acting injectable naltrexone for opioid use disorder compared to placebo or oral naltrexone. The updated literature search for AB 1288 identified one additional systematic review (Zangiabadian et al., 2022) examining the effectiveness of long-acting injectable naltrexone to treat opioid use disorder compared to placebo or oral naltrexone.

Findings from one systematic review (Jarvis et al., 2018) summarizes evidence from 16 prospective studies that long-acting injectable naltrexone decreases opioid use relative to a placebo. A systematic review by Zangiabadian et al. (2022) found that injectable naltrexone significantly improved retention in treatment versus placebo (OR = 0.86 [95% CI: 1.16 to 2.97]; 2 studies) but did not have any significant impacts on being opioid-free without relapse.

One RCT published after this systematic review compared retention in treatment and opioid use during treatment among adults randomized to receive either oral naltrexone (n=32 people) or long-acting injectable naltrexone (n=28 people) (Sullivan et al., 2019). The authors found that retention in treatment was significantly higher among participants receiving long-acting injectable naltrexone but found no significant difference between the treatment groups in the proportion of opioid-positive urine tests after 24 weeks of follow-up. A cohort study of over 46,000 adults in a nationally representative commercial claims database found that no statistically significant reduction in overdose for those treated with either oral naltrexone (n=7782 people) (HR = 0.93; 95% CI: 0.71 to 1.22) or long-acting injectable naltrexone (n=1386 people) (HR = 0.74; 95% CI: 0.42 to 1.31) compared to no treatment (Morgan et al., 2019).

**Summary of findings regarding the effectiveness of long-acting injectable naltrexone for opioid use disorder:** There is a *preponderance of evidence* from two systematic reviews, one additional RCT, and one additional cohort study that long-acting injectable naltrexone is effective for treatment retention and abstinence compared to placebo or oral naltrexone.

**Figure 10. The Effectiveness of Long-Acting Injectable Naltrexone for Opioid Use Disorder Versus Placebo or Oral Naltrexone**


## Alcohol Use Disorder

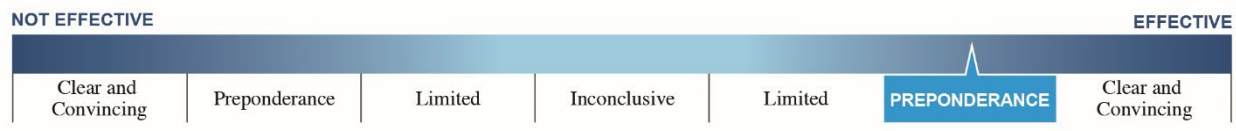
CHBRP's 2020 analysis of SB 854 identified one systematic review (Jonas et al., 2014) and one additional cohort study (Leighty and Ansara, 2019) examining the effectiveness of long-acting injectable naltrexone for alcohol use disorder. The updated literature search for AB 1288 identified two additional systematic reviews (Kedia et al., 2022; Murphy IV et al., 2022) examining the effectiveness of long-acting injectable naltrexone to treat alcohol use disorder compared to placebo or oral naltrexone.

The systematic review by Jonas et al. (2014) included four RCTs comparing long-acting injectable naltrexone to placebo (n = 1,299 people) and did not find any significant association between long-acting injectable naltrexone and return to any drinking or heavy drinking (Jonas et al., 2014). Pooled results from two trials (n = 939 people) found a significant reduction in the number of heavy drinking days among participants randomized to long-acting injectable naltrexone (weighted mean difference -4.6% [95% CI: -8.5% to -0.56%). A systematic review by Kedia et al. (2022) including 11 RCTs found that long-acting injectable naltrexone positively impacted participant's drinking behaviors compared to placebo, including reducing the mean time to first drinking or heavy drinking day, the number of drinking or heavy drinking days, the percentage of heavy drinking days, and increased the mean number of days abstinent. A meta-analysis by Murphy et al. (2022) including seven RCTs found that long-acting injectable naltrexone reduced the mean number of drinking days per month (WMD = -2.0; 95% CI: -3.4 to -0.6; p=0.03) and mean number of heavy drinking days per month (WMD = -1.2; 95% CI: -2.1 to -0.2; p=0.02).

One retrospective cohort study compared median time to relapse among Veterans Affairs patients with alcohol use disorder treated with either oral or long-acting injectable naltrexone and found that median time to relapse was significantly longer for those treated with long-acting injectable versus oral naltrexone (150.5 days vs. 50.5 days) (Leighty and Ansara, 2019).

**Summary of findings regarding the effectiveness of long-acting injectable naltrexone for alcohol use disorder:** There is a *preponderance of evidence* from three systematic reviews and one additional cohort study that long-acting injectable naltrexone is effective at reducing return to drinking compared to a placebo or oral naltrexone.

**Figure 11. The Effectiveness of Long-Acting Injectable Naltrexone for Alcohol Use Disorder Versus Placebo or No Medication**




## Comparative Effectiveness of Buprenorphine Products, Methadone, and Long-Acting Injectable Naltrexone

### *Buprenorphine or buprenorphine-naloxone combination versus methadone*

CHBRP's 2020 analysis of SB 854 identified four systematic reviews (Mattick et al., 2014; Nielsen et al., 2016; Thomas et al., 2014; Timko et al., 2016) and one additional study (Hser et al., 2016) examining the comparative effectiveness buprenorphine products versus methadone for opioid use disorder. The previous CHBRP review also identified three systematic reviews comparing the effectiveness and safety of buprenorphine and methadone for maintenance treatment of pregnant women with opioid use disorder (Minozzi et al., 2014; Thomas et al., 2014; Zedler et al., 2016). The updated literature search for AB 1288 identified an update to a previously included systematic review (Nielsen et al., 2022) and two additional systematic reviews (Lim et al., 2022; Ma et al., 2020) examining the comparative effectiveness of these medications to treat opioid use disorder.

A large number of studies have compared the effectiveness of methadone to buprenorphine or buprenorphine-naloxone combination for maintenance treatment of opioid use disorder. A smaller number of studies have compared naltrexone to buprenorphine or buprenorphine-naloxone combination treatment for maintenance or induction to treatment with long-acting injectable naltrexone. Comparative studies of maintenance medications have examined effects on retention in treatment, abstinence from use of opioids, and birth outcomes. CHBRP did not identify any studies that examined the relative effectiveness of maintenance medications used to treat opioid use disorder on transmission of hepatitis C or HIV or on engagement in behaviors that increase risk for contracting hepatitis C or HIV.

A Cochrane review by Mattick et al. (2014) compared methadone to different formulations of buprenorphine (i.e., sublingual solution, sublingual tablets, combined buprenorphine-naloxone sublingual tablet and an implant). The authors found that compared to methadone, buprenorphine retains fewer people in treatment when doses are flexibly delivered (adjusted to participant need) (5 studies; 788 people; RR=0.83; 95% CI: 0.72 to 0.95) and at low fixed doses (3 studies; 253 subjects; RR=0.67; 95% CI: 0.52 to 0.87). If fixed medium or high doses are used, buprenorphine and methadone are equally effectiveness for retaining people in treatment (7 studies; 780 people; RR=0.87; 95% CI: 0.69 to 1.10) and suppressing illicit opioid use (4 studies; 476 people; SMD=0.25; 95%CI: -0.08 to 0.58).

A systematic review of four studies (three RCTs and one systematic review; sample sizes: 196–1,497 people) concluded that the efficacy of buprenorphine is dose dependent. For comparisons at medium-dose ranges, evidence is mixed. Some studies showed similar effects of methadone and buprenorphine products, but others suggest that methadone improved treatment retention or reduces illicit opioid use. Only one RCT (sample size: 220 people) reviewed in this study compared high doses of buprenorphine and methadone, and it showed similar outcomes in terms of days in treatment (mean of 96 and 105 days, respectively) or percentage of patients with 12 or more consecutive negative opioid screens (26% vs. 28%, respectively) (Thomas et al., 2014).

Timko et al. (2016) identified three RCTs that compared methadone to buprenorphine or buprenorphine-naloxone. The authors found that methadone was associated with better retention in treatment than buprenorphine-naloxone at 4 months (73.9% vs. 45.9%) and at 6 months (74.0% vs. 46.0%; 57.6%).

An RCT published after the RCTs included in the systematic reviews compared outcomes for persons treated with buprenorphine or buprenorphine-naloxone to persons treated with methadone for an average of 4.5 years following 24 weeks of treatment (Hser et al., 2016). The authors reported that persons treated with buprenorphine or buprenorphine-naloxone were less likely to abstain from using opioids than people treated with methadone (57.2% vs. 68.3%) because they received less ongoing treatment after the 24-week trial ended. The RCT found no statistically significant difference in mortality between people treated with the two medications.

In a systematic review of three RCTs (n = 408 people) Nielsen et al. (2016) found no difference between the effects of methadone and buprenorphine or buprenorphine-naloxone in self-reported opioid use (RR=0.37; 95% CI: 0.08 to 1.63) or opioid positive urine drug tests (RR=0.81; 95% CI: 0.56 to 1.18), retention in treatment (RR=0.69; 95% CI: 0.39 to 1.22), and adverse events (RR=1.10; 95% CI: 0.64 to 1.91). An updated systemic review by Nielsen et al. (2022) including one additional RCT (4 RCTs total, n = 447 people) found that self-reported opioid use and retention in treatment favored methadone use over buprenorphine or buprenorphine-naloxone (RR=0.49 [95% CI: 0.28 to 0.86] for self-reported opioid use and RR=1.21 [95% CI: 1.02 to 1.43] for retention in treatment). The review found no difference between the effects of methadone and buprenorphine or buprenorphine-naloxone in opioid positive urine tests (RR=0.81; 95% CI: 0.57 to 1.17) or adverse events (RR=1.13; 95% CI: 0.66 to 1.93). A meta-analysis by Ma et al. (2020) including 30 studies (n = 370,611 people) found that the all-cause mortality rate during treatment was lowest among participants taking naltrexone (but does not stratify by oral versus injectable), followed by buprenorphine treatment (crude mortality rate [CMR] = 0.38; 95% CI: 0.31 to 0.46) and methadone treatment (CMR = 1.05; 95% CI: 0.86 to 1.25). After terminating treatment, all-cause mortality rates for patients terminating naltrexone treatment and methadone treatment were similar (CMR = 1.97; 95% CI: 0.0 to 5.18 and CMR=2.03; 95% CI: 1.67 to 2.39, respectively), whereas patients terminating buprenorphine treatment had the lowest all-cause mortality rate (CMR = 0.80; 95% CI: 0.38 to 1.22) and had lower mortality risk than patients treated with methadone after treatment termination (RR = 0.81; 95% CI: 0.70 to 0.93).

A network meta-analysis by Lim et al. (2022) compared treatment retention between buprenorphine, methadone, naltrexone (including both injectable and oral), and controls. Compared to control, treatment retention was highest for methadone, followed by buprenorphine and naltrexone (including both injectable and oral). The relative risk of treatment retention for methadone compared naltrexone was 1.69 (95% CI: 1.30 to 2.24) and 1.22 (95% CI: 1.06 to 1.40) compared to buprenorphine.

**Summary of findings regarding the comparative effectiveness of buprenorphine products versus methadone to treat opioid use disorder in a general population:** There is a *preponderance of evidence* from seven systematic reviews and four additional RCTs that the impact of methadone is similar or better than buprenorphine or buprenorphine-naloxone on retention in treatment and abstinence from opioids.

**Figure 12. Comparative Effectiveness of Buprenorphine Products vs. Methadone to Treat Opioid Use Disorder in a General Population (Similar Effectiveness or Favors Methadone)**

### Pregnant persons with opioid use disorder

CHBRP's 2020 analysis SB 854 identified three systematic reviews (Minozzi et al., 2013; Thomas et al., 2014; Zedler et al., 2016) comparing the effectiveness and safety of buprenorphine and methadone for maintenance treatment of pregnant women with opioid use disorder. The updated literature search for AB 1288 identified an update to a previously included systematic review (Minozzi et al., 2020) and two additional systematic reviews (Bivin et al., 2021; Kinsella et al., 2022) examining the comparative effectiveness of these medications to treat opioid use disorder in pregnant persons.

Minozzi et al. (2013) and Thomas et al. (2014) found that when the medication was dosed adequately, methadone and buprenorphine or buprenorphine-naloxone combination treatment showed similar reduction in illicit opioid use during pregnancy but that those treated with methadone were more likely to remain in treatment. Thomas et al. (2014) also found that rates of neonatal abstinence syndrome were similar for infants born to patients treated with either buprenorphine or methadone but that symptoms were less severe for infants who were exposed to buprenorphine in utero. Zedler (2016) found that buprenorphine and buprenorphine-naloxone were associated with lower risk of preterm birth, greater birthweight, and larger head circumference than methadone and that rates of fetal spontaneous deaths and fetal/congenital abnormalities were similar for the two medications. In a review of four RCTs, Minozzi et al. (2013) found three RCTs that compared birthweight. Birthweight was higher in the buprenorphine group in the two trials that could be pooled (mean difference [MD] -365.45 g; 95% CI: -673.84 to -57.07; two studies, 150 newborns). The third double-blind RCT reported that there was no statistically significant difference between buprenorphine and methadone groups (sample size: 18). The reported APGAR score (two studies, 163 newborns) and number of newborns treated for neonatal abstinence syndrome (three studies, 166 newborns) did not differ significantly between groups. One RCT (sample size: 131 people) comparing methadone with buprenorphine reported side effects. For the pregnant person, there was no statistically significant difference; for the newborns in the buprenorphine group there were significantly fewer serious side effects (RR=4.77; 95% CI: 0.59 to 38.49). An updated systematic review by Minozzi et al. (2020) did not identify any additional trials comparing the effectiveness and safety of buprenorphine and methadone for maintenance treatment of opioid use disorder during pregnancy.

A systematic review by Bivin et al. (2021) including 12 studies concluded that buprenorphine treatment during pregnancy was associated with shorter hospital stays, shorter length of treatment for neonatal abstinence syndrome, and less need for pharmacotherapy to treat neonatal abstinence syndrome compared to methadone. There was not conclusive evidence that treatment with buprenorphine products versus methadone was associated with fewer cases of neonatal abstinence syndrome. A systematic review by Kinsella et al. (2022) including 20 studies (n = 7,251 people) found that buprenorphine, compared to methadone, was associated with improved birthweight (WMD, 196.61 [95% CI: 135.76 to 257.46]) and associated with nonsignificant improvements in prematurity risk and risk for neonatal abstinence syndrome.

**Summary of findings regarding the comparative effectiveness of buprenorphine products versus methadone to treat opioid use disorder in pregnant persons:** There is a *preponderance of evidence* from six systematic reviews that buprenorphine products are associated with better newborn medical outcomes (i.e., birthweight, APGAR scores, neonatal abstinence syndrome) than methadone, but pregnant persons receiving buprenorphine products were less likely to remain in treatment compared to those receiving methadone.

**Figure 13. Comparative Effectiveness of Buprenorphine Products vs. Methadone to Treat Opioid Use Disorder in Pregnant Persons (Favors Buprenorphine Products)**

### *Buprenorphine-naloxone combination versus long-acting injectable naltrexone*

CHBRP's 2020 analysis SB 854 identified two RCTs (Lee et al., 2018; Tanum et al., 2017) and one cohort study (Morgan et al., 2019) examining the comparative effectiveness of buprenorphine products versus long-acting injectable naltrexone for opioid use disorder. The updated literature search for AB 1288 identified three follow-up analyses of a previous included RCT (Greiner et al., 2021; Greiner et al., 2022; Haeny et al., 2020), one new RCT (Opheim et al., 2021), and one new cohort (Shirk et al., 2021) study examining the comparative effectiveness of these medications to treat opioid use disorder.

One RCT included in CHRBP's 2020 analysis of SB 854 assessed outcomes after 12 weeks of treatment with either long-acting injectable naltrexone or buprenorphine-naloxone (Tanum et al., 2017) and found no statistically significant difference between the two medications in the length of time people remained in treatment or their abstinence from misuse of opioids (as measured by negative urine tests). Persons who received long-acting injectable naltrexone reported less craving for heroin compared to those on buprenorphine-naloxone but were more likely to report symptoms of withdrawal.

A second RCT (X:BOT) included in CHRBP's 2020 analysis of SB 854 examined outcomes after 24 weeks of treatment (Lee et al., 2018). The authors found that participants were less likely to successfully initiate treatment with long-acting injectable naltrexone than with buprenorphine-naloxone, due to the need to completely detoxify from opioid prior to starting naltrexone but not prior to starting buprenorphine-naloxone, which led patients assigned to receive long-acting injectable naltrexone to have a higher relapse rate than patients who received buprenorphine-naloxone. This finding is consistent with the systematic review discussed previously in the section on the Effectiveness of Buprenorphine Products, Methadone or Long-Acting Injectable Naltrexone (Jarvis et al., 2018) which included studies that have compared long-acting injectable naltrexone to a placebo. Among patients who successfully initiated treatment, there were no statistically significant differences in relapse rates or in abstinence from use of opioids (measured by negative urine tests and self-report) (Lee et al., 2018).

Haeny et al. (2020) reported similar results in a secondary analysis including a subgroup of 73 Black participants in the X:BOT trial. Of those randomized to long-acting injectable naltrexone, only 59.5% successfully initiated treatment compared to 91.6% of participants randomized to buprenorphine-naloxone. Among participants who successfully initiated treatment, there were no significant differences in treatment retention rates or relapse. Greiner et al. (2021) examined outcomes among the 75% of X:BOT participants (n=428) who attended the 36-week follow-up visit. Just over half of those participants (52.6%, n=225 people) were still receiving treatment for opioid use disorder; 39.1% (n=88 people) were being treated with long-acting injectable naltrexone and 53.3% (n=120 people) were being treated with buprenorphine-naloxone (the remaining participants were now being treated with methadone). The authors found that more patients treated with long-acting injectable naltrexone reported past-month abstinence from opioids compared to those treated with buprenorphine-naloxone (44% versus 24%, odds ratio 2.47 [95% CI: 1.63 to 3.74, as estimated in a secondary analysis Greiner et al. (2022)]). There were no differences in relapse rates, opioid use days overdose events or past-month substance use between participants taking long-acting injectable naltrexone compared with buprenorphine-naloxone.

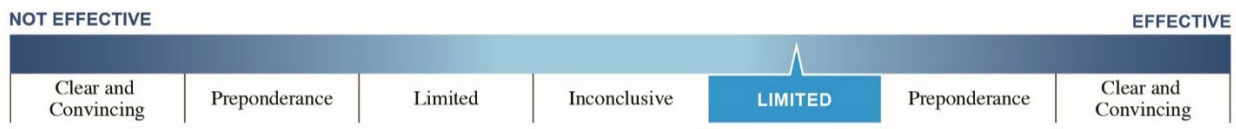
One additional RCT (Opheim et al., 2021; n = 143 people) identified in the updated literature review for AB 1288, conducted in Norway, assessed outcomes after 12 weeks of treatment with either long-acting injectable naltrexone or buprenorphine-naloxone as well as after a 36-week follow-up period wherein participants could choose to continue treatment with either long-acting injectable naltrexone or buprenorphine-naloxone. Participants who were randomized to 12 weeks of treatment with long-acting injectable naltrexone had a significantly reduced risk of relapse to heroin or other illicit opioids compared to participants randomized to buprenorphine-naloxone. There was no significant difference in time to first relapse between participants continuing with or switching to long-acting injectable naltrexone; however, in the group switching to long-acting injectable naltrexone, there were more relapses to other illicit opioids during the first four weeks of the 36-week follow-up period compared to participants continuing on long-acting injectable naltrexone (HR=0.45; 95% CI: 0.22 to 0.94).

CHBRP's 2020 analysis of SB 854 included one cohort study of over 46,000 adults in a nationally representative commercial claims database that found that those on buprenorphine therapy had a statistically significant reduced risk of overdose compared to no treatment (adjusted hazard ratio [HR] = 0.40, 95% CI: 0.35 to 0.46), while those on long-acting injectable naltrexone therapy were not at significantly reduced risk of overdose (HR = 0.74, 95% CI: 0.42 to 1.31) (Morgan et al., 2019).

Based on retrospective medical record review, one additional cohort study (Shirk et al., 2021) identified in the updated literature review for AB 1288 assessed 90-day treatment outcomes for 79 patients diagnosed with opioid use disorder and treated with long-acting injectable naltrexone or buprenorphine-naloxone at one Veterans Health Administration (VA) hospital. The authors did not find any difference in 60-day or 90-day treatment retention rates between patients taking long-acting injectable naltrexone versus buprenorphine-naloxone. Patients taking buprenorphine-naloxone were more likely to have positive urine tests (19.2% for opiates and 13.5% for other illicit substances) compared to patients taking long-acting injectable naltrexone (3.7% for opiates and 11.1% for other illicit substances), but these differences were not statistically significant.

**Summary of findings regarding the comparative effectiveness of buprenorphine products versus long-acting injectable naltrexone to treat opioid use disorder:** There is *limited evidence* from three RCTs and two cohort study that buprenorphine or buprenorphine-naloxone is of similar effectiveness compared to long-acting injectable naltrexone on treatment retention, relapse rates or overdose. One RCT that compared long-acting injectable naltrexone to orally administered buprenorphine-naloxone found that people have more difficulty initiating treatment with long-acting injectable naltrexone and were more likely to relapse, and one cohort study found that overdose rates were higher among patients taking long-acting injectable naltrexone compared to buprenorphine.

**Figure 14. Comparative Effectiveness of Buprenorphine Products vs. Long-Acting Injectable Naltrexone to Treat Opioid Use Disorder — Buprenorphine vs. Long-Acting Injectable Naltrexone (Similar Effectiveness)**




## Harms Associated with Buprenorphine Products, Methadone, and Long-Acting Injectable Naltrexone

### *Buprenorphine products and methadone*

Patients who take methadone or buprenorphine to treat opioid use disorder may experience side effects that are similar to those of opioids, such as nausea, vomiting, constipation, muscle aches, cramps, constipation, fever, cravings, irritability, and inability to sleep (SAMHSA, 2018). People using methadone may also experience difficulty breathing, lightheadedness, hives, rash, chest pain, rapid heart rate, and hallucinations (SAMHSA, 2018). They also have an increased risk of overdose during the first few weeks of treatment (Sordo et al., 2017).

There is also a risk that people will misuse methadone or buprenorphine due to their opioid effects (SAMHSA, 2018). This risk is higher with buprenorphine than methadone because people are often prescribed a supply of buprenorphine to take on their own, whereas people receiving methadone are usually required to take their medication at a methadone clinic. Because relapse is common among people who receive all forms of treatment for opioid use disorder, risk of overdose when a person resumes consumption of opioids should be considered when treatment decisions are made (Saucier et al., 2018). Despite these harms, professional organizations, including SAMHSA, recommend use of these medications to treat opioid use disorder.

**Summary of findings regarding harms associated with buprenorphine products and methadone for opioid use disorder:** People treated with methadone and buprenorphine may experience side effects similar to those of opioids. People who receive methadone have a greater risk of opioid overdose during the first few weeks of treatment compared to prior to starting treatment and compared to those starting buprenorphine.

### *Long-acting injectable naltrexone*

People who take long-acting injectable naltrexone to treat opioid use disorder or alcohol use disorder may experience side effects such as nausea, vomiting, headaches, dizziness, fatigue, anxiety, and somnolence. Some patients may also experience pain, tenderness, or other injection-site reactions at the injection site (SAMHSA, 2015).

Initiation and discontinuation of treatment with naltrexone ER carries added risk of harm for people with concurrent opioid use or opioid use disorder. Unlike methadone and buprenorphine, which can be used safely while a patient continues to use opioids, patients must withdraw from all opioids before beginning treatment with naltrexone. Some patients are unable to do this and may not start the medication, relapse, and/or overdose. Lee et al. (2018) found that inductions onto opiate use disorder medication were less likely to be successful for patients assigned to long-acting injectable naltrexone, and relapse was more likely if assigned to long-acting injectable naltrexone, compared to being assigned to sublingually administered buprenorphine. The authors also found a higher number of overdose events for patients who were assigned to long-acting injectable naltrexone but did not begin treatment (n=8) compared to patients assigned to buprenorphine who did not take the medication (n=1), although the study was not powered to detect statistically significant differences for overdose.

**Summary of findings regarding harms associated with long-acting injectable naltrexone for opioid or alcohol use disorder:** People treated with long-acting injectable naltrexone may experience side effects or injection site reactions. Initiating long-acting injectable naltrexone is associated with a higher risk of opioid overdose compared to initiating buprenorphine because people must abstain from opioids before initiating treatment and may be sensitive to lower doses of opioids if they relapse.

# APPENDIX D COST IMPACT ANALYSIS: DATA SOURCES, CAVEATS, AND ASSUMPTIONS

With the assistance of CHBRP's contracted actuarial firm, Milliman, Inc, the cost analysis presented in this report was prepared by the faculty and researchers connected to CHBRP's Task Force with expertise in health economics.[33] Information on the generally used data sources and estimation methods, as well as caveats and assumptions generally applicable to CHBRP's cost impacts analyses are available at CHBRP's website.[34]

This appendix describes analysis-specific data sources, estimation methods, caveats, and assumptions used in preparing this cost impact analysis.

## Analysis-Specific Data Sources

Current coverage of the medications addressed by AB 1288 was determined by a survey of the largest (by enrollment) providers of health insurance in California. Benefit coverage responses to an earlier survey[35] were verified through a new supplemental survey and review of current claims. In addition, CalPERS, was queried regarding related benefit coverage.

For this analysis, CHBRP relied on CPT® codes to identify relevant services. CPT copyright 2022 American Medical Association. All rights reserved. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. CPT is a registered trademark of the American Medical Association.

## Determining Public Demand for the Proposed Mandate

CHBRP reviews public demand for benefits by comparing the benefits provided by self-insured health plans or policies (which are not regulated by the DMHC or CDI and therefore not subject to state-level mandates) with the benefits that are provided by plans or policies that would be subject to the mandate.

Among publicly funded self-insured health insurance policies, the preferred provider organization (PPO) plans offered by CalPERS have the largest number of enrollees. Prior authorization requirements are present for these enrollees for the medications addressed by AB 1288.

To further investigate public demand, CHBRP used the bill-specific coverage survey to ask plans and insurers who act as third-party administrators for (non-CalPERS) self-insured group health insurance programs whether the relevant benefit coverage differed from what is offered in group market plans or policies that would be subject to the mandate. The responses indicated that there were no substantive differences.

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[33] CHBRP's authorizing statute, available at https://chbrp.org/about_chbrp/index.php, requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact.
[34] See method documents posted at https://www.chbrp.org/about/analysis-methodology/cost-impact-analysis; in particular, see *2022 Cost Analyses: Data Sources, Caveats, and Assumptions*.
[35] *SB 854 Health Care Coverage: Substance Use Disorders*, available at chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.chbrp.org/sites/default/files/bill-documents/SB854/sb854-FullReport.pdf.

## Second-Year Impacts on Benefit Coverage, Utilization, and Cost

CHBRP has considered whether continued implementation during the second year of the benefit coverage requirements of AB 1288 would have a substantially different impact on utilization of either the tests, treatments, or services for which coverage was directly addressed, the utilization of any indirectly affected utilization, or both. CHBRP reviewed the literature and consulted content experts about the possibility of varied second-year impacts and determined the second year's impacts of AB 1288 would be substantially the same as the impacts in the first year. Minor changes to utilization and expenditures are due to population changes between the first year postmandate and the second year postmandate.

# REFERENCES


Abraham AJ, Yarbrough CR. Availability of medications for the treatment of alcohol use disorder in U.S. counties, 2016–2019. *Journal of Studies on Alcohol and Drugs*. 2021;82(6):689-99. https://doi.org/10.15288/jsad.2021.82.689.

Accurso AJ, Rastegar DA. The Effect of a Payer-Mandated Decrease in Buprenorphine Dose on Aberrant Drug Tests and Treatment Retention Among Patients with Opioid Dependence. *Journal of Substance Abuse Treatment*. 2016;61:74-79.

Alanis-Hirsch K, Croff R, Ford JH, Johnson K, Chalk M, Schmidt L, McCarty D. Extended-release naltrexone: a qualitative analysis of barriers to routine use. *Journal of Substance Abuse Treatment*. 2016; 62:68-73.

American College of Obstetricians and Gynecologists (ACOG). *Frequently Asked Questions for Teens: Lesbian, Gay, Bisexual, Transgender, and Queer (LBGTQ) Teens.* September 2022. Available at: https://www.acog.org/womens-health/faqs/lgbtq-teens. Accessed January 11, 2023.

American Journal of Managed Care*. An overview of medication-assisted treatment for opioid and alcohol use disorders. Perspectives in Medication-Assisted Treatment*, 2020. Available at: https://www.ajmc.com/view/an-overview-of-medication-assisted-treatment-for-opioid-and-alcohol-use-disorders. Accessed March 28, 2023.

American Medical Association (AMA). Survey quantifies time burdens of prior authorization. 2017. Available at:https://www.ama-assn.org/practice-management/prior-authorization/survey-quantifies-time-burdens-prior-authorization. Accessed March 24, 2023.

American Medical Association (AMA). What is prior authorization? 2022. Available at: https://www.ama-assn.org/practice-management/prior-authorization/what-prior-authorization. Access March 19, 2023.

American Psychiatric Association (APA). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. DSM-5. Washington, DC: American Psychiatric Association, 2013.

American Society of Addiction Medicine (ASAM). Public Policy Statement: Definition of Addiction. April 12, 2011. Available at: https://www.asam.org/resources/definition-of-addiction. Accessed March 17, 2018.

American Society of Addiction Medicine (ASAM). Definition of Addiction. September 15, 2019. Available at: www.asam.org/resources/definition-of-addiction. Accessed January 11, 2023.

American Society of Addiction Medicine (ASAM). The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. 2020a. Available at: https://sitefinitystorage.blob.core.windows.net/sitefinity-production-blobs/docs/default-source/guidelines/npg-jam-supplement.pdf?sfvrsn=a00a52c2_2. Accessed: March 7, 2023

American Society of Addiction Medicine (ASAM). The ASAM clinical practice guidelines on alcohol withdrawal management. 2020b. Available at: https://www.asam.org/docs/default-source/quality-science/the_asam_clinical_practice_guideline_on_alcohol-1.pdf. Accessed March 6, 2023.

American Society of Addiction Medicine (ASAM). Regulation of the Treatment of Opioid Use Disorder with Methadone. October 2021. Available at: https://www.asam.org/advocacy/public-policy-statements/details/public-policy-statements/2021/11/16/the-regulation-of-the-treatment-of-opioid-use-disorder-with-methadone. Accessed March 2023.

Andraka-Christou B, Capone MJ. A qualitative study comparing physician-reported barriers to treating addiction using buprenorphine and extended-release naltrexone in U.S. office-based practices. *International Journal of Drug Policy*. 2018;54:9-17.

Andraka-Christou B, Page C, Schoebel V, Buche J, Haffajee RL. Perceptions of buprenorphine barriers and efficacy among nurse practitioners and physician assistants. *Addiction Science & Clinical Practice*. 2022;17(43).

Baxter LE, Sr, Campbell A, Deshields M, Levounis P, Martin JA, McNicholas L, et al. Safe methadone induction and stabilization: Report of an expert panel. *Journal of Addiction Medicine*. 2013;7(6):377–386

Bivin B, Waring A, Alves P. Buprenorphine compared with methadone in opioid-dependent pregnant women: How does it affect neonatal abstinence syndrome*? Journal of the American Association of Nurse Practitioner*s. 2021;33(2):119-125.

Blanco C, Iza M, Schwartz RP, Rafful C, Wang S, Olfson M. Probability, and predictors of treatment-seeking for prescription opioid use disorders: a national study. *Drug and Alcohol Dependence*. 2013;131:143–148.

California Department of Health Care Services (DHCS). Costs of Substance Abuse in the California. May 2, 2013. Available at: https://www.dhcs.ca.gov/provgovpart/Documents/GPAC%20Cost%20Presentation%20May%202nd%202013%20final.pdf. Accessed March 24, 2021.

California Department of Health Care Services (DHCS). Behavioral Health Information Notice No: 21-075. December 2021. Available at: https://www.dhcs.ca.gov/Documents/BHIN-21-075-DMC-ODS-Requirements-for-the-Period-2022-2026.pdf. Accessed March 2023.

California Department of Health Care Services (DHCS). California Medication-assisted Treatment Expansion Project: Prescriber Resources. February 2023. Available at: https://www.dhcs.ca.gov/individuals/Pages/Prescriber-Resources.aspx#:~:text=Physicians%20require%20%208%20hours%20of,treatment%20of%20opioid%20use%20disorder. Accessed March 2023.

California Department of Health Care Services (DHCS). California response to the overdose crisis. 2023a. Available at: https://californiamat.org/wp-content/uploads/2020/05/MAT_Flyers_DHCS_Opioid_Crisis.pdf. Accessed March 6, 2023.

California Department of Health Care Services (DHCS). The California MAT expansion project flyer. 2023b. Available at: https://californiamat.org/wp-content/uploads/2023/02/mat-infographic_Feb_2023.pdf. Accessed March 6, 2023.

California Department of Public Health (CDPH). California Opioid Overdose Surveillance Dashboard. 2019. https://discovery.cdph.ca.gov/CDIC/ODdash. Accessed February 23, 2021.

California Department of Public Health (CDPH). California Opioid Overdose Surveillance Dashboard. 2023. https://discovery.cdph.ca.gov/CDIC/ODdash. Accessed March 7, 2023.

California Health Benefits Review Program (CHBRP). Analysis of California Senate Bill 854 Health Care Coverage: Substance Use Disorders. Berkeley, CA; 2020.

California Health Care Foundation (CHCF). California Health Care Almanac, Substance Use in California: A Look at Addiction and Treatment. California Health Care Foundation, 2018. Available at: https://www.chcf.org/wp-content/uploads/2018/09/SubstanceUseDisorderAlmanac2018.pdf. Accessed February 3, 2020.

California Health Care Foundation (CHCF). California Health Care Almanac, Substance Use in California: Prevalence and Treatment. California Health Care Foundation, 2022. Available at: https://www.chcf.org/wpcontent/uploads/2022/01/SubstanceUseDisorderAlmanac2022.pdf. Accessed February 28, 2023.

Castillo-Carniglia A, Keyes KM, Hasin DS, Cerda M. Psychiatric comorbidities in alcohol use disorder. *Lancet Psychiatry*. 2019;6(12):1068-1080.

Centers for Disease Control and Prevention (CDC). Medication-assisted treatment for opioid use disorder study (MAT study). 2019. Available at: https://www.cdc.gov/opioids/Medication-Assisted-Treatment-Opioid-Use-Disorder-Study.html#print. Accessed March 6, 2023.

Centers for Disease Control and Prevention (CDC). National Center for Chronic Disease Prevention and Health Promotion, Division of Population Health. Alcohol and Public Health: Alcohol-Related Disease Impact (ARDI). 2013. Available at: https://nccd.cdc.gov/dph_ardi/Default/Default.aspx. Accessed March 3, 2020.

Centers for Disease Control and Prevention (CDC). NCHHSTP Social Determinants of Health: Frequently Asked Questions. Available at: www.cdc.gov/nchhstp/socialdeterminants/faq.html. Accessed August 27, 2015.

Centers for Disease Control and Prevention (CDC). Prescription Opioids. 2017. Available at: Prescription Opioids | Opioids | CDC. Accessed April 5, 2023.

Centers for Disease Control and Prevention (CDC). Transgender Persons. September 14, 2022. Available at: https://www.cdc.gov/lgbthealth/transgender.htm. Accessed January 11, 2023.

Centers for Disease Control and Prevention (CDC). Opioid Use Disorder. 2022a. Available at: Opioid Use Disorder | Disease or Condition of the Week | CDC. Accessed April 5, 2023.

Centers for Disease Control and Prevention (CDC). Substance Use Disorders. 2022b. Available at: https://www.cdc.gov/dotw/substance-use-disorders/index.html. Accessed April 5, 2023.

Centers for Disease Control and Prevention (CDC). Polysubstance Use Facts. 2022c. Available at: Polysubstance Use Facts (cdc.gov). Accessed April 7, 2023.

Centers for Medicare & Medicaid Services (CMS). Behavioral Health Terms. 2022. Available at: www.cms.gov/outreach-education/american-indianalaska-native/behavioral-health/behavioral-health-terms. Accessed December 9, 2022.

Clark RE, Baxter JD, Barton BA, Aweh G, O'Connell E, Fisher WH. The impact of prior authorization on buprenorphine dose, relapse rates, and cost for Massachusetts Medicaid beneficiaries with opioid dependence. *Health Services Research*. 2014;49(6):1964-1979.

Clemans-Cope L, Wissoker DA, Epstein M. California County Fact Sheets: Treatment Gaps in Opioid-Agonist Medication-Assisted Therapy (OA-MAT) and Estimates of How Many Additional Prescribers Are Needed. Urban Institute. March 2018. Available at: https://www.urban.org/policy-centers/health-policy-center/projects/california-county-fact-sheets-treatment-gaps-opioid-agonist-medication-assisted-therapy-oa-mat-and-estimates-how-many-additional-prescribers-are-needed. Accessed April 1, 2018.

Clemans-Cope L, Epstein M, Wissoker D, Aarons J. California opioid use disorder and treatment needs: California totals, 2019 fact sheet. 2019. Available at: https://www.urban.org/sites/default/files/2020/01/31/all_counties.pdf. Accessed March 25, 2023.

Corrigan PW and Nieweglowksi K. Stigma and the public health agenda for the opioid crisis in America. *International Journal of Drug Policy.* 2018;59:44-49.

Davis CN, O'Neill SE. Treatment of alcohol use problems among rural populations: a review of barriers and considerations for increasing access to quality care. *Current Addiction Reports*. 2022;9:432-444.

Dennis M, Scott CK. Managing addiction as a chronic condition. *Addiction Science & Clinical Practice*. 2007;4(1):45-55.

Dhanani LY, Harris EL, Mirto J, Franz, B. Barriers to working with patients who misuse opioids and physician burnout: implications for medical education. *Substance Use & Misuse*. 2022;57(8):1177-1184.

Erol A, Karpyak VM. Sex and gender-related differences in alcohol use and its consequences: Contemporary knowledge and future research considerations. *Drug and Alcohol Dependence*. 2015;156:1–13. doi: 10.1016/j.drugalcdep.2015.08.023.

Esser MB, Sherk A, Liu Y, et al. Deaths and years of potential life lost from excessive alcohol use-United States, 2011-2015. *Morbidity and Mortality Weekly Report*. 2020;69(39):1428-1433.

Fan AZ, Chou SP, Zhang H, Jung J, Grant BF. Prevalence and correlates of past-year recovery from DSM-5 alcohol use disorder: results from national epidemiologic survey on alcohol and related conditions-III. *Alcoholism: Clinical and Experimental Research*. 2019;43(11):2406-2420.

Feder KA, Krawcyzk N, Saloner B. Medication-assisted treatment for adolescents in specialty treatment for opioid use disorder. *Journal of Adolescent Health*. 2017;60(6):747-750.

Ferries E, Racsa P, Bizzell B, Rhodes C, Suehs B. Removal of prior authorization for medication-assisted treatment: Impact on opioid use and policy implications in a Medicare Advantage population. *Journal of Managed Care & Specialty Pharmacy*. 2021;27(5):596-606.

Fisher DG, Reynolds GL, D'Anna LH, Hosmer DW, Hardan-Khalil K. Failure to Get into Substance Abuse Treatment. *Journal of Substance Abuse Treatment*. 2017;73:55-62.

Foreman M, Jeferson T, deLaViez B, Park JK, Reily P, Quarterman B. *Substance Abuse under the ADA*. In: Sharing the Dream: Is the ADA Accommodating All? U.S. Commission on Civil Rights (USCCR). 2000. Available at: https://www.usccr.gov/files/pubs/ada/ch4.htm. Accessed April 10, 2023.

Fullerton CA, Kim M, Thomas CP, et al. Medication-assisted treatment with methadone: assessing the evidence. *Psychiatric Services*. 2014;65(2):146-157.

Furr-Holden D, Milam AJ, Wang L, Sadler R. African Americans now outpace whites in opioid-involved overdose deaths: a comparison of temporal trends from 1999 to 2018. *Addiction*. 2021;116:677–683. doi: 10.1111/add.15233.

Gardner JW, Sanborn JS. Years of potential life lost (YPLL)—what does it measure? *Epidemiology* (Cambridge, Mass.). 1990;1(4):322-329.

Garrett R, Young SD. The role of misinformation and stigma in opioid use disorder treatment uptake. *Substance Use & Misuse*. 2022;57(8):1332-1336.

Glynn SJ. Gender Wage Inequality: What We Know and How We Can Fix It. Washington Center for Equitable Growth. 2018. Available at: https://equitablegrowth.org/research-paper/gender-wage-inequality. Accessed September 21, 2020.

Gomes T, Tadrous M, Mamdani MM, Paterson JM, Juurlink DN. The burden of opioid-related mortality in the United States. *JAMA Network Open.* 2018;1(2):e180217. doi:10.1001/jamanetworkopen.2018.0217.

Goodwin LR Jr, Sias SM. Severe substance use disorder viewed as a chronic condition and disability. *Journal of Rehabilitation*. 2014;80(4):42-49.

Gowing L, Farrell MF, Bornemann R, Sullivan LE, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. *Cochrane Database of Systematic Reviews*. 2011(8):Cd004145.

Greiner MG, Shulman M, Choo T-H, et al. Naturalistic follow-up after a trial of medications for opioid use disorder: Medication status, opioid use, and relapse. *Journal of Substance Abuse Treatment*. 2021;131:7.

Greiner MG, Shulman M, Scodes J, et al. Patient Characteristics Associated with Opioid Abstinence after Participation in a Trial of Buprenorphine versus Injectable Naltrexone. *Substance Use & Misuse*. 2022;57(11):1732-1742.

Hadland SE, Bagley SM, Rodean J. Receipt of timely addiction treatment and association of early medication treatment with retention in care among youths with opioid use disorder. JAMA *Pediatrics*. 2018;172(11):1029-1037.

Haeny AM, Montgomery L, Burlew AK, et al. Extended-release naltrexone versus buprenorphine-naloxone to treat opioid use disorder among black adults. *Addictive Behaviors*. 2020;110.

Haffajee RL, Andraka-Christou B, Attermann J, Cupito A, Buche J, Beck AJ. A mixed-method comparison of physician-reported beliefs about and barriers to treatment with medications for opioid use disorder. *Substance Abuse Treatment, Prevention, and Policy*. 2020;15(69).

Haffajee RL, Lin LA, Bohnert AS, Goldstick JE. Characteristics of US counties with high opioid overdose mortality and low capacity to deliver medications for opioid use disorder. *JAMA Network Open*. 2019;2(6):e196373. doi:10.1001/jamanetworkopen.2019.6373.

Haight BR, Learned SM, Laffont CM, et al. Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2019;393(10173):778-790.

Han B, Jones CM, Einstein EB, Powell PA, Compton WM. Use of medications for alcohol use disorder in the US: results from the 2019 National Survey on Drug Use and Health. *JAMA Psychiatry*. 2021;78(8):922-24.

Healthy People 2020 (HP2020). Social Determinants of Health. 2014. Office of Disease Prevention and Health Promotion. Available at: https://wayback.archive-it.org/5774/20220413203948/https://www.healthypeople.gov/2020/topics-objectives/topic/social-determinants-of-health. Accessed August 6, 2021.

Hill LG, Light AE, Green TC, Burns AL, Zadeh PS, Freeman PR. Perceptions, policies, and practices related to dispensing buprenorphine for opioid use disorder: a national survey of community-based pharmacists. *American Pharmacists Association*. 2023;63:252-260.

Hser YI, Evans E, Huang D, et al. Long-term outcomes after randomization to buprenorphine/naloxone versus methadone in a multi-site trial. *Addiction*. 2016;111(4):695-705.

Huhn AS, Berry MS, Dunn KE. Review: sex-based differences in treatment outcomes for persons with opioid use disorder. *American Journal of Addiction*. 2019;28(4):246-261.

Jarvis BP, Holtyn AF, Subramaniam S, et al. Extended-release injectable naltrexone for opioid use disorder: a systematic review. *Addiction*. 2018;113(7):1188-1209.

Javed A, Lee C, Zakaria H, et al. Reducing the stigma of mental health disorders with a focus on low- and middle-income countries. *Asian Journal of Psychiatry*. 2021;58:102601

Jiménez JA, Demeter NE, Pinsker EA. Deaths from Excessive Alcohol Use in California, 2020-2021. Sacramento, CA: California Department of Public Health. January 2023. Available at: https://www.cdph.ca.gov/Programs/CCDPHP/sapb/CDPH%20Document%20Library/Deaths_from_Excessive_Alcohol_Use_in_California_2020_2021.pdf. Accessed March 21, 2023.

Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. *JAMA*. 2014;311(18):1889-1900.

Jones CM, Campopiano M, Baldwin G, McCance-Katz E. National and State Treatment Need and Capacity for Opioid Agonist Medication-Assisted Treatment. *American Journal of Public Health*. 2015;105(8): e55-e63.

Jones CM, McCance-Katz EF. Co-occurring substance use and mental disorders among adults with opioid use disorder. *Drug and Alcohol Dependence*. 2019;197:78-82.

Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. *Journal of Addiction Medicine*. 2015;9(5):358-67. doi: 10.1097/ADM.0000000000000166

Karpyak VM, Biernacka JM, Geske JR, et al. Gender-specific effects of comorbid depression and anxiety on the propensity to drink in negative emotional states. *Addiction*. 2016;111(8):1366–1375.

Kedia SK, Ahuja N, Dillon PJ, Jones A, Kumar S, Satapathy S. Efficacy of Extended-Release Injectable Naltrexone on Alcohol Use Disorder Treatment: A Systematic Review. *Journal of Psychoactive Drugs*. 2022:1-13.

Kelly JF, Greene MC, Bergman BG, White WL, Hoeppner BB. How many recovery attempts does it take to successfully resolve an alcohol or drug problem? Estimates and correlates from a national study of recovering US adults. *Alcoholism: Clinical and Experimental Research*. 2019;43(7):1533-44.

Keyes KM, Rutherford C, Hamilton A, et al. What is the prevalence of and trend in opioid use disorder in the United States from 2010 to 2019? Using multiplier approaches to estimate prevalence for an unknown population size. *Drug and Alcohol Dependence Reports*. 2022;3.

Khan S, Okuda M, Hasin DS, et al. Gender differences in lifetime alcohol dependence: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Alcohol: Clinical and Experimental Research*. 2013;37(10):1696–1705. doi: 10.1111/acer.12158.

Khullar D, Chokshi D. Health, Income, & Poverty: Where We Are & What Could Help. Health Affairs Health Policy Brief. October 4, 2018. Available at: www.healthaffairs.org/do/10.1377/hpb20180817.901935/full. Accessed September 21, 2020.

Kinsella M, Halliday LOE, Shaw M, Capel Y, Nelson SM, Kearns RJ. Buprenorphine Compared with Methadone in Pregnancy: A Systematic Review and Meta-Analysis. *Substance Use & Misuse*. 2022;57(9):1400-1416.

Knopf A. AMA urges states to stop prior authorizations for buprenorphine. *Alcoholism & Drug Abuse Weekly*. 2021;33(37):6.

Knudsen HK, Havens JR, Lofwall MR, Studts JL, Walsh SL. Buprenorphine physician supply: Relationship with state-level prescription opioid mortality. *Drug and Alcohol Dependence*. 2017;173(Suppl 1):S55-S64.

Kochnar R, Cilluffo A. Key Findings on the Rise in Income Inequality Within America's Racial and Ethnic Groups. Pew Research Center. July 12, 2018. Available at: www.pewresearch.org/fact-tank/2018/07/12/key-findings-on-the-rise-in-income-inequality-within-americas-racial-and-ethnic-groups. Accessed September 21, 2020.

Krebs E, Kerr T, Wood E, Nosyk B. Characterizing Long-Term Health Related Quality of Life Trajectories of Individuals With Opioid Use Disorder. *Journal of Substance Abuse Treatment*. 2016;67:30-37.

Kreek MJ, Reed B, Butelman ER. Current status of opioid addiction treatment and related preclinical research. *Science Advances*. 2019;5(10):eaax9140.

Krueger EA, Fish JN, Upchurch DM. Sexual Orientation Disparities in Substance Use: Investigating Social Stress Mechanisms in a National Sample. *American Journal of Preventive Medicine*. 2020;58(1): 59–68. doi:10.1016/j.amepre.2019.08.034.

Latronica, JR. Increasing access to medications for opioid use disorder: policy analysis and proposals. *Journal of Addictive Diseases*. 2021;39(3):421-424.

Lee JD, Nunes EV, Jr., Novo P, et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial. *Lancet*. 2018;391(10118):309-318.

Legal Action Center (LAC). Spotlight on Legislation Limiting the Use of Prior Authorization for Substance Use Disorder Services and Medications. May 2020. Available at: https://www.lac.org/assets/files/Prior-Authorization-Spotlight-FINAL-use-this-one.pdf. Accessed March 2023.

Leighty AE, Ansara ED. Treatment outcomes of long-acting injectable naltrexone versus oral naltrexone in alcohol use disorder in veterans. *Mental Health Clinician*. 2019;9(6):392-396.

Leone B, Di Nicola M, Moccia L, et al. Gender-related psychopathology in opioid use disorder: Results from a representative sample of Italian addiction services. *Addictive Behaviors*. 2017;71:107–110.

Lim J, Farhat I, Douros A, Panagiotoglou D. Relative effectiveness of medications for opioid-related disorders: A systematic review and network meta-analysis of randomized controlled trials. *PLoS ONE*. 2022;17(3 March).

Ling W, Casadonte P, Bigelow G, et al. Buprenorphine implants for treatment of opioid dependence: a randomized controlled trial. *JAMA*. 2010;304(14):1576-1583.

Ludici A, Girolimetto R, Volponi G, Eletto A. Dual diagnosis and application problems in the use of the construct. a review of literature. *The Journal of Nervous and Mental Disease.* 2020;208(3):181-189.

Ma J, Bao YP, Wang RJ, et al. Effects of medication-assisted treatment on mortality among opioids users: a systematic review and meta-analysis. *Molecular Psychiatry*. 2020;24(12):1868-1883.

MacArthur GJ, Minozzi S, Martin N, et al. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. *Bmj*. 2012;345:e5945.

Mackey K, Veazie S, Anderson J, Bourne D, Peterson K. Barriers and facilitators to the use of medications for opioid use disorder: a rapid review. *Journal of General Internal Medicine*. 2020;35(suppl 13):S954-S63.

Marino LA, Campbell, Nunes EV, Sederer LI, Dixon LB. Factors influencing buprenorphine prescribing among physicians in New York state. *Journal of Addiction*. 2019;2019:7832752 https://doi.org/10.1155/2019/7832752.

Mark TL, Parish WJ, Zarkin GA. Association of Formulary Prior Authorization Policies With Buprenorphine-Naloxone Prescriptions and Hospital and Emergency Department Use Among Medicare Beneficiaries. *JAMA Network Open*. 2020;3(4):e203132.

Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. The Cochrane database of systematic reviews. 2009;(3):Cd002209.

Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database of Systematic Reviews*. 2014;(2):Cd002207.

Mauro PM, Gutkind S, Annunziato EM, Samples H. Use of medication for opioid use disorder among US adolescents and adults with need for opioid treatment. 2019. *JAMA Network Open*. 2022;5(3):e223821. doi:10.1001/jamanetworkopen.2022.3821.

McCabe SE, West BT, Hughes TL, Boyd CJ. Sexual orientation and substance abuse treatment utilization in the United States: results from a national survey. *Journal of Substance Abuse Treatment.* 2013;44(1):4-12.

McCarty D, Priest KC, Korthius PT. Treatment and prevention of opioid use disorder: challenges and opportunities. *Annual Review of Public Health*. 2018;39:525-541.

McKay JR, Hiller-Sturmhöfel S. Treating alcoholism as a chronic disease. *Alcohol Research & Health*. 2011;33(4):356-370.

McNeely J, Kumar PC, Rieckmann T, et al. Barriers and facilitators affecting the implementation of substance use screening in primary care clinics: a qualitative study of patients, providers, and staff. *Addiction Science & Clinical Practice*. 2018;13(1):8.

McQuaid RJ, Malik A, Moussouni K, Baydack N, Stargardter M, Morrisey M. Life in recovery from addiction in Canada. Ottawa, Canada: Canadian Centre on Substance Use and Addiction. 2017:84.

Minozzi S, Amato L, Bellisario C, Davoli M. Maintenance treatments for opiate -dependent adolescents. *Cochrane Database of Systematic Reviews*. 2014(6):Cd007210.

Minozzi S, Amato L, Bellisario C, Ferri M, Davoli M. Maintenance agonist treatments for opiate-dependent pregnant women. *Cochrane Database of Systematic Reviews*. 2013(12):Cd006318.

Minozzi S, Amato L, Jahanfar S, Bellisario C, Ferri M, Davoli M. Maintenance agonist treatments for opiate-dependent pregnant women. *Cochrane Database of Systematic Reviews.* 2020;11(11):Cd006318.

Mintz CM, Hartz SM, Fisher SL, Ramsey AT, Geng EH, Grucza RA, Bierut LJ. A cascade of care for alcohol use disorder: using 2015-2019 national survey on drug use and health data to identify gaps in past 12-month care. *Alcohol: Clinical and Experimental Research*. 2021;45(6):1276-1286.

Mooney A, Giannella E, Glymour M, et al. Racial/Ethnic Disparities in Arrests for Drug Possession After California Proposition 47, 2011–2016. *American Journal of Public Health*. 2018;108(8): 987-993.

Morgan JR, Schackman BR, Weinstein ZM, Walley AY, Linas BP. Overdose following initiation of naltrexone and buprenorphine medication treatment for opioid use disorder in a United States commercially insured cohort. *Drug and Alcohol Dependency*. 2019;200:34-39.

Murphy IV CE, Wang RC, Montoy JC, Whittaker E, Raven M. Effect of extended-release naltrexone on alcohol consumption: a systematic review and meta-analysis. *Addiction*. 2022;117(2):271-281.

National Cancer Institute (NCI). NCI Dictionary of Cancer Terms: Premature Death. 2019. Available at: www.cancer.gov/publications/dictionaries/cancer-terms/def/premature-death. Accessed August 29, 2019.

National Center for Drug Abuse Statistics (NCDAS). Alcohol abuse statistics. 2023. Available at: https://drugabusestatistics.org/alcohol-abuse-statistics/#:~:text=Most%20American%20adults%20consume%20alcohol,Alcohol%20Use%20Disorder%20in%202020. Accessed March 7th, 2023.

National Conference of State Legislature (NCSL). As Opioid Overdoses Surge, States Expand Treatment. May 2022. Available at: https://www.ncsl.org/resources/details/as-opioid-overdoses-surge-states-expand-treatment. Accessed March 2023.

National Institute on Alcohol Abuse and Alcoholism (NIAAA). Alcohol Facts and Statistics. 2018. Available at: https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/alcohol-facts-and-statistics. Accessed February 2019.

National Institute on Alcohol Abuse and Alcoholism (NIAAA). Minority Health and Health Disparities. 2019. Available at: https://wwNrs/diversity-health-disparities. Accessed January 12, 2019.

National Institute on Alcohol Abuse and Alcoholism (NIAAA). Alcohol treatment in the United States. 2023. Available at https://www.niaaa.nih.gov/alcohols-effects-health/alcohol-topics/alcohol-facts-and-statistics/alcohol-treatment-united-states. Accessed March 26, 2023.

National Institute on Drug Abuse (NIDA). Drug Abuse and Addiction: One of America's Most Challenging Public Health Problems. 2005. Available at: https://archives.drugabuse.gov/publications/drug-abuse-addiction-one-americas-most-challenging-public-health-problems. Accessed March 2020.

National Institute on Drug Abuse (NIDA). Substance Use and SUDs in LGBT Populations. 2017. Available at: https://www.drugabuse.gov/related-topics/substance-use-suds-in-lgbt-populations. Accessed April 2020.

National Institute on Drug Abuse (NIDA). Comorbid Substance Use Disorders. 2018. Available at: https://www.drugabuse.gov/longdesc/table-1-comorbid-substance-use-disorders. Accessed February 2019.

National Institute on Drug Abuse (NIDA). Common comorbidities with substance use disorders research report. 2020. Available at: https://nida.nih.gov/download/1155/common-comorbidities-substance-use-disorders-research-report.pdf?v=5d6a5983e0e9353d46d01767fb20354b. Accessed March 30, 2023.

National Institute on Drug Abuse (NIDA). The Science of Drug Use and Addiction: The Basics. February 2023. Available at: http://archives.nida.nih.gov/publications/media-guide/science-drug-use-addiction-basics. Accessed April 7, 2023.

National Institutes of Health (NIH), Office of Research on Women's Health. Sex and Gender. 2019; Available at: https://orwh.od.nih.gov/sex-gender. Accessed August 30, 2019.

Nguyen TD, Chua KP, Andraka-Christou B, Bradford WD, Simon K. Trends in buprenorphine coverage and prior authorization requirements in US commercial formularies, 2017-2021. *JAMA Health Forum*. 2022a;3(7):e221821. doi:10.1001/jamahealthforum.2022.1821

Nguyen T, Ziedan E, Simon K, Miles J, Crystal S, Samples H, Gupta S. Racial and ethnic disparities in buprenorphine and extended-release naltrexone filled prescriptions during the COVID-19 pandemic. *JAMA Network Open*. 2022b;5(6):e2214765. doi:10.1001/jamanetworkopen.2022.14765.

Nielsen S, Larance B, Degenhardt L, Gowing L, Kehler C, Lintzeris N. Opioid agonist treatment for pharmaceutical opioid dependent people*. Cochrane Database of Systematic Reviews*. 2016;(5):Cd011117.

Nielsen S, Tse WC, Larance B. Opioid agonist treatment for people who are dependent on pharmaceutical opioids*. Cochrane Database of Systematic Reviews*. 2022;9(9):Cd011117.

Nolan S, Dias Lima V, Fairbairn N, et al. The impact of methadone maintenance therapy on hepatitis C incidence among illicit drug users. *Addiction*. 2014;109(12):2053-2059.

Opheim A, Gaulen Z, Solli KK, et al. Risk of Relapse Among Opioid-Dependent Patients Treated With Extended-Release Naltrexone or Buprenorphine-Naloxone: A Randomized Clinical Trial. *American Journal on Addictions*. 2021;30(5):453-460.

Paschen-Wolff MM, Velasquez R, Aydinoglo N, Campbell ANC. Simulating the experience of searching for LGBTQ-specific opioid use disorder treatment in the United States. *Journal of Substance Abuse Treatment,* 2022;140. doi: 10.1016/j.jsat.2022.108828

Parish WJ, Mark TL, Zarkin GA, Weber E. The association of Medicare Part D prior authorization for buprenorphine–naloxone with adherence to opioid use disorder treatment guidelines in the United States. *Addiction*. 2022;117(1):141-150.

Peltier MR, Verplaetse TL, Mineur YS, et al. Sex differences in stress-related alcohol use. *Neurobiology of Stress*. 2019;10:100149. doi: 10.1016/j.ynstr.2019.100149.

Pew Research Center. Medications for Opioid Use Disorder Improve Patient Outcomes. December 2020. Available at: https://www.pewtrusts.org/en/research-and-analysis/fact-sheets/2020/12/medications-for-opioid-use-disorder-improve-patient-outcomes. Accessed March 2023.

Philbin MM, Greene ER, Martins SS, LaBossier NJ, Mauro PM. Medical, Nonmedical, and Illegal Stimulant Use by Sexual Identity and Gender. *American Journal of Preventive Medicine*. 2020;59(5):686-696. doi: 10.1016/j.amepre.2020.05.025

Qato DM, Watanabe JH, Clark KJ. Federal and state pharmacy regulations and dispensing barriers to buprenorphine access at retail pharmacies in the US. *JAMA Health Forum.* 2022;3(8):e222839. doi:10.1001/jamahealthforum.2022.2839.

Rosenthal RN, Lofwall MR, Kim S, Chen M, Beebe KL, Vocci FJ. Effect of Buprenorphine Implants on Illicit Opioid Use Among Abstinent Adults With Opioid Dependence Treated With Sublingual Buprenorphine: A Randomized Clinical Trial. *JAMA*. 2016;316(3):282-290.

Saini J, Johnson B, Qato DM. Self-reported treatment need and barriers to care for adults with opioid use disorder: the US national survey on drug use and health, 2015 to 2019. *American Journal of Public Health*. 2022;112(2):284e295.

Saitz R, Larson MJ, LaBelle C, Richardson J, Samet JH. The case for chronic disease management for addiction. *Journal of Addiction Medicine*. 2008;2(2):55-65.

Saucier R, Wolfe D, Dasgupta N. Review of Case Narratives from Fatal Overdoses Associated with Injectable Naltrexone for Opioid Dependence. *Drug Safety.* 2018;41(10):981-988.

Schuckit, MA. Treatment of opioid-use disorders. *New England Journal of Medicine*. 2016;375:357-368.

Sharma A, Kelly SM, Mitchell SG, Gryczynski J, O'Grady KE, Schwartz RP. Update on barriers to pharmacotherapy for opioid use disorders. *Current Psychiatry Reports.* 2017;19(35).

Shirk SD, Ameral V, Kraus SW, et al. Buprenorphine Naloxone and Extended Release Injectable Naltrexone for the Treatment of Opioid Use Disorder Among a Veteran Patient Sample: A Retrospective Chart Review. *Journal of Dual Diagnosis*. 2021;17(3):207-215.

Society for Adolescent Health and Medicine (SAHM). Medication for adolescents and young adults with opioid use disorder. *Journal of Adolescent Health*. 2021;68:632-636.

Sordo L, Barrio G, Bravo MJ, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *Bmj*. 2017;357:j1550.

Sublocade. What is the sublocade REMS (risk evaluation and mitigation strategy)? 2022. Available at: Sublocade REMS - Homehttps://www.sublocaderems.com/#Main. Accessed March 30, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). Medication for the Treatment of Alcohol Use Disorder: A Brief Guide. HHS Publication No. (SMA) 15-4907. Rockville, MD. 2015. Available at: Medication for the Treatment of Alcohol Use Disorder: A Brief Guide (samhsa.gov)https://store.samhsa.gov/sites/default/files/d7/priv/sma15-4907.pdf. Accessed March 26, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). Treatments for Substance Use Disorders. Last updated August 9, 2016. Available at: https://www.samhsa.gov/treatment/substance-use-disorders. Accessed April 6, 2018.

Substance Abuse and Mental Health Services Administration (SAMHSA). Treatments for Substance Use Disorders. 2018. Available at: https://www.samhsa.gov/treatment/substance-use-disorders. . Accessed April 6, 2018.

Substance Abuse and Mental Health Services Administration (SAHMSA). Behavioral Health Barometer: California, Volume 6: Indicators as measured through the 2019 National Survey on Drug Use and Health and the National Survey of Substance Abuse Treatment Services. HHS Publication No. SMA–20–Baro–19–CA. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2020. Available at:

https://www.samhsa.gov/data/sites/default/files/reports/rpt32821/California-BH-Barometer_Volume6.pdf. Accessed March 7, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). Medications for opioid use disorder: for healthcare and addiction professionals, policymakers, patients, and families. . Treatment Improvement Protocol TIP 63. 2021a. Available at: https://store.samhsa.gov/sites/default/files/pep21-02-01-002.pdf. Accessed March 24, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). Center for Behavioral Health Statistics and Quality. Racial/ethnic differences in substance use, substance use disorders, and substance use treatment utilization among people aged 12 or older (2015-2019). 2021b. Available at: https://www.samhsa.gov/data/sites/default/files/reports/rpt35326/2021NSDUHSUChartbook.pdf. Accessed March 20, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). Key substance use and mental health indicators in the United States: results from the 2021 National Survey on Drug Use and Health (NSDUH). 2022a. Available at: https://www.samhsa.gov/data/sites/default/files/reports/rpt39443/2021NSDUHFFRRev010323.pdf . Accessed March 28, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). 2020 National Survey on Drug Use and Health: Lesbian, Gay, or Bisexual (LGB) Adults. 2022b. Available at: https://www.samhsa.gov/data/sites/default/files/reports/rpt37929/2020NSDUHLGBSlides072522.pdf. Accessed April 5, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). 2020 NSDUH detailed tables. 2022c. Available at: https://www.samhsa.gov/data/report/2020-nsduh-detailed-tables. Accessed March 30, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). The national survey on drug use and health: 2020. 2022d. Available at: Slides for the 2020 National Survey on Drug Use and Health (samhsa.gov)https://www.samhsa.gov/data/sites/default/files/reports/slides-2020-nsduh/2020NSDUHNationalSlides072522.pdf. Accessed March 30, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). National survey on drug use health (NSDUH) 2021 state estimates of substance use and mental disorders. 2023a. Available at: 2021 NSDUH: Model-Based Estimated Prevalence for States | CBHSQ Data (samhsa.gov)https://www.samhsa.gov/data/report/2021-nsduh-state-prevalence-estimates. Accessed March 15, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). Removal of DATA waiver (x-waiver) requirement. 2023b. Available at: Removal of DATA Waiver (X-Waiver) Requirement | SAMHSAhttps://www.samhsa.gov/medications-substance-use-disorders/removal-data-waiver-requirement. Accessed March 26, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). What is methadone? 2023c. Available at: What is Methadone? | SAMHSAhttps://www.samhsa.gov/medications-substance-use-disorders/medications-counseling-related-conditions/methadone. Accessed March 21, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). Opioid Treatment Program Directory. 2023d. Available at: OTP Directory (samhsa.gov)https://dpt2.samhsa.gov/treatment/. Accessed March 26, 2023.

Substance Abuse and Mental Health Services Administration (SAMHSA). Medications, counseling, and related conditions. 2023e. Available at: Medications, Counseling, and Related Conditions | SAMHSAhttps://www.samhsa.gov/medications-substance-use-disorders/medications-counseling-related-conditions. Accessed March 25, 2023.

Sudhinaraset M, Wigglesworth C, Takeuchi DT. Social and Cultural Contexts of Alcohol Use: Influences in a Social-Ecological Framework. *Alcohol Research*. 2016;38(1):35-45.

Sullivan MA, Bisaga A, Pavlicova M, et al. A Randomized Trial Comparing Extended-Release Injectable Suspension and Oral Naltrexone, Both Combined With Behavioral Therapy, for the Treatment of Opioid Use Disorder. *American Journal of Psychiatry*. 2019;176(2):129-137.

Tanum L, Solli KK, Latif ZE, et al. Effectiveness of Injectable Extended-Release Naltrexone vs Daily Buprenorphine-Naloxone for Opioid Dependence: A Randomized Clinical Noninferiority Trial. *JAMA Psychiatry*. 2017a;74(12):1197-1205.

Thomas CP, Fullerton CA, Kim M, et al. Medication-assisted treatment with buprenorphine: assessing the evidence. *Psychiatric Services.* 2014;65(2):158-170.

Timko C, Schultz NR, Cucciare MA, Vittorio L, Garrison-Diehn C. Retention in medication-assisted treatment for opiate dependence: A systematic review. *Journal of Addictive Diseases*. 2016;35(1):22-35.

Tsui JI, Evans JL, Lum PJ, Hahn JA, Page K. Association of opioid agonist therapy with lower incidence of hepatitis C virus infection in young adult injection drug users. *JAMA Internal Medicine*. 2014;174(12):1974-1981.

U.S. Department of Health and Human Services (HHS), Office of the Surgeon General. Facing Addiction in America: The Surgeon General's Spotlight on Opioids. Washington, DC: HHS, September 2018. https://addiction.surgeongeneral.gov/sites/default/files/OC_SpotlightOnOpioids.pdf Accessed January 8, 2019.

U.S. Department of Health and Human Services Department (HHS). Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder. May 2021. Available at: https://www.federalregister.gov/documents/2021/04/28/2021-08961/practice-guidelines-for-the-administration-of-buprenorphine-for-treating-opioid-use-disorder. Accessed March 2023.

U.S. Department of Justice (DOJ) Civil Rights Division. The ADA and opioid use disorder: combating discrimination against people in treatment or recovery. 2022. Available at: https://www.ada.gov/resources/opioid-use-disorder/. Accessed April 5, 2023.

U.S. Food & Drug Administration (FDA). Information about medication-assisted treatment (MAT).2019. Available at: https://www.fda.gov/drugs/information-drug-class/information-about-medication-assisted-treatment-mat. Accessed March 6th, 2023.

University of California San Francisco (UCSF). The adopt project. 2023. Available at: https://opioidpreventionandtreatment.ucsf.edu/. Accessed March 25, 2023.

Verissimo ADO, Grella CE. Influence of Gender and Race/Ethnicity on Perceived Barriers to Help-Seeking for Alcohol or Drug Problems. *Journal of Substance Abuse Treatment*. 2017;75:54-61.

Vivitrol. Important Safety Information about VIVITROL® (naltrexone for extended-release injectable suspension). 2021. Available at: For Healthcare Professionals | Important Safety Information about VIVITROL® (naltrexone for extended-release injectable suspension)

(vivitrolhcp.com)https://www.vivitrolhcp.com/important-safety-information. Accessed March 26, 2023.

Vo HT, Robbins E, Westwood M, Lezama D, Fishman M. Relapse prevention medications in community treatment for young adults with opioid addiction. *Substance Abuse*. 2016;37(3):392–397.

Ward BW, Dahlhamer JM, Galinsky AM, Joestl SS. Division of Health Interview Statistics. Sexual Orientation and Health Among U.S. Adults: National Health Interview Survey, 2013. 2014. Available at: https://www.cdc.gov/nchs/data/nhsr/nhsr077.pdf. Accessed February 2019.

Williams EC, Achtmeyer CE, Young JP, Berger D, Litt M, Curran G, Bradley KA, Richards J, Siegel MB, Ludman EJ, Lapham GT, Forehand M, Harris AHS. Barriers to and facilitators of alcohol use disorder in pharmacotherapy in primary care: a qualitative study in five VA clinics. *Journal of General Internal Medicine*. 2018;33(3):258-267.

Wolla SA, Sullivan J. Education, Income, and Wealth. Economic Research. Federal Reserve Bank of St. Louis. January 2017. Available at: https://research.stlouisfed.org/publications/page1-econ/2017/01/03/education-income-and-wealth. Accessed September 21, 2020.

Wu L, Zhu H, Swartz MS. Treatment utilization among persons with opioid use disorder in the United States. *Drug and Alcohol Dependence*. 2016;16:117–27. https://doi.org/10.1016/j.drugalcdep.2016.10.015

Wyatt R, Laderman M, Botwinick L, Mate K, Whittington J. Achieving Health Equity: A Guide for Health Care Organizations. IHI White Paper. Cambridge, MA: Institute for Healthcare Improvement; 2016.

Zhu Y, Evans EA, Mooney LJ, Saxon AJ, Kelleghan A, Yoo C, Hser Y. Correlates of long-term opioid abstinence after randomization to methadone versus buprenorphine/naloxone in a multi-site trial. *Journal of Neuroimmune Pharmacology*. 2018;13:488-497.

Zangiabadian M, Golmohammadi S, Nejadghaderi SA, Zahmatkesh MM, Nasiri MJ, Sadeghian M. The effects of naltrexone on retention in treatment and being opioid-free in opioid-dependent people: A systematic review and meta-analysis. *Front Psychiatry.* 2022;13:1003257.

Zedler BK, Mann AL, Kim MM, et al. Buprenorphine compared with methadone to treat pregnant women with opioid use disorder: a systematic review and meta-analysis of safety in the mother, fetus and child. *Addiction.* Dec 2016;111(12):2115-2128.

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A group of faculty, researchers, and staff complete the analysis that informs California Health Benefits Review Program (CHBRP) reports. The CHBRP **Faculty Task Force** comprises rotating senior faculty from University of California (UC) campuses. In addition to these representatives, there are other ongoing researchers and analysts who are **Task Force Contributors** to CHBRP from UC that conduct much of the analysis. The **CHBRP staff** coordinates the efforts of the Faculty Task Force, works with Task Force members in preparing parts of the analysis, and manages all external communications, including those with the California Legislature. As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, **Milliman**, to assist in assessing the financial impact of each legislative proposal mandating or repealing a health insurance benefit.

The **National Advisory Council** provides expert reviews of draft analyses and offers general guidance on the program to CHBRP staff and the Faculty Task Force. CHBRP is grateful for the valuable assistance of its National Advisory Council. CHBRP assumes full responsibility for the report and the accuracy of its contents.

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CHBRP assumes full responsibility for the report and the accuracy of its contents. All CHBRP bill analyses and other publications are available at www.chbrp.org.

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