

California Health Benefits Review Program

Analysis of California Senate Bill 854 Health Care Coverage: Substance Use Disorders

A Report to the 2019–2020 California State Legislature

March 15, 2020



Key Findings

Analysis of California Senate Bill 854 Health Care Coverage: Substance Use Disorders

Summary to the 2019–2020 California State Legislature, March 15, 2020



AT A GLANCE

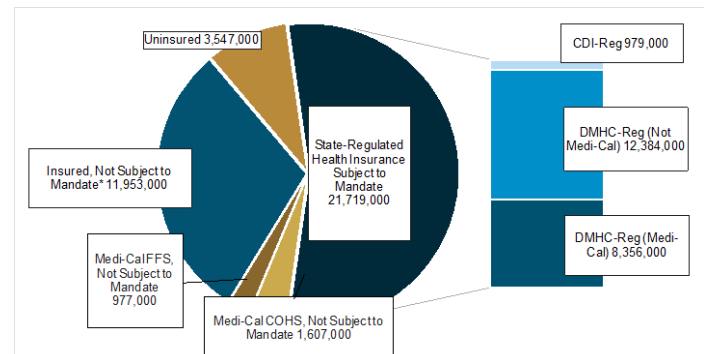
For commercial/CalPERS enrollees with coverage for outpatient prescription medications, Senate Bill (SB) 854 would require on-formulary, low-tier coverage of Food and Drug Administration (FDA) approved substance use disorder (SUD) medications and would prohibit some utilization management. It would also prohibit requiring prior authorization for coverage of counseling, the behavioral health treatment used “in conjunction” with those medications. In 2020, 62% of the 21.7 million Californians enrolled in state-regulated health insurance would have health insurance required to comply with SB 854.

1. **Benefit coverage.** Approximately 94% of commercial/CalPERS enrollees would see some change to their benefit coverage – primarily movement of some FDA approved SUD medications to a lower formulary tier.
2. **Utilization.** Commercial/CalPERS enrollee utilization would increase for many of these medications. There would be a shift between formulations of an opioid overdose reversal medication (naloxone) to greater use of the more costly auto-injector, as well as a shift from a medication used off-label for withdrawal symptoms (clonidine) to the more costly brand-name alternative (lofexidine). Increases in some related services (counseling) and decrease in others (inpatient days) would also occur.
3. **Expenditures.** Premium increases (less than 0.1%) and a decrease (less than 0.1%) in total enrollee out-of-pocket expenses for covered benefits (cost sharing) would occur.
4. **Medical effectiveness.** When successfully used as prescribed and directed, clear and convincing evidence indicates that many (but not all) FDA-approved SUD medications are effective. The effectiveness of in conjunction counseling is varies by SUD and is sometimes ineffective.
5. **Public health.** Barriers to treatment, limited patient willingness, and relapses will be limiting factors, but desirable health outcomes are expected for patients who successfully engage in treatment.

BILL SUMMARY

Senate Bill (SB) 854 would be applicable to plans and policies regulated by the California Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI). SB 854 would exempt from compliance DMHC-regulated plans enrolling Medi-Cal beneficiaries. Figure A notes the variation in health insurance among Californians. SB 854 would require plans and policies that include a pharmacy benefit to place all medications approved by the federal Food and Drug Administration (FDA) and indicated for treatment of substance use disorders (SUDs) on the formulary’s lowest tier. SB 854 would also prohibit application of step therapy (“fail first”), prior authorization, and some other utilization management protocols for the coverage of these FDA-approved SUD medications. In addition, SB 854 would prohibit application of prior authorization protocols to the coverage of behavioral health services that are “in conjunction” with the FDA-approved SUD medications.

Figure A. Health Insurance in CA



Source: CHBRP 2020.

Notes: *Medicare beneficiaries, enrollees in self-insured products, etc.

In order to analyze the impacts of SB 854, CHBRP has made several analytic assumptions, including that benefit coverage requirements: (1) would be applicable to both prescription medications generally covered through a pharmacy benefit and to medications requiring a clinician for administration, but not would not be applicable to over-the-counter medications; (2) would be applicable to covered brand-name as well as generic medications; and (3) would be applicable to all covered formulations of the medications. CHBRP has also assumed that three forms of outpatient counseling (individual, family, and group) are the “in conjunction”

with FDA-approved SUD medications” behavioral therapy for which coverage would be impacted by SB 854. Although use of other forms of behavioral health concurrent with use of FDA-approved SUD medications is not uncommon, other forms are not commonly used specifically to support compliant use of the outpatient medication – and so CHBRP has assumed that coverage for other forms not be affected by SB 584.

Should SB 854 affect the coverage of other forms of behavioral health, such as the more structured and facility based partial hospitalization or intensive outpatient therapy, the various forms of residential treatment, or detox admissions, impacts would be orders of magnitude greater that projected in this report.

CONTEXT¹

There are 11 prescription-only FDA-approved SUD medications, with one pair available in a combination format (buprenorphine-naloxone) and several available in more than one formulation (injected/pill, nasal spray/inhaler, etc.). The SUDs are opioid use disorder, alcohol use disorder, and tobacco use disorder.

However, treatments for SUDs are not limited to medications, and frequently also include residential, inpatient, and outpatient care using behavioral health counseling and/or medication, as well as mutual help groups (e.g., Alcoholics Anonymous).

Structural and attitudinal barriers to accessing any treatment for opioid use disorder, alcohol use disorder, and tobacco use disorder affect use. Structural barriers include being uninsured, utilization management protocols when insurance is present, limited provider supply, and geographic access difficulties. Attitudinal barriers include limited patient receptiveness to treatment. For many with these disorders, attitudinal barriers are the most significant barrier to treatment initiation and persistence. The stigma of addiction and the ability to acknowledge an addiction affects patient desire to seek care. Many people with opioid use disorder and/or alcohol use disorder believe they can solve the problem themselves. Similarly, limited patient readiness for treatment is also a barrier for those with tobacco use disorder: a quarter of California smokers are not interested in quitting.

Currently, CHBRP estimates that only 13.0% of commercial/CalPERS enrollees with opioid use disorder take FDA-approved SUD medications. This underuse is not necessarily related to insurance coverage for

treatment and is more likely due to other factors, such as limited willingness to enter treatment.

Similarly, only 5.0% of commercial/CalPERS enrollees with alcohol use disorder and only 5.4% of those with tobacco use disorder use take prescription-only FDA-approved SUD medications. This underuse is linked to provider practice (limited prescribing), limited willingness to enter treatment, and other treatment options that do not rely on prescription medications (e.g., over-the-counter nicotine replacement therapy, Alcoholics Anonymous).

It should be noted, as well, that even when a patient is willing, treatment adherence is difficult. Relapse rates for patients in treatment for alcohol use disorder and opioid use disorder are significant and multiple quit attempts before successful cessation is common for tobacco use disorder.

IMPACTS

Medical Effectiveness

This analysis focuses on the effectiveness the of FDA-approved SUD medications, with or without behavioral health counseling, as treatments for opioid use disorder, alcohol use disorder, or tobacco use disorder.

Effectiveness is considered through studies of outcomes and studied outcomes vary depending on the SUD. Opioid use disorder outcomes include opioid use, participation in treatment, and mortality. Alcohol use disorder outcomes include alcohol use and participation in treatment. Tobacco use disorder outcomes include reduced cigarette cravings and abstinence.

The evidence is related to use of the medications when prescribed and used as directed. As indicated in the prior discussion of structural and attitudinal barriers to treatment, as well as limited patient willingness to enter treatment and the frequency of relapse and the need for repeated tries among patients who do, many patients have difficulty “using as directed” for the recommended period.

For prescription-only medications approved by the FDA for opioid use disorder:

- There is *clear and convincing* evidence that methadone, buprenorphine, and buprenorphine-naloxone are effective.

¹ Refer to CHBRP’s full report for full citations and references.

- There is *limited* evidence that injectable naltrexone is effective.
- There is a *preponderance* of evidence that orally administered naltrexone is not effective.
- Evidence comparing medications is *limited* or *inconclusive*.
- Evidence comparing medications with medications and counseling is *inconclusive*.
- There is *insufficient* evidence to compare lofexidine (brand-name only) and off-label use of clonidine (generic available).
- Evidence comparing the auto-injector formulation of naloxone with other formulations is *inconclusive*.

For prescription-only medications approved by the FDA for alcohol use disorder:

- There is *clear and convincing* evidence that acamprosate and naltrexone are effective.
- There is limited evidence that disulfiram is not effective.
- Evidence comparing medications is *inconclusive*.
- There is *limited* evidence that medications and counseling is no more effective than medications alone.

For prescription-only medications approved by the FDA for tobacco use disorder:

- There is *clear and convincing* evidence that prescription medications are effective.
- There is a *preponderance* of evidence favoring varenicline over nicotine replacement therapy (NRT).
- There is a *preponderance* of evidence that there is no different between NRT and bupropion.
- There is *limited* evidence that medications with counseling are more effective than medications alone.

Benefit Coverage, Utilization, and Cost

For this analysis, CHBRP has estimated the impacts of requiring tier 1 formulary coverage for the 11 FDA-approved SUD medications, and prohibiting the application of prior authorization, step therapy (“fail first”), and other utilization management protocols. CHBRP also considered the impact of prohibiting prior authorization for the coverage of in conjunction behavioral counseling.

Benefit Coverage

Approximately 94% of commercial/CalPERS enrollees in plans and policies regulated by DMHC or CDI have a pharmacy benefit that would need some alteration to be compliant with SB 854 - primarily a shift to a lower formulary tier for some FDA-approved SUD medications.

Most commercial/CalPERS enrollees have on-formulary coverage for most of the FDA-approved SUD medications; all would, postmandate. Few of these enrollees have tier 1 (or no) cost sharing for most brand-name versions of these medications; all would, postmandate. Few of these enrollees have prior authorization or step therapy protocols applicable to their coverage for these medications; none would, postmandate.

SB 854’s prohibitions regarding limited numbers of visits, days, scope, or duration - on coverage for outpatient medications - seem unlikely to have any measurable impact.

All commercial/CalPERS enrollees currently have coverage for behavioral counseling in conjunction with prescribed medication for opioid use disorder, alcohol use disorder, or tobacco use disorder that is not subject to prior authorization protocols. Therefore, 100% of enrollees currently have benefit coverage that meets the behavioral counseling portion of the SB 854 mandate.

Utilization

Use of most FDA-approved SUD medication and in conjunction behavioral health counseling is expected to increase, as is the expected number of users. The broad indirect impacts SB 854 would have are decreased inpatient days and emergency room use.

Generally, more users of the FDA-approved SUD medications among commercial CalPERS enrollees would be expected and use would increase by 10% (from the current users premandate rate). The exceptions and notes regarding shifts follow:

- The increased use of the brand-name formulation of lofexidine (used to manage opiate withdrawal symptoms) would accompany a decreased use of off-label generic clonidine.
- Within the increased use of naloxone for opioid use disorder (used to treat overdoses) there would be shift such that the more costly auto-injector formulation would represent half of all filled prescriptions.
- No utilization increase is expected for methadone for opioid use disorder because it is only delivered through federally certified centers.²
- No utilization increase is expected for disulfiram for alcohol use disorder, as providers have concerns regarding its lack of effectiveness.
- No utilization increase is expected for the nasal spray formulation of nicotine replacement therapy for tobacco use disorder, as it is not well-accepted by patients.

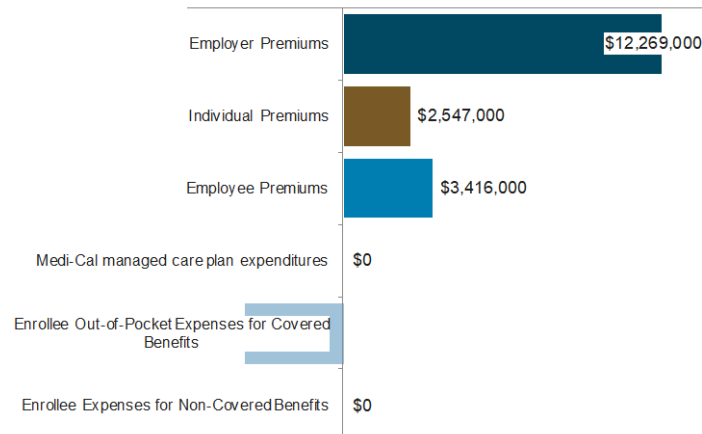
An increase in use in conjunction counseling would be expected among commercial/CalPERS enrollees using FDA-approved SUD medications.

Decreases in some related treatments and services would occur for some new (but not continuing) users of these medications. For new users of medications for opioid use disorder and alcohol use disorder, reductions in inpatient days, detox days, and emergency department visits would be expected.

Expenditures

The premium impacts noted in Figure B, represent an increases of less than 0.1% for all market segments and less than a 0.1% decrease in enrollee out-of-pocket expenses (cost sharing) for covered benefits.

Figure B. Expenditure Impacts of SB 854



Source: CHBRP, 2020.

Cost sharing impacts vary by market segment. Among commercial/CalPERS enrollees with on-formulary benefit coverage at baseline, the number of enrollees who will be impacted ranges from a low of 0.190% for CalPERS HMO to a high of 0.206% for small group DMHC-plans or CDI-regulated policies. For these enrollees, average annual out-of-pocket expenses are expected to decrease by a range of \$118.15 to \$128.75. Among commercial/CalPERS enrollees who gained on-formulary benefit coverage, the percent of enrollees who would be affected ranges from 0.035% for CalPERS HMO to 0.089% for individual plans. These enrollees are projected to have an increase in annual out-of-pocket expenses for medications, with or without behavioral counseling, by a range of \$108.14 to \$115.43. It should be noted that the per-user annual impact in the form of cost sharing savings (for commercial/CalPERS enrollees currently covered, whose medications will be mandated to be covered with Tier-1 cost sharing) and new spending (for enrollees with new access to these medications).

CalPERS

CalPERS premiums would be expected to increase less than 0.1%.

Number of Uninsured in California

No measureable impact is expected.

² Federal law restricts methadone treatment to federally certified opioid treatment programs (OTP), known as

methadone clinics, see Title 42 of the Code of Federal Regulations Part 8 (42 CFR § 8)

Public Health

In the first postmandate year, CHBRP estimates the following public health impacts:

Approximately 5,253 commercial/CalPERS enrollees with opioid use disorder and newly compliant benefit coverage would take FDA-approved substance use disorder medications, though 40% to 60% of them may experience relapse. Successful use of these medications would mean reducing illicit opioid use, opioid overdose and associated mortality, transmission of hepatitis C and HIV, and poor maternal-infant outcomes. Among those new users, SB 854 would also increase maintenance treatment retention and increase overdose reversals (through the use of naloxone).

Approximately 2,995 commercial/CalPERS enrollees with alcohol use disorder and newly compliant benefit coverage would take FDA-approved SUD medications, though 50% or more may experience relapse. Health outcomes of successful treatment would include reducing alcohol consumption and decreases in undesirable outcomes such as injuries/accidents and poor pregnancy outcomes.

Approximately 2,871 commercial/CalPERS enrollees with newly compliant benefit coverage would take FDA-approved tobacco use disorder medications, though some of them will relapse. Health outcomes of successful treatment would include increasing quit rates and sustaining abstinence, as well as decreases in undesirable outcomes, such as poor birth outcomes and smoking-exacerbated conditions (e.g., asthma and heart attacks).

Long-Term Impacts

Long-term utilization of FDA-approved medications for opioid use disorder could increase as opioid use disorder prevalence increases in the state. CHBRP estimates that the level of use per user per year predicted in 2021 would not change over time, but utilization overall would increase with additional use of opioids. Due to continuing structural and attitudinal barriers, CHBRP expects the portion of persons with opioid use disorder in treatment to remain limited, even as the total number of these persons increases. In the case of alcohol use disorder and tobacco use disorder

treatment, there is very low baseline utilization of the FDA-approved medications for the two conditions. Because plans reported few restrictions to obtaining these medications, it appears physicians and patients are not using them frequently to treat alcohol use disorder or tobacco use disorder and therefore CHBRP does not expect long-term changes.

A key barrier to treatment for any substance use disorder is patient interest and readiness. CHBRP anticipates the demand for treatment would continue as relapsed patients attempt treatment again and first-time initiators join the pool of patients seeking care. SB 854 would continue to facilitate prescription medication treatment for some enrollees (whose insurance did not previously offer compliant benefit coverage), but limited patient readiness for substance use disorder treatment and the demand-supply mismatch for regarding treatment for opioid use disorder and alcohol use disorder are likely to remain significant barriers to care in future years.

However, although the quantitative long-term impact of SB 854 on premature death associated with SUDs is unknown, it stands to reason, based on the effectiveness of FDA-approved substance use disorder medications, that there would be a reduction in premature deaths for those enrollees who successfully engage in treatment.

Benefit Mandate Structure and Unequal Racial/Ethnic Health Impacts

SB 584 would increase utilization of effective medications for tobacco use disorder among commercial/CalPERS enrollees, but would not do so among Medi-Cal beneficiaries enrolled in DMHC-regulated plans. As people of color are over-represented among Medi-Cal beneficiaries, an increase in disparate health outcomes among racial/ethnic groups is likely, should SB 854 become law.

Essential Health Benefits and the Affordable Care Act

SB 854 would alter the terms and conditions of existing benefit coverage, but would not require coverage for a new benefit and so appears unlikely to exceed the definition of EHBs in California.

A Report to the California State Legislature

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Health Care Coverage: Substance Use Disorders

March 15, 2020

California Health Benefits Review Program
MC 3116; Berkeley, CA 94720-3116
www.chbrp.org

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

REVISION HISTORY

Date	Description of Revisions
May 5, 2020	In the body of the report (page 26), the discussion of harms potentially related to use of naltrexone for treatment of opioid use disorder has been refined for better clarity.
May 5, 2020	In the body of the report, the Table 7 entry for methadone was corrected to clarify “no expected impact” as it is only available as a treatment for opioid use disorder from federally licensed clinics.



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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Table 1. SB 854 Impacts on Benefit Coverage, Utilization, and Cost, 2021

	Baseline (2021)	Postmandate Year 1 (2021)	Increase/Decrease	Change Postmandate
Benefit Coverage				
Total enrollees with health insurance subject to state-level benefit mandates (a)	21,719,000	21,719,000	0	0.0%
Total enrollees with health insurance subject to SB 854	13,363,000	13,363,000	0	0.0%
Total enrollees with OPD coverage	12,531,000	12,531,000	0	0.0%
Number of enrollees with health insurance fully compliant with SB 854	832,000	13,363,000	12,531,000	1506.1%
Percentage of enrollees with health insurance fully compliant with SB 854	6.2%	100%	94%	1506.1%
Number of enrollees with health insurance partially compliant with SB 854	12,531,000	0	-12,531,000	-100.0%
Percentage of enrollees with health insurance partially compliant with SB 854	94%	0%	-94%	-100.0%
Utilization and Cost				
<i>Number of Enrollees</i>				
Enrollees with Alcohol Use Disorder using (f)				
AUD Medication Only	6,278	8,956	2,678	42.7%
AUD Medication + Behavioral Counseling	970	1,287	317	32.7%
Enrollees with Opioid Use Disorder using (f)				
ODU Medication Only	8,514	13,294	4,781	56.2%
ODU Medication + Behavioral Counseling	916	1,388	472	51.5%
Enrollees with Tobacco Use Disorder using				
TUD Medication Only	11,361	14,098	2,737	24.1%
TUD Medication + Individual Counseling	584	718	134	22.9%
<i>Average Total Annual Unit Costs Per User</i>				
per Enrollee with Alcohol Use Disorder using				
AUD Medication Only	\$859.03	\$1,279.62	\$420.59	49.0%
AUD Medication + Behavioral Counseling	\$1,808.61	\$1,808.61	\$0.00	0.0%
per Enrollee with Opioid Use Disorder using				
ODU Medication Only	\$3,471.03	\$4,056.65	\$585.62	16.9%
ODU Medication + Behavioral Counseling	\$2,149.25	\$2,149.25	\$0.00	0.0%
per Enrollee with Tobacco Use Disorder using				
TUD Medication Only	\$943.91	\$959.34	\$15.43	1.6%
TUD Medication + Individual Counseling	\$2,034.96	\$2,034.96	\$0.00	0.0%
<i>Average Annual Out-of-Pocket Cost Per User</i>				
Average Annual Out-of-Pocket Cost per Enrollee with Alcohol Use Disorder using				
AUD Medication Only	\$125.75	\$60.74	-\$65.00	-51.7%
AUD Medication + Behavioral Counseling	\$178.51	\$178.51	\$0.00	0.0%
Average Annual Out-of-Pocket Cost per Enrollee with Opioid Use Disorder using				
ODU Medication Only	\$462.78	\$123.82	-\$338.96	-73.2%
ODU Medication + Behavioral Counseling	\$242.96	\$242.96	\$0.00	0.0%
Average Annual Out-of-Pocket Cost per Enrollee with Tobacco Use Disorder using				
TUD Medication Only	\$54.76	\$54.56	-\$0.21	-0.4%
TUD Medication + Individual Counseling	\$220.63	\$220.63	\$0.00	0.0%
<i>Total Medical Offsets from Increased Utilization of Substance Use Disorder Treatments</i>				
Alcohol Use Disorder Inpatient Days	--	-\$840,000	--	--
Alcohol Use Disorder Detox Days	--	-\$124,000	--	--
Alcohol Use Disorder ED Visits	--	-\$37,000	--	--
Opioid Use Disorder Inpatient Days	--	-\$28,614,000	--	--
Opioid Use Disorder ED visits	--	-\$9,161,000	--	--
Expenditures				
<i>Premium (expenditures) by Payer</i>				
Private Employers for group insurance	\$54,037,059,000	\$54,048,770,000	\$11,711,000	0.0217%
CalPERS HMO employer expenditures (c)	\$3,264,098,000	\$3,264,656,000	\$558,000	0.0171%
Medi-Cal Managed Care Plan expenditures (d)	\$29,218,820,000	\$29,218,820,000	\$0	0.0000%
<i>Enrollee Premiums (expenditures)</i>				
Enrollees for individually purchased insurance	\$15,689,758,000	\$15,692,305,000	\$2,547,000	0.0162%
Individually Purchased – Outside Exchange	\$4,412,875,000	\$4,413,763,000	\$888,000	0.0201%

Individually Purchased – Covered California	\$11,276,883,000	\$11,278,542,000	\$1,659,000	0.0147%
Enrollees with group insurance, CalPERS HMOs, Covered California, and Medi-Cal Managed Care (a) (b)	\$15,867,227,000	\$15,870,643,000	\$3,416,000	0.0215%
Enrollee out-of-pocket expenses				
Enrollee out-of-pocket expenses for covered benefits (deductibles, copayments, etc.)	\$12,776,801,000	\$12,773,004,000	-\$3,797,000	-0.0297%
Enrollee expenses for noncovered benefits (e)	--	--	-	-
Total Expenditures	\$130,853,763,000	\$130,868,198,000	\$14,435,000	0.0110%

Source: California Health Benefits Review Program, 2020

Notes: (a) Enrollees in plans and policies regulated by DMHC or CDI aged 0 to 64 years as well as enrollees 65 years or older in employer-sponsored health insurance. This group includes commercial enrollees (including those associated with Covered California or CalPERS) and Medi-Cal beneficiaries enrolled in DMHC-regulated plans.³

(b) Approximately 57.4% of CalPERS enrollees in DMHC-regulated plans are state retirees, state employees, or their dependents. About one in five (20.5%) of these enrollees has a pharmacy benefit not subject to DMHC.⁴ CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).

(c) Enrollee premium expenditures include contributions by employees to employer-sponsored health insurance, health insurance purchased through Covered California, and contributions to Medi-Cal Managed Care.

(d) Includes only expenses paid directly by enrollees (or other sources) to providers for services related to the mandated benefit that are not currently covered by insurance. This only includes those expenses that would be newly covered postmandate. Other components of expenditures in this table include all health care services covered by insurance.

(e) Although enrollees with newly compliant benefit coverage may have paid for some prescription medications and behavioral services related to opioid use disorder, alcohol use disorder, or tobacco use disorder before SB 854, CHBRP cannot estimate the frequency with which such situations may have occurred and therefore cannot estimate the related expense. Postmandate, such expenses would be eliminated, though enrollees with newly compliant benefit coverage might, postmandate, pay for some [tests/treatments/services] for which coverage is denied (through utilization management review), as some enrollees who always had compliant benefit coverage may have done and may continue to do, postmandate.

(f) The number of persons taking FDA-approved SUD medications is greater than in CHBRP's report on an earlier bill (CHBRP, 2019) due to inclusion in this analysis of additional medications: naltrexone IM for AUD and OUD, which is generally not covered through a pharmacy benefit, and Lofexidine for OUD, which was not available when the prior report was released but.

Key: AUD = alcohol use disorder; CalPERS = California Public Employees' Retirement System; CDI = California Department of Insurance; DMHC = Department of Managed Health Care; HMO = Health Maintenance Organizations; OPD = outpatient department; OUD = opioid use disorder; SUD = substance use disorder; TUD = tobacco use disorder

³ For more detail, see *Estimates of Sources of Health Insurance in California for 2021*, available at http://chbrp.org/other_publications/index.php.

⁴ For more detail, see *Estimates of Pharmacy Benefit Coverage in California for 2021*, available at http://chbrp.org/other_publications/index.php.

POLICY CONTEXT

The California Senate Committee on Health has requested that the California Health Benefits Review Program (CHBRP)⁵ conduct an evidence-based assessment of the medical, financial, and public health impacts of Senate Bill (SB) 854, Substance Use Disorder.

Bill-Specific Analysis of SB 854, Substance Use Disorder

SB 854 includes a benefit mandate relevant to plans and policies that provide prescription drug benefits related to substance use disorder (SUD) treatment.

SB 854 would require lowest tier formulary placement of all medications approved by the federal Food and Drug Administration (FDA) for treatment of SUDs.

SB 854 would prohibit application of prior authorization protocols to the coverage of FDA-approved SUD medications or to the coverage of their “in conjunction” behavioral health services.

SB 854 would also prohibit application to the coverage of FDA-approved SUD medications the following:

- Limits on the number of visits, days of coverage, scope, or duration of treatment, or other similar limitations;
- Requirements related to an enrollee’s prior success or failure with substance use disorder treatment; and
- Step therapy (or “fail first”) protocols.

In addition, SB 854 would prohibit coverage denials related to court orders for treatment.

The full text of SB 854 can be found in Appendix A.

Further descriptions of the utilization management protocols SB 854 would prohibit (prior authorization and step therapy) are included in the *Background on Substance Use Disorders* section of this report.

Relevant Populations

If enacted, SB 854 would affect the health insurance of approximately 13.4 million enrollees (34% of all Californians). This represents 62% of the 21.7 million Californians who will have health insurance regulated by the state that may be subject to any state health benefit mandate law — health insurance regulated by the California Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI). If enacted, the law would affect the health insurance of commercial/CalPERS enrollees in DMHC-regulated plans and CDI-regulated policies, exempting the health insurance of Medi-Cal beneficiaries enrolled in DMHC-regulated plans.

Analytic Approach

CHBRP has focused this analysis on FDA-approved SUD medications, which are currently available for three SUDs:

- Opioid use disorder
- Alcohol use disorder

⁵ CHBRP’s authorizing statute is available at www.chbrp.org/faqs.php.

- Tobacco use disorder

As there are currently no FDA-approved medications for the treatments of other SUDs (such as disorders related to use of amphetamines or cocaine), those SUDs are not included in this analysis.

CHBRP has considered SB 854’s potential impacts on the coverage of prescription-only medications that the FDA has approved as treatments for SUD — as well as the use of “in conjunction” behavioral health services. These medications are listed in Table 2. The list does not include medications that may be used off-label (without approval by the FDA for the treatment of SUDs) and the list does not include medications available over the counter (without a prescription). The list include medications used to for any of these purposes: to manage withdrawal symptoms, to reverse overdoses, or to maintain abstinence.

Table 2. Medications Related to SB 854 Coverage Requirements

Substance Use Disorder (SUD)	Prescription-only medication approved to treat SUD
Opioid Use Disorder (OUD)	<i>Buprenorphine</i>
	<i>Methadone</i>
	<i>Naloxone</i>
	<i>Naltrexone (a)(b)</i>
	<i>Combination buprenorphine/naloxone</i>
	<i>Lofexidine (b)</i>
Tobacco Use Disorder (TUD)	<i>Nicotine replacement therapy — inhaler (c)</i>
	<i>Nicotine replacement therapy — nasal spray (c)</i>
	<i>Varenicline (b)</i>
	<i>Bupropion HCL SR</i>
Alcohol Use Disorder (AUD)	<i>Acamprosate</i>
	<i>Naltrexone</i>
	Disulfiram

Source: California Health Benefits Review Program, 2020

Notes: (a) Naltrexone is used to treat both OUD and AUD. (b) Not available as a generic. (c) Nicotine replacement therapy is also available in non-prescription, over-the-counter formulations, including patch, gum, and lozenge.

Key: AUD = alcohol use disorder; OUD = opioid use disorder; SUD = substance use disorder; TUD = tobacco use disorder

Key Assumptions

In order to complete this analysis of SB 854, CHBRP has made a number of analytic assumptions.

Medication Coverage

As SB 854 specifies “on formulary” and “lowest tier,” terms related to pharmacy benefit coverage of outpatient services, CHBRP has assumed the bill would apply to the coverage of prescription-only outpatient FDA-approved SUD medications and would not apply to the coverage of medications available over the counter (OTC) without a prescription.⁶

As SB 854 is silent regarding generic status, CHBRP has assumed that if both generic and brand-name versions are covered, all coverage would have to be as specified by SB 854. CHBRP has assumed that SB 854 would not require coverage of the brand-name drug when a generic is available.

As SB 854 is silent regarding formulation (pill, injectable, patch, etc.), CHBRP has assumed that if multiple formulations are covered, all coverage would have to be as specified by SB 854. CHBRP has assumed that SB 854 would not require coverage all formulations.

As SB 854 does not exempt from compliance coverage for methadone. However, although methadone is commonly on formulary as a treatment for pain, methadone as a treatment for opioid use disorder can only be prescribed by and delivered through federally certified Opioid Treatment Programs (OTPs), which are commonly referred to as “methadone clinics.”⁷ As SB 854 does not require network expansion, CHBRP has assumed that the bill would have no effect on methadone as a treatment for opioid use disorder.

Medication Cost Sharing

As SB 854 specifies “lowest tier,” CHBRP has assumed that SB 854 would allow cost sharing for FDA-approved SUD medications. For this analysis, CHBRP has assumed SB 854 would require relevant medications not already on “tier 0” (no cost sharing) or not already on “tier 1” (standard only for generics) regardless of generic/brand-name status to become “tier 1.” “Tier 0,” which indicates “no cost sharing,” is generally restricted to a situation in which the ACA’s preventive services mandate prohibits all cost sharing.

For FDA-approved SUD outpatient medications that are administered during an office visit (and so generally covered under a medical benefit instead of a pharmacy benefit), CHBRP has assumed that cost sharing would become similar to what it would be as a “formulary tier 1” pharmacy benefit.

Behavioral Health Services Coverage

As is the case for many chronic diseases, treatment for SUDs can be lengthy (years) and can involve many forms of many treatments in a sequential or concurrent manner. By citing the FDA, SB 854 is relatively clear as to which medications are relevant. The bill is less clear as to which behavioral health treatments would be “in conjunction with” those medications.

As SB 854 references American Society of Addiction Medicine (ASAM). Based on the ASAM guide⁸ and content expert experience, this analysis assumes impact of SB 854 would be on three forms of outpatient counseling (individual, family, and group) as the forms of behavioral health that are “in conjunction with FDA-approved SUD medications.” Although use of other forms of behavioral health concurrent with use of FDA-approved SUD medications is not uncommon, other forms are not commonly used specifically to

⁶ Some formulations of nicotine replacement therapy (patch, lozenge, gum) are available over-the-counter (without a prescription). Others (nasal spray, inhaler) are prescription-only.

⁷ Federal law restricts methadone treatment to federally certified opioid treatment programs (OTP), known as methadone clinics, see Title 42 of the Code of Federal Regulations Part 8 (42 CFR § 8).

⁸ Page 38 of ASAM National Practice Guidelines linked here: <https://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-supplement.pdf?sfvrsn=24>

support compliant use of the outpatient medication – and so CHBRP has assumed that coverage for other forms not be affected by SB 584.

Should SB 854 affect the coverage of other forms of behavioral health, such as the more structured and facility based partial hospitalization or intensive outpatient therapy, the various forms of residential treatment, or detox admissions, impacts would be orders of magnitude greater than projected in this report.

Denials and Prior Success or Failure

As CHBRP has located no evidence of coverage related to treatment of SUDs being denied on the basis of prior success or failure with an SUD treatment, CHBRP has assumed that the related prohibition included in SB 854 would have no measurable impact in the first year after implementation.

Denials Related to Court Orders

As CHBRP has located no evidence of coverage related to treatment of SUDs being denied in connection with a court order, CHBRP has assumed that the related prohibition included in SB 854 would have no measurable impact in the first year after implementation.

Interaction with Existing Requirements

Although a number of federal laws and regulations restrict providers in regards to the medications specified by SB 854 (see the *Background on Substance Use Disorders* section of this report), CHBRP is aware of few state or federal benefit coverage laws or regulations that would directly interact with compliance to the outpatient SUD prescription medication and related behavioral health coverage requirements addressed in SB 854.

California Policy Landscape

California law and regulations

CHBRP is also aware of bills that are or have been considered by the California Legislature that broadly or indirectly relate to SB 584, including:

- SB 855 (Wiener – 2020): Would alter California’s mental health parity coverage law to require coverage for medically necessary treatment for SUDs. Prior years bills — including AB 154 (Beall – 2011), AB 1600 (Beall – 2010), AB 244 (Beall 2009), AB 1887 (Beall – 2008), AB 423 (Beall – 2007), and SB 572 (Perata – 2005) — have also proposed to amend the parity law so that most behavioral health conditions would be covered instead of the “severe mental illnesses” currently covered.
- SB 374 (Newman – 2017): Would have required large-group, individual, and small-group health insurance policies to provide all covered mental health and substance use disorder benefits in compliance with those provisions of federal law governing mental health parity.
- SB 1192 (Chesbro – 2004): Would have required health plans to provide coverage for medically necessary treatment of SUDs.

CHBRP is unaware of California laws or regulations that directly address cost sharing and utilization management protocols related to coverage of the outpatient medications for SUD.

However, CHBRP is aware of bills that are or have been considered by the California Legislature that include some aspect of SB 854, including:

- SB 11 (Beall – 2019): Would require a health care service plan or insurer that provides prescription medication benefits to include FDA-approved SUD medications on the formulary's lowest tier and would prohibit use of prior authorization and step-therapy utilization management protocols.
- ACR 98 (Wicks – 2019): This resolution lays out mental health/SUD statistics, Milliman statistics, and Wit v United Behavioral Health decision. It calls for DMHC, CDI, the Department of Health Care Services (DCHS), and California Attorney General to use full powers of their office to ensure parity compliance. Also calls on all coverage to be consistent with generally accepted standards of care.
- AB 2384 (Arambula – 2018): Would have mandated coverage for at least one MAT, relapse prevention and overdose reversal prescription drug for opioid use disorder; and prohibits health plans and insurers from using prior authorization, fail first, or step therapy and other utilization management requirements for at least one version of each MAT, relapse prevention and overdose reversal prescription drug.

Similar requirements in other states

CHBRP is aware of a number of bills signed into law in other states that address coverage of outpatient FDA-approved SUD medications, related behavioral health services, or MAT (which involves both):

- Iowa HF 623 (2019): Requires that the state Medicaid fee-for-service and managed care programs offer at least one form of MAT without prior authorization.
- Arkansas HB 1656 (2019): Prohibits insurers from imposing prior authorization or any other requirement other than a prescription for coverage of specified medications used for the purposes of MAT. Additionally, such MAT medications must be placed on the lowest tier of the prescription drug formulary.
- Colorado HB 18 (2018): Requires coverage for a five-day supply of first requests for FDA-approved MAT drug without prior authorization.
- Illinois SB 1707 (2018): Prohibits use of prior authorization and step therapy for all FDA-approved medications to treat SUD.
- Maryland HB 887 (2017): Prohibits individual and group health plans from requiring prior authorization for medications used to treat SUDs that contain buprenorphine, methadone, or naltrexone.
- Maryland HB 1329/SB 967 (2017): Requires individual and group health plans to cover at least one opioid overdose reversal medication that does not require prior authorization.
- Delaware SB 41 (2017): Requires individual plans and large group plans that cover prescription medications to provide 5 days of "emergency" prescription medications without prior authorization for the treatment of behavioral health conditions, including medications used to treat opioid use disorders. This includes withdrawal and management medications along with overdose reversal medications.
- New Hampshire SB 158 (2017): Prohibits renewal of prior authorization of approved MAT more frequently than once every 12 months.
- Illinois SB 1707 (2017): Prohibits prior authorization and step-therapy requirements for FDA-approved medications to treat substance use disorders; requires generic FDA-approved medications for substance use disorders to be on lowest-tier of prescription formularies; prohibits exclusions of prescription coverage and related support services for substance use disorder because they are court ordered.

Federal Policy Landscape

Federal Mental Health Parity and Addiction Equity Act

The federal Mental Health Parity and Addiction Equity Act (MHPAEA) addresses parity for mental health benefits.⁹ The MHPAEA requires that if mental health or substance use disorder services are covered, cost-sharing terms and treatment limits be no more restrictive than the predominant terms or limits applied to medical/surgical benefits. The MHPAEA applies to the large group, but the ACA requires small-group and individual market plans and policies purchased through a state health insurance marketplace to comply with the MHPAEA. This federal requirement is similar to the California mental health parity law,¹⁰ although the state law applies to some plans and policies not captured in the MHPAEA.

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 SB 854 may interact with requirements of the ACA as presently exists in federal law, including the requirement for certain health insurance to cover essential health benefits (EHBs).^{11,12}

Any changes at the federal level may impact the analysis or implementation of this bill, were it to pass into law. However, CHBRP analyzes bills in the current environment given current law and regulations.

Federally Selected Preventive Services

The ACA requires that nongrandfathered group and individual health insurance plans and policies cover certain preventive services without cost sharing when delivered by in-network providers within 12 months after a recommendation appears in any of the following:¹³

- The United States Preventive Services Task Force (USPSTF) A and B recommendations;
- The Health Resources and Services Administration (HRSA)-supported health plan coverage guidelines for women's preventive services;
- The HRSA-supported comprehensive guidelines for infants, children, and adolescents, which include:
 - The Bright Futures Recommendations for Pediatric Preventive Health Care; and
 - The recommendations of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children; and
- The Advisory Committee on Immunization Practices (ACIP) recommendations that have been adopted by the Director of the Centers for Disease Control and Prevention (CDC).

As an A recommendation, the USPSTF recommends medications approved by the FDA to treat tobacco use disorder for all non-pregnant adults who use tobacco (USPSTF, 2009). Through its interaction with

⁹ Mental Health Parity and Addiction Equity Act of 2008 (MHPAEA), as amended by the ACA.

¹⁰ H&SC Section 1374.72; IC Section 10144.5 and 10123.15.

¹¹ The ACA requires nongrandfathered small-group and individual market health insurance — including but not limited to QHPs 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.

¹² 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.

¹³ A resource on this ACA requirement is available on the CHBRP website: www.chbrp.org/other_publications/index.php.

the ACA, this results in a prevention services benefit mandate and prohibits cost sharing (regardless of formulary tier) for these medications. However, the interaction is silent in regards to:

- Whether brand-name (as well as generic) versions must be covered,
- Whether all formulations (lozenge, patch, nasal spray, etc.) must be covered, and
- Whether all covered versions/formulations must be covered without applicable cost sharing.

In terms of its interaction with SB 854, for the situations in which it is applicable, the prevention services mandate is stricter on cost sharing. The prevention service mandate prohibits cost sharing for some medications in some circumstances, a situation often referred to as being “tier 0” when the medication is on formulary, SB 584 allows “lowest formulary tier” coverage, which may include some cost sharing. However, the prevention services mandate may not be as broadly applicable as SB 854 — it may not be relevant to all covered formulations of a medication or to both brand name and generic if both are covered, as CHBRP has assumed that SB 854 would be.

Essential Health Benefits

Nongrandfathered plans and policies sold in the individual and small-group markets are required to meet a minimum standard of benefits as defined by the ACA as essential health benefits (EHBs). In California, EHBs are related to the benefit coverage available in the Kaiser Foundation Health Plan Small Group Health Maintenance Organization (HMO) 30 plan, the state’s benchmark plan for federal EHBs.^{14,15} CHBRP estimates that approximately 4 million Californians (10%) have insurance coverage subject to EHBs in 2021.¹⁶

States may require plans and policies to offer benefits that exceed EHBs.¹⁷ However, a state that chooses to do so must make payments to defray the cost of those additionally mandated benefits, either by paying the purchaser directly or by paying the qualified health plan.^{18,19} Health plans and policies sold outside of the health insurance marketplaces are not subject to this requirement to defray the costs. State rules related to provider types, cost sharing, or reimbursement methods would not meet the definition of state benefit mandates that could exceed EHBs.²⁰

As SB 854 would affect the terms and conditions of existing coverage, but would not require new coverage, it would not seem likely to exceed EHBs.

¹⁴ CCIIO, Information on Essential Health Benefits (EHB) Benchmark Plans. Available at: <https://www.cms.gov/ccio/resources/data-resources/ehb.html>.

¹⁵ H&SC Section 1367.005; IC Section 10112.27.

¹⁶ CHBRP, *Estimates of Sources of Health Insurance in California in 2021*. Available at: www.chbrp.org/other_publications/index.php.

¹⁷ ACA Section 1311(d)(3).

¹⁸ 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: <https://www.gpo.gov/fdsys/pkg/FR-2013-02-25/pdf/2013-04084.pdf>.

¹⁹ However, as laid out in the Final Rule on EHBs 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.

²⁰ Essential Health Benefits. Final Rule. A state’s health insurance marketplace would be responsible for determining when a state benefit mandate exceeds EHBs, and QHP issuers would be responsible for calculating the cost that must be defrayed.

BACKGROUND ON SUBSTANCE USE DISORDERS

Substance use disorder is the clinical diagnosis for substance use that meets criteria per the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), including impaired control, social impairment, risky use, increased tolerance, and withdrawal symptoms (APA, 2013). The American Society of Addiction Medicine (ASAM) characterizes addiction as “the inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one’s behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission” (ASAM, 2011).

There are a number of licit and illicit substances that qualify for a substance use disorder diagnosis including: opioids (heroin and misuse of prescription pain medications such as fentanyl and oxycodone), alcohol, cannabis, nicotine, inhalants, hallucinogens, amphetamine, cocaine, and sedatives. Treatments for SUD include residential, inpatient, and outpatient care using behavioral therapy, counseling, and/or prescription medication. Mutual help groups (e.g., Alcoholics Anonymous, Narcotics Anonymous) also support those with substance use disorder to quit substance use and maintain sobriety. Three substance use disorders have medications approved and indicated by the FDA for their treatment, and these three substance use disorders are included in this report: opioid use disorder, alcohol use disorder, and tobacco use disorder.

SB 854 would require state-regulated plans and policies that include a pharmacy benefit to cover all prescription medications approved and indicated by the FDA for treatment of substance use disorders. Coverage for Medi-Cal beneficiaries would be exempt from the requirements of SB 854. SB 854 would also require placement of these medications on the lowest formulary tier and would prohibit prior authorization, step therapy, or denials related to court orders. The latter three prohibitions would also be applicable to counseling used in conjunction with medication for treatment of substance use disorder. **Thirteen medications are approved by the FDA for the treatment of *opioid use disorder*, *alcohol use disorder*, and *tobacco use disorder*; Table 2 shows the only medications and disorders that meet the conditions of SB 854.**

SUDs in California: Prevalence, Mortality, Health Services Use, and Disparities

CHBRP reports the most recent data available and cites national data when California data are unavailable. In this report, misuse/abuse/dependence (or heavy drinking) rates are used as proxy measures when data on use disorders is unavailable. Data sources and prevalence rates in California vary among the three use disorders:

- Opioid use disorder prevalence is 2% among people aged 12 years and older (Clemans-Cope et al., 2018)
- Alcohol use disorder prevalence at a level that warrants consideration of pharmacotherapy is 5.51% among people aged 12 years and older (CHCF, 2018)
- Tobacco use disorder prevalence is 11.2% among adults (based on all tobacco products; CDC, 2019)

Of note, polysubstance use is common among those diagnosed with substance use disorder, and many patients have more than one substance use disorder. For example, in the U.S., among those reporting alcohol use disorder, 23.8% also report nicotine dependence, and 3.9% report a concomitant prescription opioid use disorder. Among those reporting a prescription opioid use disorder, 35.2% also reported alcohol use disorder and 45.4% reported concomitant nicotine dependence (NIDA, 2018). The diagnosis and treatment of multiple use disorders is complex and treatment and recovery rates for each substance

use disorder may vary for a single patient. It is possible for a patient to be in recovery from one SUD, but not another.

Opioid Use Disorder

The DSM-5 characterizes opioid use disorder as a pattern of opioid use (e.g., oxycodone, hydrocodone, and heroin) 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 opioid use disorder depending on the number of criteria met (APA, 2013).

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).

Opioid use disorder prevalence

The California Opioid Overdose Surveillance Dashboard estimates that two million opioids were prescribed in California in 2018 (CDPH, 2019). Clemans-Cope and colleagues (2018) defined opioid use disorder as abuse of or dependence on nonmedical use of prescription pain relievers *and/or* heroin by persons aged 12 years and older.

Opioid use disorder treatment relapse rates

Many providers consider opioid use disorder to be a chronic condition. As with most chronic conditions, medication adherence and long-term control of the condition (relapse prevention) are challenging. A literature review by McLellan et al. (2000) found that adherence rates for medications for substance use disorders in the first year of treatment (40%-60%) were similar to or higher than adherence rates for medications used to manage diabetes, asthma, and hypertension (30%-50% for type 1 diabetes; 50%-70% for asthma and hypertension) (McLellan et al., 2000). Health care professionals note that relapse 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 (NIDA, 2017).

Mortality

The CDC attributes the increase in premature mortality across the U.S. since 2013 to a significant increase in overdose deaths associated with illicitly manufactured synthetic opioids (fentanyl). Those using opioids obtained illegally (on the street) are unaware of variations in strength for every dose purchased; illicitly manufactured fentanyl appears to remain a significant problem in 2019 (CDC, 2019). After 25 years of increasing life expectancy in the U.S., researchers from the National Center for Health Statistics reported that life expectancy fell from 78.9 years in 2014 to 78.6 years in 2016 (Kochanek et al., 2017). In 2019, life expectancy increased slightly to 78.7 years (Xu, 2020). At the population level, researchers linked the overall decrease in life expectancy in part to the opioid epidemic (Dowell et al., 2017).

The California Opioid Overdose Surveillance Dashboard shows an age-adjusted mortality rate for all opioid overdose deaths of 5.23/100,000 Californians in 2017 (2,196 deaths) the highest annual rate yet reported in California (CDPH, 2018).

There are significant mortality rate differences among demographic groups. Native Americans, followed by whites, had the highest opioid overdose mortality rates in California in 2017 (17.56/100,000 and 8.9/100,000) as compared with Asians who had the lowest opioid overdose mortality rate at 0.97/100,000

(CDPH, 2018). California males were twice as likely to die from opioid overdose as females (7.32 deaths/100,000 and 3.08 deaths/100,000, respectively).

Opioid use disorder-related health services use

The California Opioid Overdose Surveillance Dashboard provides a variety of statistics about California's experience with opioid misuse, including information about emergency department use. About 10/100,000 Californians were seen in emergency departments (ED) for opioid (excluding heroin) overdose in 2017 (CDPH, 2019). Males and females have about the same rate of emergency department visits for opioid overdoses (10.4/100,000 and 10.0/100,000, respectively). Among various age cohorts, the Dashboard shows that Californians aged 55 to 69 years have the highest crude rates of emergency department visits for opioid overdose (~15/100,000), closely followed by younger patients (aged 20-29 years) (~14/100,000) (CDPH, 2019).

In contrast to the pattern of mortality rates, the California Opioid Overdose Surveillance Dashboard shows that blacks and whites have similar rates of hospitalizations for opioid overdose (11.9/100,000 and 11.6/100,000, respectively), followed by Native Americans (5.9/100,000), Latinos (4.3/100,000), and Asians (1/100,000) (CDPH, 2019). See the *Benefit Coverage, Utilization, and Cost Impacts* section for discussion about estimated cost offsets attributable to SB 854.

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).

Alcohol use disorder is the third leading cause of preventable mortality in the U.S. 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).

Alcohol use disorder prevalence

The California Health Care Foundation estimates that 6.4% of Californians aged 12 years and older reported "meeting criteria for abuse of or dependence on alcohol."

The national rate of alcohol use disorder is estimated to be 6.2% among adults aged 18 and older (NIAAA, 2018). The 2017 Behavioral Risk Factor Surveillance Survey data show that males and females have similar rates of heavy drinking²¹ (proxy indicator for alcohol use disorder) (6.6% and 6.0%, respectively). More significant differences were reported by age cohort and race/ethnicity. Heavy drinking was highest among those aged 18 to 34 years, followed by those aged 55 to 64 years (7.3% and 6.0% respectively) (CDC, 2015). Differences among racial ethnic groups exist with non-Hispanic whites reporting higher rates of heavy drinking than blacks (non-Hispanic) and Hispanics (8.7%, 4.5%, and 5.2%, respectively) (CDC, 2015).

Although Hispanics and blacks have relatively lower rates of alcohol use disorders than do non-Hispanic whites, ethnic and racial disparities exist for alcohol-related diseases, problems, and deaths in these groups (NIAAA, 2019). For example, Hispanics and blacks have a higher risk for developing alcohol-related liver disease and subsequent cirrhosis mortality than whites. Self-reported rates of DUI are highest among mixed race and Native Americans and Alaska Natives (NIAAA, 2019).

²¹ Behavioral Risk Factor Surveillance System Survey defines heavy drinking as males consuming >14 drinks/week and females consuming >7 drinks/week. CHBRP uses this as a proxy indicator of alcohol use disorder.

The National Institute on Drug Abuse reports a series of statistics regarding disparities in alcohol misuse/abuse according to sexual orientation (NIDA, 2017). For example, 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).

Alcohol use disorder treatment relapse rates

Of the substance use disorders that have medication treatment options, alcohol use disorder is the disorder least associated with medication-assisted treatment. An estimated one-third of people with alcohol use disorder receive treatment (medication and/or counseling); fewer than 10% of these use alcohol use disorder prescription drug treatment (Jonas et al., 2014; NIAAA, 2018). Generally, alcohol use disorder is treated in specialty facilities, or patients choose to attempt abstinence through mutual-help organizations such as Alcoholics Anonymous. Alcohol use disorder is treated less commonly through primary care (Jonas et al., 2014).

Alcohol use disorder-related mortality

The CDC Alcohol-Related Disease Impact database reports the number of alcohol-attributable deaths due to excessive alcohol consumption. In California, of the 10,671 alcohol-attributed deaths in 2013 (most recent data), 5,558 deaths were due to chronic conditions associated with liver disease/cirrhosis (more than 3,500 deaths), followed by stroke (193), hypertension (238), and cancer (325) (CDC, 2013). The remaining 5,113 deaths were from acute causes, including more than 1,000 motor vehicle deaths, 1,000 homicides, 800 suicides, and 600 falls resulting in death (CDC, 2013).

Alcohol use disorder-related health service use.

Among the 119,600 non-fatal emergency room visits and 30,000 non-fatal hospitalizations for alcohol-related injuries and poisonings in 2014, men, whites, and Hispanics experienced disproportionate representation similar to the death rates.

Tobacco Use Disorder

The DSM-5 characterizes tobacco use disorder as a pattern of tobacco use (e.g., smoking, chewing) 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 tobacco use disorder depending on the number of criteria met (APA, 2013).

Public health campaigns, smoking policy changes (tobacco taxation, tobacco sales restrictions, workplace restrictions, etc.), and the ACA requirement for coverage of cessation therapies by many plans and policies have contributed to California having the second lowest rate of adult smoking in the U.S. (11.4%). However, California still has the largest number of smokers due to the size of its population (3.2 million adult smokers) (CDPH, 2018). Cigarette use combined with other tobacco product (e.g., cigars, chewing tobacco) use gives an overall tobacco-use prevalence rate of 16.4% of adult Californians. (Vaping is excluded from this discussion because e-cigarettes do not contain tobacco.) CDPH also reports significant variation in smoking prevalence among subpopulations. For example, there is a three-fold difference between the populations with the highest and the lowest smoking rates: 24.2% of American Indians as compared with 8.6% of Asian/Pacific Islanders. African Americans have the second highest rate of smoking in California (20.7%) followed by whites (13.0%) and Hispanics (11.5%).

Treatment and cessation rates for tobacco use disorder

Table 3 shows the prevalence of smoking cessation methods that California smokers reported using (one or more) to quit smoking in the past year, based on the 2016-2017 California Adult Tobacco Survey (CDPH, 2018). Prior research has shown that former smokers recalled an average of 4.7 quit attempts before successfully abstaining (CDPH, 2018). This number is likely an undercount; Chaiton et al. found that quit attempt estimates may be low because chronic smokers who attempt to quit several times rely on their memory for the number of quit attempts and tend to undercount them (Chaiton et al., 2016).

Table 3. Methods (One or More) Used to Quit Cigarette Smoking in the Past Year among Adults in California Aged 18-64, 2016-2017

Method	2016	2017
Quit Cold Turkey	67.4%	67.0%
Medication (e.g., bupropion, varenicline)	6.7%	5.7%
Nicotine Patches, Gum, or Lozenges	18.5%	19.2%
Counseling	4.1%	5.6%
Self-Help Materials	5.9%	10.6%
California Smokers' Helpline	7.3%	4.6%
Electronic Smoking Devices*	19.5%	14.6%

Source: California Health Benefits Review Program, 2020, adapted from CDPH, 2018.

Note: * Electronic smoking devices are not an FDA-approved method of smoking cessation.

Tobacco use disorder morbidity and mortality

Tobacco use is the leading cause of preventable illness and death in the United States and California. The CDC estimates that smoking and exposure to tobacco smoke account for approximately 40,000 deaths annually in California and that 440,000 youth today will die prematurely due to tobacco exposure. There is a robust body of literature demonstrating poor health outcomes associated with smoking, including cardiopulmonary disease, cancer, dental disease, and poor fetal outcomes (e.g., low birthweight, stillbirth, preterm delivery). The California Department of Public Health (CDPH) reported that current smokers have the highest rate of chronic obstructive pulmonary disease (12.7%) followed by never smokers (5.5%) and former smokers (4.8%). Rates of smoking-attributable mortality for lung cancer for men was 85% (5,175) and 64% (3,625 deaths) for women in 2016 (CDPH, 2018). Among the 10 categories of cancer, nine categories of cardiovascular disease, and five categories of respiratory disease, the smoking attributable mortality rate was above 60% accounting for more than 20,000 preventable deaths in California in 2014 (CDPH, 2018).

Unmet Needs for Opioid Use Disorder, Alcohol Use Disorder, and Tobacco Use Disorder Treatment

Opioid use disorder: In calculating the opioid use disorder treatment gap in California, Clemans-Cope et al. (2018) estimated that about 20% with opioid use disorder will seek medication-assisted treatment based on study findings from Wu et al. (2016) that considered opioid-related treatment received by people with opioid use disorder in the U.S. See the Structural and Attitudinal Barriers to Opioid Use

Disorder, Alcohol Use Disorder, and Tobacco Use Disorder Treatment subsection for discussion about contributing factors to unmet need for treatment.

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 (Jonas et al., 2014). In 2017, 5.41% of Californians aged 12 years and older reporting a need for but not receiving alcohol use disorder treatment (and 9.93% among those aged 18–25 years) (SAMHSA, 2017). See the Structural and Attitudinal Barriers to Opioid Use Disorder, Alcohol Use Disorder, and Tobacco Use Disorder Treatment subsection for discussion about contributing factors to unmet need for treatment.

Tobacco use disorder: Based on California Health Interview Survey data, 72% percent of adult smokers in California thought about quitting in the next six months and 58% percent made an attempt in the past year. Prescription medications were used by 5.7% smokers, who may report using more than one cessation method simultaneously (CDPH, 2018).

Structural and Attitudinal Barriers to Opioid Use Disorder, Alcohol Use Disorder, and Tobacco Use Disorder Treatment

Barriers to accessing treatment for opioid use disorder, alcohol use disorder, and tobacco use disorder include drug utilization management techniques (see side bar), provider supply, geographic access, and patient receptiveness to treatment. According to the Pew Foundation, two key barriers to the use of medications for opioid use disorder are limited insurance coverage for medications and limited provider supply.

Patient Attitudinal Barriers

For many with opioid use disorder, alcohol use disorder, and tobacco use disorder, attitudinal barriers are the most significant barrier to treatment initiation and persistence (Blanco et al., 2013). The stigma of addiction and the ability to acknowledge a use disorder affects patient desire 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). Many people with opioid use disorder and/or alcohol use disorder believe they can solve the problem themselves (Rapp et al., 2006). Rapp et al. (2006) tested a Barrier to Treatment Inventory tool to assess barriers to treatment from the substance abusers' perspective. They reported significant correlation among six of the seven barrier factors: absence of a problem; negative social support; fear of treatment; privacy concerns; time conflict; poor treatment availability; and admission difficulty.

As with opioid use disorder and alcohol use disorder, patient readiness for treatment also presents a barrier for those with tobacco use disorder. The California Health Information Survey (CHIS) data shows that a quarter of smokers in California are not interested in quitting. For those who attempt to quit, repeated efforts are needed, with an average of 4.7 quit attempts reported by former smokers before successful cessation (CDPH, 2018).

Prescription Drug Utilization Management

These tools help insurance carriers manage the cost or safety of use of outpatient prescription medications. In addition to minimizing the use of more expensive prescription medications, these techniques are used sometimes for clinical reasons such as promoting adherence to clinical recommendations for specific illnesses or protecting enrollees from outdated or potentially dangerous medications (PBMI, 2015). As discussed further in the *Benefit Coverage, Utilization, and Cost Impacts* section, most enrollees in DMHC-regulated plans and CDI-regulated policies have formulary coverage for prescription medications approved and indicated by the FDA to treat substance use disorders. (See box for definitions of prescription drug utilization management techniques.)

Provider Supply

Although formulary coverage and utilization management may provide some barrier to treatment, provider supply including regulatory and geographic access to existing providers, as well as the number of appropriate providers per capita, and provider attitudes can also pose structural barriers to treatment and are more difficult to address through legislated benefit mandates.

Significant prescribing restrictions limit access to opioid use disorder medications. Federal law restricts methadone treatment (for opioid use disorder) to federally certified opioid treatment programs (“methadone clinics”). Methadone must be initiated through admission to a certified methadone clinic. Initially, patients must take their daily methadone treatment under direct clinical supervision. Once a patient is stabilized, it is possible for some patients to take methadone at home in between required clinic visits. Federal guidelines recommend a minimum 12-month treatment plan, and many patients continue with methadone for years (SAMHSA, 2015). (Due to the federal restrictions, CHBRP assumes SB 854 would not change administration, payment, or barriers to methadone treatment. See the *Benefit Coverage, Utilization, and Cost Impacts* section for further discussion.) Clemans-Cope et al. (2018) reported that there are 152 SAMHSA-certified methadone clinics in California, which can treat 46,430 patients simultaneously.

Patients may also face supply issues or geographical barriers to accessing Vivitrol (naltrexone), as it needs to be injected by a provider. A provider office would need to have the drug, and patients would need to travel to the provider’s office.

In order to prescribe buprenorphine for opioid use disorder, another FDA-approved treatment, federal law requires health care providers to receive special training and certification called a DATA 2000 Waiver. Providers (physicians, physician assistants, and nurse practitioners) can treat no more than 30

Prescription Drug Utilization Management Techniques

The following are used to help health plans and insurers control costs and manage patient safety (PBMI, 2015):

Formulary. The formulary is a list of prescription medications that the health plan or insurer agrees to pay for in whole or in part.

Tier. Formularies divide the covered medications into tiers, each tier having a distinct cost-sharing level. Prescription medications in the lower tiers (0-2), usually generics and preferred brand-name medications, are less costly to both the enrollee and to the health plan or insurer than medications listed in upper tiers (3-5).

Prior authorization. This utilization management tool requires providers to submit documentation of medical need to the health plan for approval of coverage for some prescription medications.

Step therapy. This utilization management tool (sometimes referred to as “fail first”) requires an enrollee to try and fail one or more formulary-required medications prior to receiving coverage for the initially preferred drug. Step therapy protocols usually recommend starting with a drug that is less expensive (generics) and/or has more “post-marketing safety experience.”

simultaneous patients during first year of waiver, and must reapply to increase to 100 patients. Addiction medicine physicians may treat up to 275 patients at a time (SAMHSA, 2018). In 2018, there were 5,821 physicians waived to prescribe buprenorphine in California (CHCF, 2018). Several studies suggest that, of certified buprenorphine providers, only 44% to 66% actually prescribe the medication for opioid use disorder, and most do not choose to reach their maximum-allowed patient caseload (Hutchinson et al., 2014; Jones et al., 2015; Walley et al., 2008). This leads to wait lists in some areas, which have been shown to decrease uptake of opioid use disorder medications by people with opioid use disorder (Fisher et al., 2017). A recent treatment capacity analysis by Clemans-Cope et al. (2018) estimated that an additional 3,500 to 4,100 providers would need to be trained and certified to treat the opioid use disorder population in California.

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, lack of office space and support resources, time pressure, or personal beliefs against using medications to treat opioid use disorder (HHS, 2016; McNeely et al., 2018). Many providers are reticent to prescribe medication to treat alcohol use disorder, despite more than 10 years of provider education campaigns from government entities and the American Medical Association (SAMHSA, 2015). Other reasons for provider nonparticipation include prior training to refer to patients with alcohol use disorder to specialty treatment centers and systemic division between physical and behavioral health care (SAMHSA, 2015). Wessell et al. found that key facilitators to increasing primary care providers' prescribing alcohol use disorder medication included provider exposure to evidence and case studies, limited referral options to specialty treatment clinics for their patients (provider-of-last resort), receptive patients, early successful patient outcomes, and low-cost (generic oral naltrexone) availability of alcohol use disorder medication (Wessell et al., 2014).

Medications for treating tobacco use disorder and alcohol use disorder do not require special provider training or waivers, thus these disorders do not face the same provider supply barrier described for opioid use disorder.

Lack of availability for providers for counseling services may also affect enrollees with opioid use disorder and alcohol use disorder. However, because of the barriers facing enrollees to access FDA-approved medications to treat substance use disorder, provider shortage of counselors is not projected to impact utilization as a result of this bill, because access to counseling services would need to be in conjunction with access to FDA-approved medications in order to fall under the bill's purview (see the *Benefit Coverage, Utilization, and Cost Impacts* section for more information).

Disparities²² and Social Determinants of Health²³ in Substance Use Disorders

SDoH include factors outside of the traditional medical care system that influence health status and health outcomes (e.g., income, education, geography, etc.). See the *Long-Term Impacts* section for a full discussion.

²² 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).

²³ CHBRP defines social determinants of health as conditions in which people are born, grow, live, work, learn, and age. These social determinants of health (economic factors, social factors, education, physical environment) are shaped by the distribution of money, power, and resources and impacted by policy (adapted from: (CDC, 2014; Healthy People 2020, 2019)). See CHBRP's SDoH white paper for further information: http://chbrp.com/analysis_methodology/public_health_impact_analysis.php.

MEDICAL EFFECTIVENESS

As discussed in the *Policy Context* section, SB 854 would mandate coverage for all FDA-approved medications used to treat substance use disorders and stipulates requirements about utilization management. Additionally, SB 854 would mandate coverage for cognitive, behavioral, and mental health therapies (hereafter called behavioral therapies) prescribed in conjunction with FDA-approved substance use disorder (SUD) medications. The medical effectiveness review summarizes findings from evidence²⁴ on the effectiveness of medications that the FDA has approved for treatment of SUD, the effectiveness of behavioral therapy in conjunction with medication, and the impact of utilization management techniques on use of these medications and outcomes. Additional information on SUDs for which there are FDA-approved medications is included in the *Background on Substance Use Disorders* section.

As indicated in the *Background on Substance Use Disorders* section, the FDA has approved prescription medications to treat opioid use disorder, alcohol use disorder, and tobacco use disorder. Opioid use disorder encompasses abuse of short-acting opioids, such as heroin and morphine, and semi-synthetic opioids such as oxycodone and hydrocodone. Alcohol use disorder involves compulsive use of alcohol and inability to control alcohol intake. Tobacco use disorder encompasses use of all forms of tobacco. (See the *Background on Substance Use Disorders* section for more detailed definitions of these SUDs.)

The FDA has approved different medications for each of these disorders. Table 4 lists the medications the FDA has approved, the SUD(s) they are used to treat, their role in treatment, and how the medication is administered. Multiple forms of behavioral therapy are provided in conjunction with medications to treat substance use disorders, including individual and group counseling. Specific types of therapy provided include cognitive behavioral therapy, contingency management, motivational enhancement therapy, and facilitation of participation in 12-step programs (SAMHSA, 2016).

Table 4. FDA-Approved Prescription Medications for Opioid, Alcohol, and Tobacco Use Disorders and Approved Uses

Substance Use Disorder(s)	Medication	Role in Treatment	Mode of Administration
Opioid Use Disorder	Naloxone	Reverse overdose	Injection (by bystander, syringe or autoinjector), nasal spray
Opioid Use Disorder	Lofexidine	Manage withdrawal symptoms	Tablet
Opioid Use Disorder	Buprenorphine (including buprenorphine-naloxone)	Manage withdrawal symptoms, maintain abstinence from opioids	Tablet, film, injection (by medical provider), implant
Opioid Use Disorder	Methadone	Manage withdrawal symptoms, maintain abstinence from opioids	Tablet, liquid(a)
Opioid Use Disorder, Alcohol Use Disorder	Naltrexone	Maintain abstinence from opioids or abstinence from or reduction in alcohol consumption	Tablet, injection (by medical provider)

²⁴ Much of the discussion below is focused on reviews of available literature. However, as noted on page 11 of the *Medical Effectiveness Analysis and Research Approach* document posted at http://chbrp.com/analysis_methodology/medical_effectiveness_analysis.php, 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.

Substance Use Disorder(s)	Medication	Role in Treatment	Mode of Administration
Alcohol Use Disorder	Acamprosate	Maintain abstinence from alcohol	Tablet
Alcohol Use Disorder	Disulfiram	Maintain abstinence from alcohol	Tablet
Tobacco Use Disorder	Nicotine replacement therapy	Maintain abstinence from tobacco use	Inhaler, nasal spray(b)
Tobacco Use Disorder	Bupropion sustained release (SR)	Maintain abstinence from tobacco use	Tablet
Tobacco Use Disorder	Varenicline	Maintain abstinence from tobacco use	Tablet

Source: California Health Benefits Review Program, 2020.

Notes: (a) SB 854 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) Other forms of nicotine replacement therapy (i.e., patch, gum, and lozenge) are available over the counter.

Research Approach and Methods

Studies of FDA-approved SUD medications and relevant behavioral treatments were identified through searches of PubMed, the Cochrane Library, EMBASE, Scopus, and PsycINFO. Websites maintained by the following organizations that produce and/or index meta-analyses and systematic reviews were also searched: the Agency for Healthcare Research and Quality (AHRQ), the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health Service (NHS) Centre for Reviews and Dissemination, the National Institute for Health and Care Excellence (NICE), and the Scottish Intercollegiate Guideline Network. The search was limited to abstracts of studies published in English and current through January 27, 2020, and the search was conducted in the following manner:

- For SUD medications and utilization management, the search only included articles published since January 2019 because CHBRP previously reviewed older literature on medications for these disorders for its report on SB 11, which was issued in 2019.
 - The exception is for injectable naltrexone, which was not covered in the report for SB 11 but was covered in the report for AB 2384 (issued in 2018); the search for articles on injectable naltrexone included articles published since January 2018.
- For combined behavioral therapies and medications for opioid use disorder, the search only included articles published since January 2018 because CHBRP previously reviewed older literature on this treatment approach in its report on AB 2384, which was issued in 2018.
- For combined behavioral therapies and medications for alcohol use disorder, the search was limited to articles published since January 2006 to capture the COMBINE trial.
- For combined behavioral therapies and medications for tobacco use disorder, the search was limited to articles published after January 2015, to account for the most recent USPSTF Tobacco Cessation review.

Of the 558 articles found in the literature review, 94 were reviewed for potential inclusion in this report on SB 854, and a total of 20 new studies were included in the medical effectiveness review for this report. The other articles were eliminated because they did not address FDA-approved medications or counseling for SUD, 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 and the process used to grade the evidence for each outcome measure is presented in Appendix B.

The conclusions below are based on the best available evidence from peer-reviewed and grey literature.²⁵ 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 questions:

1. What is the effectiveness of FDA-approved medications for treatment of SUDs compared to no treatment or a placebo?
2. What is the relative effectiveness of FDA-approved medications used treat SUDs?
3. What are the harms associated with FDA-approved medications used treat SUDs?
4. How does health plans' use of utilization management techniques (such as prior authorization and step therapy) affect use of FDA-approved medications for SUDs?
5. Does the combination of medication and behavioral, cognitive or mental health services improve outcomes for persons treated for SUDs relative to either medication or behavioral therapy alone?

Methodological Considerations

SB 854 could be interpreted as only affecting coverage for FDA-approved medications for SUDs that are typically covered as part of a pharmacy benefit (i.e., medications that are administered orally, intra-nasally or by self-injection). However, since the language of the bill is unclear, the medical effectiveness review also discusses the injectable or implanted formulations for opioid- and alcohol use disorders that are typically covered as part of a medical benefit. CHBRP did not review literature on medications that are prescribed for alcohol use disorder but do not carry an FDA indication for this purpose, such as baclofen, gabapentin, topiramate, and valproic acid. In addition, CHBRP did not review studies of bupropion extended release (XL) because that formulation of bupropion is not FDA approved for treatment of tobacco use disorder. CHBRP also did not review literature on the effectiveness of transdermal and intravenous formulations of buprenorphine because the FDA has only approved these formulations of buprenorphine for the treatment of chronic pain.

CHBRP focused on medications used for long-term, maintenance treatment of opioid use disorder. CHBRP also reviewed an opioid-reversal medication and a medication for opioid withdrawal symptoms as these medications are commonly prescribed for persons with opioid use disorder for symptoms associated with the disorder, even though they are not used to treat opioid use disorder.

The systematic reviews CHBRP cited included overlapping groups of studies of FDA-approved medications for SUDs. Thus, the conclusions of these systematic reviews regarding the effectiveness of these medications are not independent of one another.

²⁵ 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 http://chbrp.com/analysis_methodology/medical_effectiveness_analysis.php.

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.

In the context of SUDs, several types of behavioral interventions are used to help people control urges, remain abstinent, and assist patients in coping with the emotional strife that often accompanies addiction (Dutra et al., 2008). Behavioral counseling interventions can be delivered in different treatment modalities (e.g., inpatient, outpatient) and in a variety of formats (e.g., individual, group, digital). After review of the literature, and discussion with the content expert, CHBRP determined that most behavioral, cognitive, or mental health services prescribed in conjunction with or supplementary to medications for SUDs are outpatient counseling interventions; counseling in conjunction with medication therapy for SUDs is uncommon in partial hospitalization or intensive outpatient therapy settings. As such, CHBRP limited the medical effectiveness review to outpatient counseling in conjunction to medications for SUD. Counseling for SUD may be delivered as individual (i.e., one-on-one), family or group (i.e., two or more on one) counseling, in-person or via telecommunication, and employ multiple techniques including cognitive-behavioral therapy, contingency management, 12-step facilitation therapy, motivational interviewing or motivational enhancement therapy, family therapy, and others (Carroll and Onken, 2005). The term counseling is used broadly throughout this report to describe the range of formats in which counseling for SUD may be delivered.

Outcomes Assessed

Studies of FDA-approved medications 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 FDA-approved medications plus counseling for opioid use disorder have primarily examined abstinence from opioid use, treatment attendance, retention in treatment, and psychiatric symptoms.

Studies of FDA-approved medications 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. Studies of FDA-approved medications plus counseling for alcohol use disorder have primarily examined abstinence from alcohol use and time until heavy drinking.

Studies of FDA-approved medications for tobacco use disorder have primarily examined outcomes related to cessation of tobacco use. Outcomes assessed include reduced cigarette cravings during treatment, abstinence during treatment, and abstinence of tobacco at follow up. Some studies have examined effects of medications on birth outcomes for pregnant women treated for tobacco use disorder, including rates of miscarriage, stillbirth, preterm birth (less than 37 weeks), low birthweight, admissions of babies to neonatal intensive care, and infant development. Studies of FDA-approved medications plus counseling for tobacco use disorder have primarily examined smoking cessation.

Study Findings

This following section summarizes CHBRP's findings regarding the strength of evidence for the effectiveness of FDA-approved medications for SUDs, relevant behavioral treatments, and utilization management. 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.

Opioid Use Disorder Treatments

Opioid use disorder: FDA-approved prescription maintenance medications versus placebo or no medication

Research has demonstrated the effectiveness of FDA-approved medications 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).

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 (≥ 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 ($\geq 80\%$ 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, SB 854 would affect coverage 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, SB 854 is likely to have a limited impact on costs associated with methadone treatment. CHBRP decided to include methadone in its medical effectiveness review despite SB 854’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/1000 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).

Naltrexone

In contrast to methadone and buprenorphine, which can be administered while a person tapers off misuse of opioids, people must complete detoxification 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 Cochrane review of 13 RCTs (1,158 total people; sample sizes: 20–280 people) (Minozzi et al., 2011) found that there was no statistically significant difference between treatment with oral naltrexone and treatment with placebo or no pharmacological agent with respect to retention or abstinence.

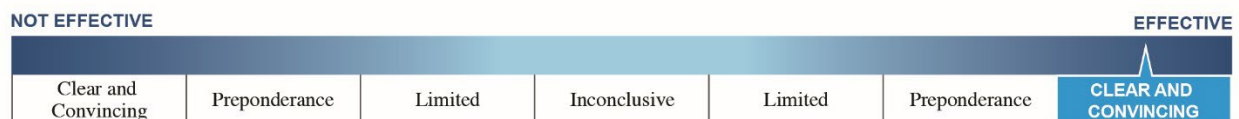
An extended release intramuscular injectable formulation of naltrexone has been developed to provide a longer acting form of the medication that does not depend on a patient taking a medication on a daily basis. Findings from one systematic review (Jarvis et al., 2018) found limited evidence that extended-release naltrexone decreases opioid use relative to a placebo.

One RCT has compared retention in treatment and opioid use during treatment among adults randomized to receive either oral naltrexone (sample size: 32 people) or extended-release intramuscular injectable naltrexone (sample size: 28 people) (Sullivan et al., 2019). The authors found that retention in treatment was significantly higher among participants receiving extended-release intramuscular 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 (sample size: 7782 people) (HR = 0.93, 95% CI: 0.71 to 1.22) or extended-release naltrexone (sample size: 1386 people) (HR = 0.74, 95% CI: 0.42 to 1.31), compared to no treatment (Morgan et al., 2019).

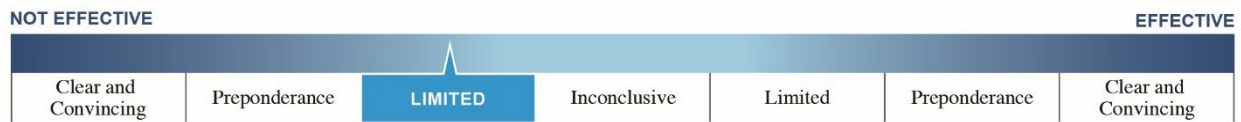
Summary of findings regarding the effectiveness of buprenorphine and methadone: There is clear and convincing evidence from 10 systematic reviews and five RCTs that buprenorphine (including buprenorphine-naloxone) and methadone are more effective than a placebo or no treatment with regard to retention 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 1. FDA-Approved Medication for Opioid Use Disorder Versus Placebo or No Medication – Methadone and Buprenorphine



Summary of findings regarding the effectiveness of oral naltrexone versus placebo or injectable naltrexone: There is limited evidence from one systematic review, one RCT published after the systematic review, and one cohort study that oral naltrexone is not effective for treatment retention, abstinence, or overdose prevention compared to placebo or injectable naltrexone.

Figure 2. FDA-Approved Medication for Opioid Use Disorder Versus Placebo or No Medication, or vs. Extended-Release Naltrexone – Naltrexone Oral



Summary of findings regarding the effectiveness of injectable naltrexone ER versus placebo or oral naltrexone: There is limited evidence from one systematic review, one RCT published after the systematic review, and 1 cohort study that injectable naltrexone ER is effective for treatment retention and abstinence, but not for overdose prevention, compared to placebo or oral naltrexone.

Figure 3. FDA-approved Medication for Opioid Use Disorder Versus Placebo or No Medication – Naltrexone Injectable (ER)



Opioid use disorder: Comparison of FDA-approved maintenance medications

Buprenorphine or buprenorphine-naloxone combination versus methadone

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 extended release 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. CHBRP also did not identify any studies of the relative impact of maintenance medications used to treat opioid use disorder on mortality.

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 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 six RCTs (607 people) that addressed the impact of medication treatment on people who are addicted to legal opioid prescription medications (as opposed to heroin and other illegal opioids), 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).

Three systematic reviews compared the effectiveness and safety of buprenorphine and methadone for maintenance treatment of pregnant women with opioid use disorder. 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 among pregnant women but that pregnant women 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 mothers treated with buprenorphine or methadone but that symptoms were less severe for infants whose mothers were treated with buprenorphine. 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 people). 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 people) and number of newborns treated for neonatal abstinence syndrome (three studies, 166 subjects) did not differ significantly between groups. One RCT (sample size: 131 people) comparing methadone with buprenorphine reported side effects. For the mother 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).

Buprenorphine-naloxone combination versus extended-release naltrexone

Two RCTs have compared the effectiveness of extended-release naltrexone and buprenorphine-naloxone. One RCT assessed outcomes after 12 weeks of treatment (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 extended-release naltrexone reported less craving for heroin compared to those on buprenorphine-naloxone but were more likely to report symptoms of withdrawal. A second RCT examined

outcomes after 24 weeks of treatment (Lee et al., 2018). The authors found that participants were less likely to successfully initiate treatment with extended-release naltrexone than with buprenorphine-naloxone which led patients assigned to receive extended-release naltrexone to have a higher relapse rate than patients who received buprenorphine-naloxone. This finding is consistent with findings of studies that have compared extended-release naltrexone to a placebo (Jarvis et al., 2018). 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). Finally, a cohort study of over 46,000 adults in a nationally representative commercial claims database 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 extended release naltrexone therapy were not at significantly reduced risk of overdose (HR = 0.74, 95% CI: 0.42 to 1.31) (Morgan et al., 2019).

Summary of findings regarding the comparative effectiveness of buprenorphine versus methadone to treat opioid use disorder: There is inconclusive evidence from seven systematic reviews and four RCTs published after the systematic reviews about the impact of methadone relative to buprenorphine or buprenorphine-naloxone on retention in treatment and abstinence from opioids. There is limited evidence that buprenorphine and buprenorphine-naloxone are associated with better birth outcomes than methadone, but women receiving buprenorphine or buprenorphine-naloxone were less likely to remain in treatment than women who receive methadone.

Figure 4. Comparative Effectiveness of Different FDA-Approved Medications Used to Treat Opioid Use Disorder – Buprenorphine vs. Methadone



Summary of findings regarding the comparative effectiveness of buprenorphine versus extended-release naltrexone to treat opioid use disorder: There is limited evidence from two RCTs and one cohort study about the impact of extended-release naltrexone relative to buprenorphine or buprenorphine-naloxone. One of two RCTs that compare extended-release injectable naltrexone to orally administered buprenorphine-naloxone have found that people have more difficulty initiating treatment with extended-release naltrexone and were more likely to relapse, and one cohort study found that overdose rates were higher among patients taking naltrexone formulations compared to buprenorphine formulations.

Figure 5. Comparative Effectiveness of Different FDA-approved Medications Used to Treat Opioid Use Disorder – Buprenorphine vs. Extended-Release Naltrexone (Favors Buprenorphine)



Opioid Use Disorder: Harms Associated with Use of FDA-Approved Prescription Medications

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.

Initiation and discontinuation of treatment with naltrexone ER carries added risk of harm. 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) that inductions onto opiate use disorder medication were less likely to be successful for patients assigned to naltrexone ER, and relapse was more likely if assigned to naltrexone ER, compared to being assigned to sublingually administered buprenorphine. The authors also found a higher number of overdose events for patients who were assigned to 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.

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).

SAMHSA has concluded that the benefits of these medications with regard to mortality, HIV transmission, hepatitis C infection, and birth outcomes outweigh the harms associated with them (SAMHSA, 2015).

Summary of findings regarding harms associated with FDA-approved prescription medications 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. Naltrexone is associated with a higher risk of opioid overdose because people must abstain from opioids before initiating treatment and may be sensitive to lower doses of opioids if they relapse. SAMHSA has concluded that the benefits of these medications outweigh the harms.

Opioid use disorder: FDA-approved prescription medications for symptom management

Naloxone for overdose reversal: syringe-delivered versus intranasal versus auto-injector

The FDA has approved syringe-delivered injections (subcutaneous, intramuscular, or intravenous), auto-injector (intramuscular or subcutaneous) and intranasal formulations of naloxone for reversal of an opioid overdose. Paramedics and emergency department clinicians have used syringe-delivered intramuscular naloxone for many years and recent studies suggest that lay people can also administer the medication by this route effectively. All forms of naloxone have been found to reverse opioid overdoses (Boyer, 2012; Chou et al., 2017; Kim et al., 2009). Two studies that compared syringe-delivered intramuscular and intranasal formulations of naloxone found that the efficacy of intramuscular naloxone (2 mg) and intranasal naloxone (2 mg/1 mL) are similar (Chou et al., 2017). There were also no differences in adverse events associated with naloxone, which include agitation, nausea, and vomiting. Currently, the intranasal and auto-injectable are used by laypersons for opioid overdose. Pharmacokinetic studies for the auto-injector and intranasal formulation show adequate naloxone exposure to reverse opioid overdose with either formulation (Ryan and Dunne, 2018). Professional guidelines and content expert opinion do not suggest either intranasal or auto-injector over the other (ASAM, 2014).

Summary of findings regarding the comparative effectiveness of different routes of naloxone administration for opiate overdose: There is inconclusive evidence from limited studies that any route of naloxone is more effective than another. Professional guidelines and content expert opinion do not support either the intranasal or the auto-injector over the other for layperson use.

Figure 6. Comparative Effectiveness of Different Routes of administration of FDA-approved Naloxone for Opiate Overdose Management



Lofexidine for management of withdrawal symptoms versus placebo and versus clonidine

In 2018 the FDA approved lofexidine for management of symptoms of opioid withdrawal after decades of use in Europe for this indication (Pergolizzi et al., 2019). Two RCTs have found that lofexidine is more effective than a placebo for alleviating withdrawal symptoms as indicated by scores on instruments that measure opioid withdrawal symptoms (Fishman et al., 2019; Gorodetzky et al., 2017). People with less severe withdrawal symptoms may be more willing to abstain from using illicit opioids and to take other medications that the FDA has approved for maintenance treatment. Both RCTs found that persons who received lofexidine were more likely to complete the study than persons who received a placebo.

In 2016, a Cochrane systematic review compared lofexidine against placebo for the management of withdrawal symptoms (Gowing et al., 2009). In the single included study reporting on lofexidine versus placebo, they found that those treated with lofexidine versus placebo had lower withdrawal symptom scores and higher treatment retention (Yu et al., 2008).

The 2016 Cochrane review also compared clonidine, a medication that is used off-label for withdrawal symptoms, to lofexidine for the management of withdrawal symptoms. They found insufficient data in three studies for a quantitative comparison in efficacy between the two medications. They did conclude that lofexidine had a better safety profile than clonidine as lofexidine did not reduce blood pressure to the same extent as clonidine (Gowing et al., 2009).

Summary of findings regarding the comparative effectiveness of lofexidine versus placebo or clonidine for management of withdrawal symptoms: There is limited evidence from one systematic review including one RCT, and two additional RCTs published after the systematic review about the effectiveness of lofexidine on withdrawal symptoms compared to placebo. There is insufficient evidence from one systematic review including three RCTs to compare lofexidine to clonidine for the management of withdrawal symptoms.

Figure 7. Comparative Effectiveness of FDA-approved Lofexidine for Management of Withdrawal Symptoms vs. Placebo

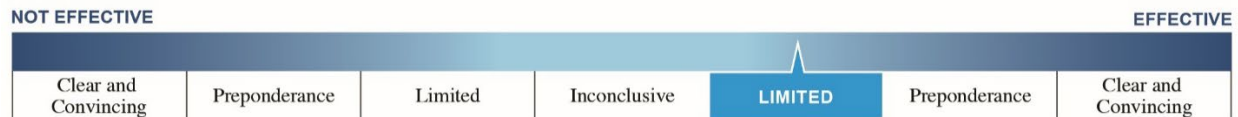


Figure 8. Comparative Effectiveness of FDA-Approved Lofexidine for Management of Withdrawal Symptoms vs. Off-label clonidine



Opioid use disorder: Effects of utilization management on use of FDA-approved prescription medications for opioid use disorder and outcomes

CHBRP found two studies that addressed the impact of utilization management on use of medications to treat opioid use disorder or patient outcomes. 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 per day. After the prior authorization policy was implemented the number of people prescribed doses of buprenorphine-naloxone greater than 24 mg per 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 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.

Accurso and Rastegar (2016) conducted a retrospective study (n=297 people) on the effect of a change in insurer policy, in which the insurer of a subset of patients in an office-based practice 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 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 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).

Summary of findings regarding the effects of utilization management for FDA-approved medications for opioid use disorder: There is insufficient evidence to assess the impact of utilization management on use of FDA-approved medications to treat opioid use disorder and patient outcomes. Buprenorphine is the only medication that has been assessed and studies have only examined the effects of prior authorization for high doses.

Opioid use disorder: Counseling plus FDA-approved maintenance medications versus medication alone

In a Cochrane review of 35 RCTs (4,319 participants), Amato et al. (2011) evaluated the efficacy of providing specific behavioral therapy treatments in conjunction with maintenance medications (methadone or buprenorphine) for opioid use disorder, including cognitive behavioral therapy, community reinforcement, contingency management, intensive supportive-expressive therapy, 12-step therapy, interpersonal psychotherapy, and standard counseling. The authors concluded that adding behavioral therapy to maintenance medications does not increase retention in treatment (27 studies, 3124 subjects, sample sizes: 24–542), abstinence from opiates during and after treatment (eight studies, 1002 subjects, sample sizes: 50–335), and compliance (three studies, 346 subjects, sample sizes: 40–198). The authors also found that adding behavioral therapy to medication maintenance treatment does not reduce psychiatric symptoms or depression (three studies, 279 subjects, sample sizes: 44–151). However, the authors noted that the control treatment in the RCTs typically included a counseling component and that their results should be interpreted as indicating that adding specific, structured behavioral therapy interventions to standard counseling and maintenance medications does not improve retention, abstinence, compliance, psychiatric symptoms, or depression.

Dugosh (2016) conducted a systematic review that included 27 recent empirical studies that were not included in the three summarized systematic reviews on treatment attendance, retention, and completion;

opioid use; and counseling session attendance. The most widely studied behavioral therapy interventions examined in conjunction with maintenance medications for opioid use disorder were contingency management and cognitive behavioral therapy, with the majority of studies focusing on the impact of adding behavioral therapy to methadone treatment (14 studies). There were 8 studies examining the efficacy of counseling in conjunction with buprenorphine, 3 studies on counseling in conjunction with oral naltrexone and 2 studies on counseling in conjunction with injectable naltrexone. For methadone, the authors concluded that counseling interventions in conjunction with medication had a significant effect on increased treatment attendance, lower treatment dropout rates and decreased opioid use. Significant effects were also shown on secondary outcomes: decreased HIV risk, improved psychosocial functioning, improved adherence to psychiatric medications, reduce alcohol use and reduce fear of detoxification. The authors note that the comparison groups (non-counseling groups) varied across studies and the majority were not methadone-only conditions. For buprenorphine, the authors conclude that the findings were less robust. They did find significant effects, with significant effects in only 3 of the 8 studies; significant effects were seen on treatment retention, attendance at group visits, reduction in opioid use and improved buprenorphine adherence. For oral naltrexone, all 3 studies demonstrated positive effects on treatment retention, treatment attendance or oral naltrexone adherence. The authors again note that comparison group varied across studies and the majority were not comprised of medications alone. For injectable naltrexone, the 2 studies demonstrated significant effects on treatment retention and completion, but no significant differences in opioid use.

Summary of findings regarding the effects of medication plus counseling versus medication alone for opioid use disorder: There is a preponderance of evidence from 1 systematic review including 14 heterogeneous studies that counseling in conjunction with methadone is effective for increased treatment attendance, decreased treatment dropout rates, decreased opioid use, decreased HIV risk, improved psychosocial functioning, improved adherence to psychiatric medications, reduced alcohol use and reduced fear of detoxification. There is limited evidence from 1 systematic review including 8 heterogeneous studies that counseling in conjunction with buprenorphine is effective for increased treatment retention, increased attendance at group visits, increased medication adherence, and reduced in opioid use. It should be noted that the findings of this systematic review is tempered by the findings of an older systematic review of 35 studies of methadone or buprenorphine that showed no effect of counseling in conjunction with these medications on treatment retention, abstinence from opioids, treatment compliance or reduction in psychiatric symptoms. There is limited evidence from 1 systematic review including 5 studies that counseling in conjunction with naltrexone, oral or injectable, is effective on treatment retention, attendance, adherence and/or completion.

Figure 9. Medication Plus Behavioral Therapy Versus Medication Alone for Opioid Use Disorder – Methadone

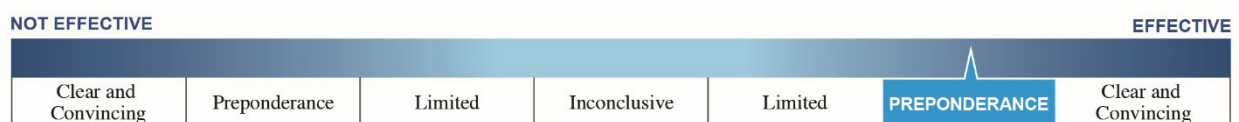


Figure 10. Medication Plus Behavioral Therapy Versus Medication Alone for Opioid Use Disorder – Buprenorphine and Naltrexone (oral and injectable)



Alcohol Use Disorder Treatments

Alcohol use disorder: FDA-approved prescription medications versus placebo or no medication

Acamprosate

A systematic review (122 RCTs, one cohort study; 22,803 people) comparing acamprosate to placebo found that significantly fewer subjects treated with acamprosate returned to any drinking (19 trials) and had significantly fewer drinking days (13 trials) than those treated with placebo. There was no significant difference for return to heavy drinking (seven trials), drinking days (one trial), or drinks per drinking day (one trial) between acamprosate and placebo (Jonas et al., 2014).

A meta-analysis (Donoghue et al., 2015) (22 RCTs; 5,236 people) of the efficacy of acamprosate found the risk of returning to any drinking at 6 months was significantly lower for people receiving acamprosate than for people receiving a placebo. There was little difference in the risk of participants discontinuing treatment for any reason.

Naltrexone

A systematic review (122 RCTs, one cohort study; 22,803 people) comparing naltrexone (either oral or injection) to placebo found patients treated with naltrexone were significantly less likely to return to any drinking (21 trials) or heavy drinking (23 trials), and had significantly fewer drinking days (19 trials), or heavy drinking days (11 trials), and had fewer drinks per drinking day (11 trials) (Jonas et al., 2014). The review did not report results of head-to-head comparisons of oral versus injectable naltrexone; however, results of the meta-analysis only found significant associations with return to any or heavy drinking for 50 mg/day oral naltrexone versus placebo, but not for 100 mg/day oral or injectable naltrexone. The strength of evidence for oral naltrexone was considered “moderate” whereas the strength of evidence for injectable naltrexone was considered “low,” likely due to the limited number of studies assessing injectable naltrexone (four studies) compared with oral formulations (40 studies).

One meta-analysis (Donoghue et al., 2015) (27 RCTs; 4,199 people) that examined the efficacy of orally administered naltrexone found the risk of individuals returning to any drinking at approximately 3 months was reduced significantly for the naltrexone group, as was the risk of individuals relapsing to heavy drinking at 3 months. There was no statistically significant difference in the risk of discontinuing treatment for any reason.

A systematic review (four studies; 798 people; 273 diagnosed with a psychotic disorder) (Sawicka and Tracy, 2017) of orally administered naltrexone in individuals with both psychosis and alcohol use disorder, found most studies, including those that were more robust methodologically, concluded that people who received naltrexone had fewer drinking days and fewer heavy drinking days than people who received a placebo.

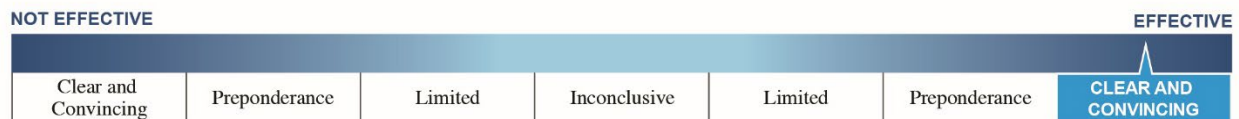
One retrospective cohort study compared median time to relapse among Veteran’s Affairs patients with alcohol use disorder treated with either oral or injectable naltrexone and found that median time to relapse was significantly longer for those treated with injectable versus oral naltrexone (150.5 days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

Disulfiram

A systematic review (122 RCTs, one cohort study; 22,803 people) with three RCTs (729 people) comparing disulfiram to placebo found there was no significant difference in return to any drinking and no statistically significant difference in percentage of drinking days between disulfiram and placebo (Jonas et al., 2014).

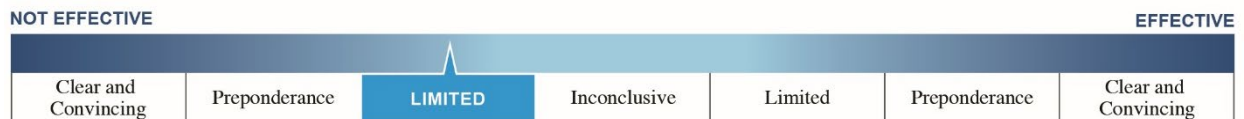
Summary of findings regarding the effectiveness of acamprosate and naltrexone for alcohol use disorder: There is clear and convincing evidence from three systematic reviews that acamprosate and naltrexone are more effective than a placebo or no treatment with regard to return to drinking, return to heavy drinking, percentage of drinking days, and percentage of heavy drinking days. One cohort study suggests that injectable naltrexone may result in longer time to relapse than oral naltrexone.

Figure 11. FDA-Approved Medications for Alcohol Use Disorder Versus Placebo or No Medication – Acamprosate and Naltrexone



Summary of findings regarding the effectiveness of disulfiram for alcohol use disorder: There is limited evidence from one systematic review that disulfiram does not reduce the risk that a person will return to drinking or have a lower percentage of drinking days.

Figure 12. FDA-Approved Medications for Alcohol Use Disorder Versus Placebo or No Medication – Disulfiram



Alcohol use disorder: Comparison of FDA-approved prescription medications for maintaining abstinence from alcohol

Acamprosate versus naltrexone

A systematic review (122 RCTs, one cohort study; 22,803 people) found that both acamprosate and oral naltrexone were associated with reduction in return to drinking but found no statistically significant difference between the two medications for return to any drinking (three studies; 800 participants), return to heavy drinking (four studies; 1141 people), and percentage of drinking days (two studies; 720 people) (Jonas et al., 2014).

Naltrexone versus disulfiram

A systematic review (Jonas et al., 2014) (122 RCTs, one cohort study; 22,803 people) included one RCT (254 participants) that directly compared naltrexone to disulfiram. The trial reported no statistically significant difference between disulfiram and naltrexone for number of subjects achieving total abstinence, the percentage of days abstinent, or the percentage of heavy drinking days.

A systematic review (four studies; 561 people; 128 diagnosed with a psychotic disorder) (Sawicka and Tracy, 2017) synthesized findings from two studies that compared orally administered naltrexone to disulfiram for treatment of alcohol use disorder and two studies that compared a combination of naltrexone and disulfiram to either naltrexone or disulfiram alone. None of the four studies found a statistically significant difference in the number of drinking days and the number of heavy drinking days.

Summary of findings regarding the comparative effectiveness of different medications used to treat alcohol use disorder: There is inconclusive evidence from three systematic reviews about the relative effectiveness of acamprosate, naltrexone, and disulfiram for treatment of alcohol use disorder. Findings from two studies suggest that acamprosate and naltrexone are equally effective. Studies that compared naltrexone and disulfiram did not find any differences in effects on abstinence from alcohol or heavy drinking days. No studies were identified that compared acamprosate to disulfiram.

Figure 13. Comparative Effectiveness of Different FDA-Approved Medications Used to Treat Alcohol Use Disorder – Acamprosate vs. Naltrexone vs. Disulfiram



Alcohol use disorder: Harms associated with use of FDA-approved prescription medications

Acamprosate

A systematic review (Jonas et al., 2014) (122 RCTs, one cohort study; 22,803 people) of 10 RCTs (sample sizes: 100 to 612 people) examining acamprosate found, compared with placebo, patients treated with acamprosate had a statistically significant higher risk of anxiety, diarrhea, and vomiting. No clinically significant differences were found for quality of life for acamprosate compared with placebo.

Naltrexone

Jonas et al. (2014) reported results from 10 trials (31 to 618 people) on health outcomes for naltrexone compared to placebo. Those treated with naltrexone had a statistically significant higher risk of dizziness, nausea, vomiting, aftertaste, blurred vision, confusion, constipation, drowsiness, dry mouth, loss of appetite, and tremors relative to persons who received a placebo. Six RCTs of naltrexone reported mortality rates; no study found more than one death in each treatment group.

One systematic review (Donoghue et al., 2015) (27 RCTs; 4,199 people) found there was a significantly greater risk of participants in the naltrexone group discontinuing treatment due to adverse events compared to placebo.

Disulfiram

Jonas et al. (2014) reported results from one study (254 people) comparing disulfiram combined with naltrexone, disulfiram combined with placebo, naltrexone alone, and placebo alone showed that patients who received disulfiram had side effects including aftertaste, blurred vision, confusion, constipation, drowsiness, dry mouth, loss of appetite, nausea, and tremors more often than patients in the placebo group. There were no statistically significant between-group differences for other adverse events.

Summary of findings regarding harms associated with FDA-approved prescription medications for alcohol use disorder: Use of FDA-approved prescription medications for alcohol use disorder is associated with mild to moderate side effects, including aftertaste, anxiety, blurred vision, confusion, constipation, diarrhea, dizziness, drowsiness, dry mouth, loss of appetite, nausea, tremors, and vomiting.

Alcohol use disorder: Effects of utilization management on use of FDA-approved prescription medications for alcohol use disorder and outcomes

No studies were identified that assessed the impact of utilization management on use of FDA-approved prescription medications for alcohol use disorder or treatment outcomes.

Alcohol use disorder: Counseling plus FDA-approved prescription medications versus medication alone

Acamprosate

One RCT (Wolwer et al., 2011) compared the rate of drinking relapse among 371 recently abstinent alcohol-dependent patients who were randomized to receive 6 months of treatment with either acamprosate and treatment as usual, acamprosate plus counseling, or placebo plus counseling. At the 6-month follow-up there were no statistically significant differences in the rate of relapse between the three study groups.

Acamprosate and/or Naltrexone

One large-scale multisite RCT, the COMBINE Study (Anton et al., 2006), compared percent days abstinent from alcohol consumption and time to first heavy drinking day among recently abstinent persons with a diagnosis of primary alcohol dependence²⁶ who were randomized to nine study arms: eight groups received medical management²⁷ plus 16 weeks of treatment with naltrexone, or acamprosate, or both medications, and/or placebo, with or without an intensive counseling intervention²⁸, and the ninth group was assigned to receive the counseling intervention alone with no pills and, therefore, no medical management.

Although all study groups showed a substantial reduction in drinking at the end of the 16-week study period compared to baseline (73.1% vs. 25.2% days abstinent), the only significant difference in percent days abstinent between the study interaction groups was observed for the naltrexone by naltrexone plus counseling interaction ($p=0.009$). Participants receiving placebo and no counseling had the lowest mean percent days abstinent (75.1%) compared with either naltrexone alone (80.6%) or counseling alone (79.2%). Only the comparison of naltrexone alone (with medication management) versus placebo was statistically significant for percent days abstinent (effect size 0.22 [97.5% CI: 0.03 to 0.40]). At the end of the 12-month follow-up period, the naltrexone by counseling interaction for percent days abstinent was no longer significant; however, the naltrexone plus counseling exhibited the highest mean percent days abstinent out of all study groups (67.3%) when adjusted for clinical center and baseline drinking (Anton et al., 2006; Donovan et al., 2008).

Anton et al. (2006) also assessed the time to first heavy drinking day at the end of the 16-week study period. No significant effects were observed for any of the groups who received acamprosate or any of the groups that included the counseling intervention; only the group who received naltrexone alone exhibited a significantly reduced risk of returning to one day of heavy drinking over the study period as compared with persons who received placebo (hazard ratio 0.78 [97.5% CI: 0.63 to 0.97]). At the 12-month follow-up assessment no groups exhibited a significant reduction in risk of returning to heavy drinking (Anton et al., 2006; Donovan et al., 2008).

²⁶ As defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*

²⁷ Medical management was delivered over nine in-person sessions with licensed health care professionals (e.g., physicians or nurses) during which patients received advice regarding abstinence, education about their medications, and a medication adherence plan. After the first appointment patients were asked about adherence barriers, adverse effects, and overall functioning.

²⁸ The counseling intervention was delivered over twenty 50-minute sessions with licensed behavioral health specialists and integrated aspects of cognitive behavioral therapy, 12-step facilitation, motivational interviewing, and support system involvement. The content of the sessions was tailored to the patient's individual needs.

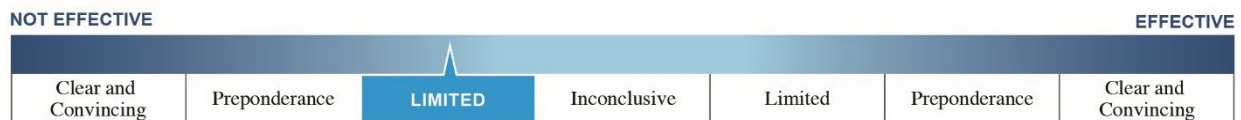
Ancillary and subgroup analyses of the primary COMBINE study cohort assessing the likelihood of reducing drinking frequency over time (Gueorguieva et al., 2010) and drinking abstinence among persons with frequent drinkers in their close social network (Worley et al., 2015) found that counseling plus naltrexone (but not acamprosate) was more effective than naltrexone alone. In contrast, ancillary and subgroup analyses of assessing secondary drinking measures (e.g., number of drinking days, days of paid work), quality of life outcomes (LoCastro et al., 2009), or baseline drinking habits (Gueorguieva et al., 2012) have not observed any additional benefit of treatment with medication (naltrexone or acamprosate) plus counseling beyond those effects provided with the medications alone or counseling alone.

Disulfiram

CHBRP did not identify any studies that compared receipt of disulfiram alone to receipt of disulfiram plus behavioral counseling for treatment of alcohol use disorder.

Summary of findings regarding the effects of medication plus counseling versus medication alone for alcohol use disorder: There is limited evidence from two RCTs that treatment for alcohol use disorder with medication plus counseling does not confer a significant benefit beyond treatment with medications alone, or medication with minimal counseling, on abstinence from drinking or time to heavy drinking day. There is insufficient evidence to assess effects on other outcomes, such as mortality, psychiatric outcomes, HIV risk behaviors, or birth outcomes because the studies did not report findings for these outcomes. The two studies that CHBRP identified examined the combination of acamprosate or naltrexone and counseling; CHBRP did not identify any studies that assessed the differential effectiveness of the combination of disulfiram and counseling compared with disulfiram alone.

Figure 14. Counseling Plus Medication vs. Medication Alone for Alcohol Use Disorder



Tobacco Use Disorder Treatments

Tobacco use disorder: FDA-approved prescription medications versus placebo or no medication

Nicotine replacement therapy

Two systematic reviews (Hartmann-Boyce et al., 2018; Patnode et al., 2015) found that nicotine replacement therapy is associated with greater likelihood of smoking cessation than placebo or psychotherapy alone. These systematic reviews included RCTs of nicotine inhalers and nicotine nasal spray, the two forms of nicotine replacement therapy for which a prescription is required, as well nicotine patches, gum, and lozenges, which are available without a prescription.

A systematic review (Hartmann-Boyce et al., 2018) (136 studies) comparing any type of nicotine replacement therapy and a placebo or non-nicotine replacement therapy control group concluded that there is high-quality evidence that nicotine replacement therapy increases quit rates at six months or longer in adults. The systematic review (131 trials, 133 comparisons; 64,600 people) found that each of the six forms of nicotine replacement therapy studied (gum, patch, inhalator, tablets/lozenges, intranasal spray, oral spray) significantly increased the rate of cessation compared to placebo or no nicotine replacement therapy. Pooled estimates from four RCTs of nicotine inhalers indicate that people who were treated with nicotine inhalers were 1.9 times as likely to abstain from smoking as people who received a

placebo. Pooled estimates from four RCTs of nicotine nasal spray indicate that people treated with nicotine nasal spray were twice as likely to abstain from smoking as people who received a placebo.

A systematic review of reviews (54 systematic reviews) (Patnode et al., 2015) comparing any type of nicotine replacement therapy with placebo or no nicotine replacement therapy (nine reviews; 51,265 people). Four of the RCTs included in these systematic reviews examined nicotine inhalers and four examined nicotine nasal spray. The authors concluded that all forms of nicotine replacement therapy, including inhalers and nasal spray, significantly increased the rate of smoking cessation compared with placebo or no nicotine replacement therapy. Participants who received some type of nicotine replacement therapy were 1.6 times more likely to achieve abstinence at 6 months or longer compared with participants in a control group. Seventeen percent of persons who received any form of nicotine replacement therapy abstained from smoking for 6 months or more versus 10% of people who received a placebo or no nicotine replacement treatment.

Six of the RCTs included in these systematic reviews included in Patnode et al. (2015) review of reviews directly compared different types of nicotine replacement therapy (e.g., patch versus nasal spray). None of these RCTs found statistically significant differences in rates of abstinence from smoking, which suggests that the benefits of forms of nicotine replacement therapy for which a prescription is required are similar to those of forms of nicotine replacement therapy that are available without a prescription. Nine trials (n=4,664) that compared people who received two types of nicotine replacement therapy to people who received a single type of nicotine replacement therapy were 1.4 times more likely to abstain from smoking.

Bupropion SR

In a systematic review of reviews (54 systematic reviews) (Patnode et al., 2015) (three reviews; 13,728 people) found a statistically significant benefit to taking bupropion SR versus taking a placebo or no pharmacotherapy on smoking abstinence at 6 months.

A meta-analysis (six trials; sample size: 5–61) comparing bupropion SR to placebo in people with tobacco use disorder who also have a serious mental illness, found bupropion SR more effective (defined as self-reported sustained smoking cessation, verified biochemically at the longest reported time-point) than placebo (Roberts et al., 2016).

One small RCT of 65 pregnant women (Nanovskaya et al., 2017) found individual smoking cessation counseling along with bupropion SR sustained release increased smoking cessation rates and reduced cravings and total nicotine withdrawal symptoms during the treatment period. However, there was no significant difference in abstinence rates between groups at the end of bupropion treatment and at the end of pregnancy, perhaps because of the small sample size.

Varenicline

A systematic review (Cahill et al., 2016) found high-quality evidence that participants who received varenicline at standard dose (1.0 mg twice a day) had between a two- and a three-fold chance of successful long-term smoking cessation compared to participants who received a placebo (27 trials, 12,625 people). Varenicline at lower or variable doses was also shown to be effective (four trials, 1,266 people) and lower dose regimens reduced the incidence of adverse events (four trials).

These findings were consistent with those of a previous systematic review of reviews (Patnode et al., 2015). The authors conducted a meta-analysis and concluded that participants who received varenicline were twice as likely to abstain from smoking six months or more after treatment ended than participants who received a placebo (14 trials, 6,166 people).

A systematic review (three RCTs; 744 people) on the effectiveness of varenicline in smokeless tobacco cessation found significantly higher 7-day point prevalence of smokeless tobacco abstinence at 12 weeks

(48% vs. 33%) but not at 26 weeks (49% vs. 39%) among participants who received varenicline than among participants who received a placebo (Schwartz et al., 2016).

One small RCT (60 participants) of clinically stable adult patients with bipolar disorder found significantly more subjects quit smoking with varenicline than with placebo (48.4% vs. 10.3%) at 3 months. At the end of non-treatment follow-up at 6 months, a higher percentage of varenicline-treated subjects remained abstinent compared to placebo (19.4% vs. 6.9%), while psychopathology scores remained stable (Chengappa et al., 2014).

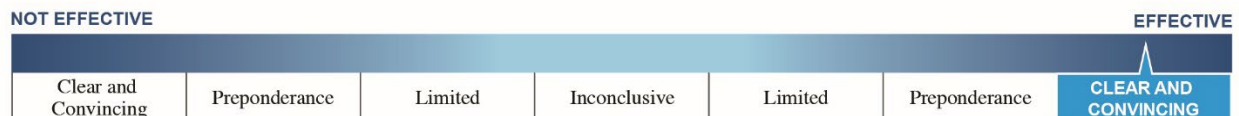
One small RCT (33 participants) found varenicline to be effective for increasing smoking abstinence rates in smokers with alcohol abuse or dependence. This study showed varenicline may also decrease alcohol consumption in this population of smokers (Hurt et al., 2018).

Three meta-analyses found varenicline appears to be significantly more effective than placebo in assisting with smoking cessation and reduction in people with severe mental illness (Ahmed et al., 2018; Roberts et al., 2016; Wu et al., 2016). A meta-analysis (eight studies; 398 people) comparing varenicline to placebo in people found that persons with severe mental illness who received varenicline were more likely to abstain from smoking and smoked fewer cigarettes per day than persons with severe mental illness who received a placebo (mean reduced daily cigarettes was 6.39) (Wu et al., 2016). Another meta-analysis (five RCTs; sample size: 5–128) comparing varenicline to placebo in people with tobacco use disorder who also have a mental illness, found varenicline more effective (defined as self-reported sustained smoking cessation, verified biochemically at the longest reported time-point) than placebo (Roberts et al., 2016).

A meta-analysis (four RCTs; 239 people) of patients with schizophrenia, found varenicline treatment significantly reduced the number of cigarettes consumed per day and expired carbon monoxide levels relative to placebo (Ahmed et al., 2018). One systematic review found varenicline is not superior to placebo for smoking cessation in people with schizophrenia (Kishi and Iwata, 2015). Moreover, there was no significant difference in the discontinuation rate due to all causes, clinical deterioration, or side effects between varenicline and placebo (Kishi and Iwata, 2015). The difference between Kishi and Iwata (2015) conclusion and those of the other three meta-analyses reflect differences in the RCTs included in the meta-analysis. Kishi and Iwata only included RCTs that enrolled persons with schizophrenia whereas Wu et al (2016) and Roberts et al (2016) also included RCTs that enrolled people with bipolar disorder. Kishi et al (2015) also did not include an RCT that Ahmed et al (2018) included in their meta-analysis because the RCT had not been published at the time Kishi and Iwata completed their analysis.

Summary of findings regarding the effects of FDA-approved prescription medications versus placebo or no medication for treatment of tobacco use disorder: There is clear and convincing evidence from one systematic review of reviews, nine systematic reviews, and three RCTs that people who use nicotine replacement therapy, bupropion SR, or varenicline have higher rates of smoking cessation than people who receive a placebo or no medication for smoking cessation.

Figure 15. FDA-Approved Medications for Tobacco Use Disorder Versus Placebo or No Medication



Tobacco use disorder: Comparison of FDA-approved prescription medications for maintaining abstinence from tobacco

Nicotine replacement therapy versus bupropion SR

A systematic review of reviews (Patnode et al., 2015) identified two systematic reviews of studies that compared nicotine replacement therapy to bupropion SR. Neither review found a statistically significant difference in the rates of smoking cessation 6 months or more after treatment ended, suggesting that the effectiveness of nicotine replacement therapy and bupropion SR do not differ (eight RCTs; 4,086 people).

Nicotine replacement therapy versus varenicline

There is evidence that varenicline is more effective than nicotine replacement therapy (Baker et al., 2016; Cahill et al., 2016; Chang et al., 2016; Rohsenow et al., 2017).

A systematic review (Cahill et al., 2016) found moderate evidence that varenicline is more effective than nicotine replacement therapy as measured by point prevalence abstinence at 24 weeks (eight RCTs; 6,264 people). Participants who received varenicline were 1.25 times (95% CI: 1.14 to 1.37) more likely to abstain from smoking at 24 weeks than participants who received nicotine replacement therapy.

Three studies not included in the systematic reviews found varenicline more effective than nicotine patch for tobacco cessation (Chang et al., 2016; Gray et al., 2015; Rohsenow et al., 2017). One comparative effectiveness study (Chang et al., 2016) (11,968 participants), found varenicline was associated with greater odds of abstinence compared with nicotine replacement patch, at 1 week, 1 month, and 6 months after initiation of treatment. Varenicline was also associated with higher odds of abstinence in 6 months, in both smokers with severe dependence on tobacco and smokers with light/moderate dependence. A 4-week RCT (140 females) showed that relative to the nicotine patch, varenicline more than doubled the odds of abstinence upon completion of treatment, although this difference diminished at post-treatment follow-up and was no longer statistically significant (Baker et al., 2015). Another RCT (Rohsenow et al., 2017; 137 people) found varenicline improved the odds of achieving at least 3 months of smoking abstinence in smokers with substance use disorders who were trying to stop, compared with transdermal nicotine patches and that the effect was independent of whether a person had a history of major depressive disorder.

Two studies found no difference in smoking abstinence or quit rates between nicotine replacement therapy and varenicline. One RCT (1,086 people) found that treatment, including 12 weeks of open label treatment with nicotine patch, varenicline, or combination nicotine replacement therapy (nicotine patch plus nicotine lozenges) produced no significant differences in biochemically confirmed rates of smoking abstinence at 26 or 52 weeks (Baker et al., 2016). One RCT (737 people, including those with medical and psychiatric comorbidities) found that participants who received varenicline were more likely to be continuously abstinent from smoking at 22 weeks after initiation of treatment than participants who received nicotine replacement monotherapy or combination nicotine replacement therapy, but that the difference was no longer statistically significant at 52 weeks following initiation of treatment (Tulloch et al., 2016).

Bupropion SR versus varenicline

A systematic review (Cahill et al., 2016) found high-quality evidence (five RCTs; 5877 people) that varenicline is superior to bupropion for sustained abstinence at 6 months post treatment.

Another systematic review (Roberts et al., 2016) found both varenicline and bupropion had superior treatment efficacy to placebo and were not different from each other. In the review, one trial found when comparing varenicline with bupropion, in terms of treatment efficacy, there was no significant advantage for one treatment over the other.

Nicotine replacement therapy versus nicotine replacement therapy plus bupropion SR

Thurgood et al.'s (2016) systematic review of RCTs of smoking cessation treatment for persons who have both tobacco use disorder and another SUD, identified two RCTs (253 participants) that compared receipt of nicotine replacement therapy alone to receipt of nicotine replacement therapy plus bupropion SR. The RCTs found no statistically significant difference in point prevalence and continuous abstinence from smoking between the two groups.

Varenicline versus nicotine replacement therapy plus varenicline

One meta-analysis (three RCTs; 904 participants) examined both early outcomes (rate of abstinence from tobacco assessed before or at the end of treatment) and late outcomes (assessed after the end of the treatment). The authors identified one RCT that found that nicotine replacement therapy plus varenicline is more effective than varenicline alone, if nicotine patch treatment is administered prior to a participant's target date for tobacco cessation (Chang et al., 2015). Two RCTs in which nicotine patch treatment was not administered prior to a participant's target quit date found no statistically significant difference in abstinence rates before, at, or after the end of treatment.

Varenicline versus bupropion SR plus varenicline

One systematic review (Vogeler et al., 2016) of three prospective clinical trials and one retrospective outcome research study (N=1,193 people) found combination bupropion SR and varenicline displayed greater efficacy in smoking cessation than varenicline monotherapy as measured by 4-week smoking abstinence and prolonged abstinence (continuous abstinence from week 2 to weeks 12 and 26 of the study). One retrospective study included in the systematic review found that combination bupropion SR and varenicline was associated with a higher rate of continuous abstinence at 52 weeks than varenicline monotherapy (55% vs. 32%) but this finding was not replicated in the prospective trials.

Summary of findings regarding the comparative effectiveness of different medications used to treat tobacco use disorder: The preponderance of evidence from studies that have compared nicotine replacement therapy to varenicline suggests that varenicline is more effective than nicotine replacement therapy. RCTs that have compared nicotine replacement therapy to bupropion SR have found no statistically significant differences in tobacco cessation outcomes. There is limited evidence that combining varenicline with bupropion SR may improve abstinence from smoking relative to varenicline alone.

Figure 16. Comparative Effectiveness of Different FDA-Approved Medications Used to Treat Tobacco Use Disorder – Varenicline vs. Nicotine Replacement Therapy (Favors Varenicline)

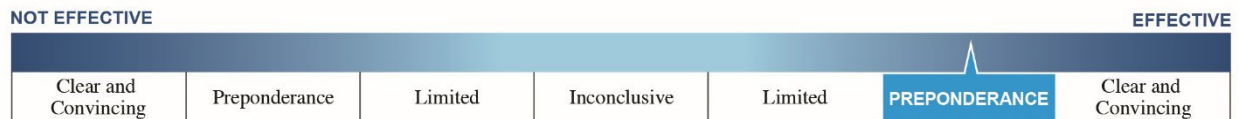


Figure 17. Comparative Effectiveness of Different FDA-Approved Medications Used to Treat Tobacco Use Disorder – Nicotine Replacement Therapy vs. Bupropion SR



Tobacco use disorder: Harms associated with use of FDA-approved prescription medications

Nicotine replacement therapy

One Cochrane review (Hartmann-Boyce et al., 2018) found that persons who received nicotine replacement therapy had higher odds of chest pains or palpitations relative to control. However, the authors found that chest pains and palpitations were rare in both groups and serious adverse events were extremely rare.

One systematic review (Coleman et al., 2015) (eight studies; 2,199 participants) found no statistically significant differences in birth outcomes, including rates of miscarriage, stillbirth, preterm birth (less than 37 weeks), low birthweight, mean birthweight, admissions of babies to neonatal intensive care or neonatal deaths. One RCT (1,050 participants) of women whose infants were followed to two years of age, found those born to women who had been randomized to NRT were more likely to have healthy development. (Coleman et al., 2015).

In a systematic review of possible serious adverse health effects of nicotine replacement therapy, Lee and Farris (2017) evaluated 34 epidemiological studies and clinical trials regarding the effect of exposure to nicotine replacement therapy on risk of cancer, reproductive/developmental effects, cardiovascular disease, stroke and/or other serious adverse health effects. The authors found many limitations in the evidence, most significantly short-term exposure (≤ 12 weeks) and follow-up to NRT product use in most of the studies, failure to control for changes in smoking behavior following NRT use, and limited information on serious adverse health effects by type of NRT product used. The only serious adverse health effects associated with NRT exposure was an increase in respiratory congenital abnormalities reported in one study. Limited evidence indicated a *lack* of effect between NRT exposure and serious adverse health effects for CVD and various reproduction/developmental endpoints. For cancer, stroke and other serious adverse health effects, the evidence was insufficient.

Bupropion SR

In a systematic review of reviews (54 systematic reviews) (Patnode et al., 2015), two reviews examined the harms associated with bupropion SR. One review (Mills et al., 2014) (sample size: 10,402 people) suggested no significant increased risk of any cardiovascular event for bupropion SR versus placebo. Another study (Hughes et al., 2014; n=9,631) found no statistically significant increase risk in the rate of serious adverse events, serious psychiatric events, or serious cardiovascular events among participants who received bupropion sustained SR versus placebo. There were 10 cases of seizures within seven trials that comprised between 100 and 502 individuals receiving bupropion SR (over 13,000 total participants).

Varenicline

A Cochrane review (Cahill et al., 2016) found high-quality evidence that the main adverse effect of varenicline was nausea (32 studies; 14,963 participants), which was generally mild to moderate and diminished over time. The authors also found that people who used varenicline were not at greater risk of neuropsychiatric adverse events, such as depressed mood, agitation, suicidal ideation, and suicidal behavior than persons who did not use varenicline.

One meta-analysis comparing nicotine replacement therapy plus varenicline to varenicline alone (3 RCTs; 904 participants) found the most common adverse events were nausea, insomnia, abnormal dreams, and headache, but there were no significant differences in odds of these adverse events between nicotine replacement therapy plus varenicline and varenicline alone (Chang et al., 2015).

Another meta-analysis (Schwartz et al., 2016) comparing varenicline to placebo for smokeless tobacco cessation found no statistically significant differences in adverse events reported, including nausea, sleep

disturbance, and mood disorders but interpretation is limited by high heterogeneity across studies included in the meta-analysis.

One systematic review of RCTs found there was no statistically significant difference in risk of neuropsychiatric adverse events, including risk of suicide or attempted suicide, suicidal ideation, depression, irritability, aggression, or death, between participants who received varenicline and participants who received a placebo (39 RCTs; 10,761 participants). Varenicline was associated with an increased risk of sleep disorders, insomnia, abnormal dreams, and fatigue, but a reduced risk of anxiety (Thomas et al., 2015).

Summary of findings regarding harms associated with FDA-approved prescription medications for tobacco use disorder: Use of FDA-approved prescription medications for tobacco use disorder is not associated with increased risk of serious adverse events, including poor birth outcomes, cancer, cardiovascular disease, stroke, and neuropsychiatric events. Varenicline is associated with mild to moderate side effects, including abnormal dreams, fatigue, headache, insomnia, nausea, and sleep disorders.

Tobacco use disorder: Effects of utilization management on use of FDA-approved prescription medications for tobacco use disorder and outcomes

Findings from one retrospective cohort analysis study (sample size: 15,597 people) found that prior authorization and step-therapy requirements for varenicline reduced the likelihood that people would fill a prescription for any pharmacotherapy for tobacco use disorder. Among persons enrolled in health plans included in the study, 63.9% of persons who had a claim for varenicline rejected due to a requirement for prior authorization filled a prescription for any pharmacotherapy for tobacco use disorder. Among those who faced a step therapy requirement, 46% filled a prescription for any pharmacotherapy for tobacco use disorder. This study also found that people who had higher out-of-pocket costs for pharmacotherapy for tobacco use disorder had lower odds of filling a prescription. There was a statistically significant reduction in the odds of filling a prescription for all levels of out-of-pocket costs above \$0 to \$5 (Zeng et al., 2011).

One retrospective cohort study (15,452 participants) found that among Medicare beneficiaries newly initiated on varenicline, greater out of pocket cost was associated with lower adherence, as measured by the proportion of days for which a person had medication available, and lower odds of refilling a prescription for varenicline (Suehs et al., 2014).

Summary of findings regarding the effects of utilization management for FDA-approved medications for tobacco use disorder: There is limited evidence that higher cost sharing is associated with lower rates of adherence to varenicline. This finding suggests that requiring health plans to place varenicline in the lowest tier on its formulary, which SB 854 would require, may improve adherence to varenicline. CHBRP did not identify any studies of effects of utilization management or cost sharing on use of nicotine replacement therapy or bupropion SR.

Figure 18. Impact of Utilization Management on Use of FDA-Approved Prescription Medications for Tobacco Use Disorder



Tobacco use disorder: Counseling plus FDA-approved prescription medications versus medication alone

Nicotine Replacement Therapy and Bupropion

Medication and individual counseling versus medication alone: CHBRP identified one Cochrane review of individual counseling interventions²⁹ for smoking cessation that included an evaluation of the effectiveness of combined medications and individual counseling as compared with medications alone (NRT or bupropion). In a meta-analysis of six RCTs (2,662 participants), Lancaster et al. (2017) found that persons randomized to medication interventions offered in conjunction with individual counseling were almost 25% more likely to achieve smoking abstinence as compared with persons randomized to medication interventions alone (RR 1.24; 95% CI: 1.01 to 1.51). Quit rates in the six included studies ranged from 3 to 32 percent in the combined intervention groups and 5% to 26% in the medication alone control groups. Five of the trials used some form of NRT as the medication component and one trial evaluated bupropion, but effect modification by medication type was not systematically assessed.

Another meta-analysis (eight RCTs; 2,048 participants) nested within the same Cochrane review of individual counseling for smoking cessation demonstrated that, when provided as an adjunct to medication, persons receiving higher-intensity individual counseling were about 25% more likely to achieve smoking abstinence when compared with persons who were randomized to lower-intensity individual counseling interventions (RR 1.26; 95% CI: 1.04 to 1.52).

Medication and group counseling versus medication alone: CHBRP identified one Cochrane review of group-based counseling interventions³⁰ for smoking cessation that included an evaluation of the effectiveness of combined medications and group counseling as compared with medications alone (NRT or bupropion). In a meta-analysis of five RCTs (1,523 participants), Stead et al. (2017) found that persons randomized to medication interventions offered in conjunction with group counseling did not demonstrate a significant difference in smoking abstinence at 6 months as compared with persons who were randomized to medication interventions alone (quit rates 8-30%) (RR 1.11 [95% CI: 0.93, 1.33]). Three trials used some form of NRT as the medication component and two trials evaluated bupropion, but effect modification by medication type was not systematically assessed.

Medication and any counseling versus medication alone: In a Cochrane review of 53 RCTs or quasi-RCTs (25,375 participants), Stead et al. (2016) evaluated the effectiveness of combined medications (NRT, varenicline, bupropion, cytosine, or nortriptyline) and behavioral counseling (individual or group) for smoking cessation as compared with control groups who received usual care with no medication, brief advice, or limited behavioral interventions alone (i.e., pamphlets). A meta-analysis of 52 of the 53 included studies (19,488 participants) found a statistically significant benefit of combined medication and counseling as compared with controls on smoking cessation at 6 months or more (RR 1.83 [95% CI: 1.68, 1.98]). Quit rates in the included studies ranged from 2% to 50% among participants who received combined medication and counseling and 0 to 36 percent among controls. The majority of studies in the meta-analysis offered between four and eight sessions of in-person counseling and most provided one or more types of NRT, or bupropion, as the medication component. Although the differential impacts on smoking cessation were not assessed by type of medication in this review, the authors note that other Cochrane reviews evaluating the effect of NRT alone versus control (Hartmann-Boyce et al., 2018) or bupropion alone versus control (Hughes et al., 2014) for smoking cessation observed smaller effect sizes (RR 1.55; 95% CI: 1.49 to 1.61, and RR 1.62; 95% CI: 1.49 to 1.76, respectively) than for combined medication and behavioral counseling.

²⁹ Defined by Lancaster et al. (2017) as at least one session with face-to-face contact lasting more than 10 minutes between a smoker and a counsellor trained in assisting smoking cessation.

³⁰ Defined by Stead et al. (2017) as scheduled group meetings where smokers received some form of behavioral intervention, such as information, advice and encouragement or cognitive behavioral therapy (CBT) delivered over at least two sessions.

Varenicline

CHBRP did not identify any studies that compared receipt of varenicline alone to receipt of varenicline plus behavioral counseling for treatment of tobacco use disorder.

Summary of findings regarding the effects of medication plus counseling versus medication alone for tobacco use disorder: There is limited evidence from three systematic reviews about the differential effect of combined counseling plus medication versus medication alone on smoking abstinence. Findings from two studies (one of combined counseling/medication interventions in general and one of individual counseling/medication interventions) suggest that interventions with both a medication and counseling component are more effective than medications alone for the treatment of tobacco use disorder, but one systematic review of group counseling for tobacco use disorder found that counseling conferred no additional benefit beyond medication. All three systematic reviews primarily included studies of NRT and bupropion; no studies were identified that compared varenicline and counseling versus varenicline alone.

Figure 19. Counseling Plus Medication versus Medication Alone for Tobacco Use Disorder



Summary of Findings

Table 5 summarizes evidence of the effectiveness of FDA-approved prescription medications for SUD when prescribed and used as directed, as well as the evidence about their use in combination with behavioral therapies. Evidence is reported separately for (1) prescription medication versus a placebo or no treatment, (2) comparison of different prescription medications used to treat SUD, and (3) the impact of counseling plus medications to treat SUD. Findings differ substantially by comparison.

There is limited or clear and convincing evidence from multiple RCTs that, with the exception of orally administered naltrexone for opioid use disorder and disulfiram for alcohol use disorder, medications are more effective than a placebo or no treatment for the treatment of opioid use disorder, alcohol use disorder, or tobacco use disorder. There is also limited evidence that lofexidine is effective in managing opioid withdrawal symptoms compared to placebo, but insufficient evidence about its effectiveness relative to generic clonidine. Evidence regarding the relative effectiveness of different medications for SUD differs depending on the medications that are compared to one another. There is a preponderance of evidence that combining methadone treatment with counseling is effective for opioid use disorder. There is limited evidence that the addition of counseling to buprenorphine or naltrexone (oral or injectable) is effective in treatment opioid use disorder and limited evidence that is an effective treatment for tobacco use disorder. There is limited evidence that this treatment combination is not effective for alcohol use disorder.

Most harms associated with medications for SUD are mild with the exception of naltrexone. This medication is associated with a higher rate of overdose prior to initiation of treatment because users must be abstinent from opioids before starting treatment whereas methadone and buprenorphine treatment can be initiated before a person is weaned off other opioids. There is insufficient evidence to determine the impact of prohibiting prior authorization and step therapy and requiring that all FDA-approved pharmacotherapies for SUD be placed on the lowest tier of a health plan’s formulary, with the exception of some evidence showing that higher cost sharing reduces certain medications for tobacco use disorder.

Table 5. Summary of Evidence of Medical Effectiveness of FDA-Approved Medications with or without Counseling for Substance Use Disorders (SUD) and the Impact of Utilization Management

Type of SUD	Medication vs. Placebo or No Treatment	Comparison of Different Medications	Medication plus Counseling vs. Medication	Impact of Utilization Management
Opioid Use Disorder	<p>Clear and convincing evidence favors methadone, buprenorphine (including buprenorphine-naloxone)</p> <p>Limited evidence that injectable naltrexone is effective</p> <p>Limited evidence that orally administered naltrexone is not effective</p> <p>Limited evidence that lofexidine is effective for withdrawal symptom management</p>	<p>Limited evidence favoring buprenorphine (including buprenorphine-naloxone) relative to extended-release naltrexone, and lofexidine for withdrawal symptom management</p> <p>Insufficient evidence about the impact of lofexidine relative to clonidine for withdrawal symptom management</p> <p>Inconclusive evidence about the impact of methadone relative to buprenorphine (including buprenorphine-naloxone)</p> <p>Inconclusive evidence that one route of naloxone administration is more effective than another</p>	<p>Preponderance of evidence that counseling plus methadone is effective</p> <p>Limited evidence that counseling plus buprenorphine or naltrexone (oral or injectable) is effective</p>	Insufficient evidence
Alcohol Use Disorder	<p>Clear and convincing evidence favors acamprosate and naltrexone</p> <p>Limited evidence that disulfiram is not effective</p>	Inconclusive evidence	Limited evidence that medication plus counseling is not effective	Insufficient evidence
Tobacco Use Disorder	Clear and convincing evidence favors prescription medications	<p>Preponderance of evidence favors varenicline over nicotine replacement therapy</p> <p>No difference between nicotine replacement therapy and bupropion</p>	Limited evidence that medication plus counseling is effective	Limited evidence that higher cost sharing reduces use of varenicline.

Source: California Health Benefits Review Program, 2020

BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

As discussed in the *Policy Context* section, SB 854 would require DMHC-regulated health plans and CDI-regulated health policies with commercial/CalPERS enrollees that include an outpatient pharmacy benefit to provide lowest tier on-formulary coverage for outpatient prescription medications approved by the FDA for treatment of substance use disorders (SUDs). SB 854 exempts DMHC-regulated plans enrolling Medi-Cal beneficiaries from compliance with the mandate. For coverage of those medications, SB 854 would prohibit utilization management as detailed in the *Policy Context* section. In addition, for coverage of those medications and for coverage of in-conjunction behavioral counseling, SB 854 would prohibit prior authorization protocols.

Commercial/CalPERS enrollees account for approximately 61.5% of enrollees in DMHC-regulated plans and CDI-regulated policies that would be subject to SB 854. A supermajority of these enrollees (93.8%) are in plans or policies that include outpatient pharmacy benefit coverage. The remaining 6.2% have benefit coverage considered fully compliant with this mandate, as those DMHC-plans and CDI-policies would not have to change any provisions of their coverage in response to SB 854. For more detail on the presence or absence of a pharmacy benefit among DMHC-regulated plan and CDI-regulated policy enrollees, see CHBRP's *Estimates of Pharmacy Benefit Coverage in California for 2021*.³¹

This section reports the potential incremental impacts of SB 854 on estimated baseline benefit coverage, utilization, and overall cost. The estimates are based upon the following core assumptions, informed by existing claims data on practice patterns and use of substance use disorder treatments, the *Medical Effectiveness* section, and consultation with a context expert.³² CHBRP assumes that:

- Enrollees who gain compliant coverage due to SB 854 would experience care commensurate with the typical pattern of care for enrollees who have currently compliant coverage. There would be no difference in terms of dosing or frequency of refills, and patient needs would remain constant. In other words, CHBRP assumes that enrollees who gain coverage would have similar patterns of medical need compared to those who currently have coverage.
- Reductions in cost sharing due to movement of a drug onto tier 1 of the formulary will shift use to more expensive medications, as postmandate, they would be required to be covered without prior authorization or step therapy requirements.
- Postmandate, in the absence of prior authorization or step therapy requirements for FDA-SUD medications and in the absence of prior authorization for in-conjunction behavioral counseling, CHBRP estimates that utilization of both will increase, varying by medication and accepted practice patterns as confirmed by the content expert.

See Appendix C for a detailed chart of the utilization increases per medication and counseling services.

Currently, approximately 5.0% of commercial/CalPERS enrollees with alcohol use disorder, 13.0% with opioid use disorder, and 5.4% with tobacco use disorder take FDA-approved medications to treat their conditions. Low utilization of medications to treat all three conditions is linked to many factors other than the terms and conditions of benefit coverage, such as provider practice patterns, enrollee willingness to enter treatment, and other options available to enrollees that do not rely on prescription medications (e.g., over-the-counter nicotine replacement therapy, Alcoholics Anonymous). These other factors are unlikely to change due to SB 854.

For further details on the underlying data sources and methods, please see Appendix C.

³¹ Available at http://chbrp.org/other_publications/index.php

³² Personal communication on 2/13/20 with Dr. Scott Steiger, Deputy Medical Director, Opiate Treatment Outpatient Program, University of California, San Francisco.

Baseline and Postmandate Benefit Coverage

Current benefit coverage was determined by a survey of the largest (by enrollment) providers of health insurance in California. Responses to this survey represent 92% of enrollees with commercial market health insurance that can be subject to state mandates.

Currently, 6.2% commercial/CalPERS enrollees have no outpatient pharmacy benefit coverage, and so have coverage that would not need to be altered under SB 854. However, 93.8% of these enrollees have benefit coverage that is in partial compliance with the mandate (see Table 1). All commercial/CalPERS enrollees currently have coverage for behavioral counseling in conjunction with prescribed medication for opioid use disorder, alcohol use disorder, or tobacco use disorder that is not subject to prior authorization protocols. Therefore, 100% of enrollees currently have benefit coverage that meets the behavioral counseling portion of the SB 854 mandate.

Existing benefit coverage varies by prescription medication for opioid use disorder, alcohol use disorder, and tobacco use disorder (see Table 6), but there is broad near-compliance with SB 854's requirements. On-formulary coverage is generally common and use of utilization management protocols is generally limited, such that SB 854's prohibitions regarding limited numbers of visits, days, scope, or duration - on coverage for outpatient medications - are unlikely to have an impact.

However, compliance with SB 854 would bring change (see Table 6). For example, 80% of commercial/CalPERS enrollees have on-formulary coverage for buprenorphine to treat opioid use disorder, but 0% of enrollees have this coverage in tier 1 of their prescription benefit. Additionally, 5% of enrollees have benefit coverage under which buprenorphine is subject to prior authorization, and 4% have benefit coverage that requires step therapy protocols before they can be prescribed buprenorphine.

Table 6. SB 854 Medication-Specific Baseline Benefit Coverage for Commercial/CalPERS Enrollees, 2021

Medication	% of enrollees with on-formulary medication coverage	% of enrollees with on-formulary medication coverage that is...		
		...on tier 1 of the formulary (commonly the tier for generics)	...Subject to prior authorization requirements	... Subject to step therapy protocols
<i>Opioid Use Disorder</i>				
Buprenorphine	80%	0%	5%	4%
Methadone	82%	0%	1%	4%
Naloxone	82%	0%	0%	4%
Naltrexone - Oral	80%	0%	0%	0%
Naltrexone – IM	35%	0%	5%	0%
Combination Buprenorphine/ Naloxone	80%	0%	1%	0%
Lofexidine	19%	0%	33%	33%
<i>Tobacco Use Disorder</i>				
Nicotine – Inhaler	27%	6%	0%	0%
Nicotine - Nasal Spray (a)	27%	6%	0%	0%
Varenicline	81%	60%	0%	0%
<i>Alcohol Use Disorder</i>				
Bupropion HCL SR	82%	76%	0%	0%
Acamprosate	82%	63%	1%	0%
Naltrexone – Oral	82%	82%	0%	0%
Naltrexone – IM	35%	0%	5%	0%
Disulfiram	82%	82%	0%	0%

Source: California Health Benefits Review Program, 2020.

Notes: (a) Does not include over-the-counter medication purchases, which are not part of the formulary for commercial/CalPERS enrollees.

Postmandate, benefit coverage for all commercial/CalPERS enrollees will be fully compliant with the mandate. This means that all enrollees will have on-formulary benefit coverage for prescription medications for opioid use disorder, alcohol use disorder, and tobacco use disorder, and that those medications will be available on tier 1 of the formulary (for cost sharing similar to generics), and utilization management protocols will not apply.

Baseline and Postmandate Utilization

Baseline FDA-approved medication and counseling utilization for commercial/CalPERS enrollees were based on Milliman commercial claims and enrollment data for the state of California. For a full discussion of utilization baseline and postmandate calculations, please see Appendix C.

Currently, there are 6,278 commercial/CalPERS enrollees with alcohol use disorder who use prescription medication treatment by itself, and an additional 970 use medication treatment in conjunction with counseling (see Table 1). There are 8,514 commercial/CalPERS enrollees with opioid use disorder who use prescription medication treatment by itself, and an additional 911 use medication treatment in conjunction with behavioral counseling. Finally, 11,361 commercial/CalPERS enrollees with tobacco use disorder use prescription medication treatment by itself, and an additional 584 use medication treatment with counseling. This utilization estimate does not include enrollees who purchase over-the-counter medications for tobacco use disorder.

Due to the variance in baseline use by type of medication, CHBRP estimates variation in the resulting increase in the number of commercial/CalPERS enrollees who use prescription medication, either by itself or in conjunction with counseling. These detailed estimates were aggregated into Table 1 to show overall trends, but are shown in detail in Table 7 below.

Table 7. Utilization Baseline and Postmandate of Medication for Opioid Use Disorder, Alcohol Use Disorder, and Tobacco Use Disorder, 2021

	Baseline	Postmandate	Increase/ Decrease	Change Postmandate
	Number of Users	Number of Users		
Number of Enrollees with Substance Use Disorder Using Prescription Medication	26,153	36,348	10,196	39%
<i>Opioid Use Disorder</i>				
Buprenorphine	1,300	1,842	543	42%
Buprenorphine-Naloxone	5,468	8,640	3,171	58%
Naltrexone – Oral	553	699	146	26%
Naltrexone – IM	218	600	383	176%
Naloxone	65	90	25	39%
Naloxone Auto Injector	21	34	13	60%
Lofexidine	76	391	315	414%
Methadone (a)	813	813	0	0%
<i>Alcohol Use Disorder</i>				
Campral	648	899	251	39%
Antabuse	1,459	1,862	403	28%
Naltrexone – IM Oud	317	1,079	762	240%
Generic Naltrexone	3,854	5,116	1,262	33%
<i>Tobacco Use Disorder</i>				
Verenicline	3,827	4,728	901	24%
Burpropion	7,470	9,165	1,695	23%
Nicotine (b)	64	205	141	220%

Source: California Health Benefits Review Program, 2020.

Notes: (a) Available for OUD treatment only from federally licensed clinics, so no change in methadone utilization is projected. (b) Includes prescription only inhaler and nasal spray.

Postmandate, CHBRP estimates increases in the number of commercial/CalPERS enrollees using FDA-approved SUD medications, alone or with counseling.³³ CHBRP estimates an increase of 2,678 enrollees with alcohol who would use medication treatment, and another 317 who would use medication treatment and counseling services (Table 1). Postmandate, an additional 4,781 enrollees with opioid use disorder would use medication treatment, and another 472 who would use medication treatment and counseling services. Finally, an additional 2,737 enrollees with tobacco use disorder would use medication treatment postmandate, and another 134 who would also use medication treatment and counseling services. The increases in utilization are a combination of: (1) enrollees gaining entirely new benefit coverage through the new inclusion of the medication on-formulary, and (2) enrollees who at baseline had on-formulary benefit coverage increasing their current utilization due to the change to tier 1 or the elimination of step therapy protocols. Eliminating restrictions on days of coverage would have no impact, as these restrictions do not currently cause enrollees to delay or forego care.³⁴

For commercial/CalPERS enrollees with increases in benefit coverage that are the underlying cause of increases in utilization, there is variation by type of prescription medication, as shown in Table 6 in the Baseline and Postmandate Benefit Coverage subsection above. Some medications, though, are not used often by enrollees because of difficulty in the method of administration, including the nicotine nasal spray. With input from the content expert, CHBRP estimated the change in utilization per medication type. Some medications will increase at greater rates because they currently have higher cost than generic options, and when moved to tier 1 of the formulary under SB 854, providers will change their current prescribing practices to switch to these medications.³⁵ Use of the auto-injector method of medication administration is also expected to increase, as it is preferred but currently more expensive. Additionally, lofexidine coming to market later in 2020 will change current prescribing practices, as providers now use a current medication (clonidine) for an off-label purpose. CHBRP assumes that providers will switch to prescribing lofexidine when it becomes available, but that some providers will continue to use clonidine. A detailed table of these assumptions is presented in Appendix C.

The number of commercial/CalPERS enrollees with opioid use disorder, alcohol use disorder, or tobacco use disorder who have behavioral counseling in conjunction with their medication treatment will increase due to the increased utilization of medications. Applying the medication increases to the corresponding utilization of behavioral counseling, CHBRP finds that individual therapy will increase by 83%, from 1,184 enrollees at baseline to 2,167 enrollees postmandate (Table 8). Similarly, group therapy will increase by 76%, from 1,237 currently to 2,183 postmandate. Finally, family therapy will increase 61%, from 51 enrollees currently to 82 enrollees postmandate.

³³ The number of persons, postmandate, taking FDA-approved opioid use disorder (OUD) medications and alcohol use disorder (AUD) medications is greater than in CHBRP's report on an earlier bill (CHBRP, 2019). The difference is due to inclusion in this analysis of additional medications: naltrexone IM (for AUD and OUD), which is generally not covered through a pharmacy benefit, and lofexidine (for OUD), which was not available when the prior report was released.

³⁴ Personal communication on 3/3/20 with Dr. Scott Steiger, Deputy Medical Director, Opiate Treatment Outpatient Program, University of California, San Francisco.

³⁵ Personal communication on 2/23/20 with Dr. Scott Steiger, Deputy Medical Director, Opiate Treatment Outpatient Program, University of California, San Francisco.

Table 8. Utilization Baseline and Postmandate of Counseling Services for Opioid Use Disorder, Alcohol Use Disorder, and Tobacco Use Disorder, 2021

	Baseline	Postmandate	Increase/ Decrease	Change Postmandate
Counseling Services				
Individual Therapy	1,174	1,632	458	39%
Group Therapy	1,244	1,694	450	36%
Family Therapy	52	67	15	29%

Source: California Health Benefits Review Program, 2020.

Baseline and Postmandate Per-Unit Cost

Baseline FDA-approved medication and counseling unit cost for commercial/CalPERS enrollees were based on Milliman commercial claims and enrollment data for the state of California. For a full discussion of utilization baseline and postmandate calculations, please see Appendix C

Table 1 provides estimates of average annual per enrollee unit costs of all prescription medication treatments combined, both alone and with associated behavioral counseling. Below, Table 9 provides the detailed per-unit cost of each type of prescription medication for a 30-day supply. These unit costs are not expected to change postmandate.

Although unit costs are expected to be unchanged, due to some reduction of cost sharing and the removal of utilization management protocols, CHBRP expects average annual per-user costs to change (see Table 1). This is due to the expected utilization shifts (noted in the prior subsection) to some higher unit cost formulations and or medications. For example, lofexidine costs \$2,015.94 for a 30-day supply, which is much higher than the clonidine which had been used off-label to treat opioid withdrawal symptoms, so the average annual unit cost for opioid use disorder medications would be increased by a switch in utilization from clonidine to lofexidine.

Table 9. Per-Unit Cost of Medications (30-Day Supply) for Opioid Use Disorder, Alcohol Use Disorder, and Tobacco Use Disorder, 2021

	Unit Cost
<i>Opioid Use Disorder</i>	
Buprenorphine	\$233.54
Buprenorphine-Naloxone	\$402.11
Naltrexone - Oral Oud	\$507.30
Naltrexone - IM Oud	\$1,777.83
Naloxone	\$169.21
Naloxone Auto Injector	\$6,634.15
Lofexidine	\$2,015.94
Methadone	\$2,015.94
<i>Alcohol Use Disorder</i>	
Campral	\$237.93
Antabuse	\$106.93
Naltrexone – IM Oud	\$1,611.14
Generic Naltrexone	\$132.52
<i>Tobacco Use Disorder</i>	
Verenicycline	\$480.98
Burpropion	\$59.35
Nicotine*	\$503.56

Source: California Health Benefits Review Program, 2020.

Notes: *Includes prescription only inhaler and nasal spray.

The cost per session of behavioral counseling varies by the number of persons assisted, with group therapy having the highest average cost at \$322.03 (Table 6). Family therapy has the lowest per session cost, at an average of \$181.44.

Table 10. Per-Session Unit Cost for Counseling Services for Opioid Use Disorder, Alcohol Use Disorder, and Tobacco Use Disorder, 2021

Counseling Services	Unit Cost
Individual Therapy	\$201.19
Group Therapy	\$322.03
Family Therapy	\$181.44

Source: California Health Benefits Review Program, 2020.

Baseline and Postmandate Expenditures

Table 13 and Table 14 present baseline and postmandate expenditures by market segment for DMHC-regulated plans and CDI-regulated policies. The tables present per member per month (PMPM) premiums, enrollee expenses for both covered and noncovered benefits, and total expenditures (premiums as well as enrollee expenses).

SB 854 would increase total net annual expenditures by \$14,436,000 or 0.0110% for commercial/CalPERS enrollees with DMHC-regulated plans and CDI-regulated policies. This is due to a \$18,232,000 increase in total health insurance premiums paid by employers and enrollees for newly covered benefits, adjusted by a decrease of \$3,796,000 in enrollee expenses for covered and/or noncovered benefits.

Premiums

Changes in premiums as a result of SB 854 would vary by market segment. Note that such changes are related to the number of commercial/CalPERS enrollees (see Table 1, Table 13, and Table 14), with health insurance that would be subject to SB 854.

Among DMHC-regulated privately funded plans, premium increases range from a low of \$0.1013 PMPM for individual plans to \$0.1279 PMPM for small-group plans. Among CDI-regulated privately funded policies, premium increases range from a low of \$0.0586 PMPM for small-group plans to \$0.0998 PMPM for individual plans.

Among publicly funded DMHC-regulated health plans, CalPERS HMOs are estimated to have premium increases of \$0.1056 PMPM. Medi-Cal HMOs are exempt from the mandate, and will not have any change in premiums.

Enrollee Expenses

SB 854–related changes in enrollee expenses for covered benefits (deductibles, copays, etc.) and enrollee expenses for noncovered benefits would vary by market segment. Note that such changes are related to the number of commercial/CalPERS enrollees (see Table 1, Table 13, and Table 14) with health insurance that would be subject to SB 854 expected to use the relevant medication either alone or with behavioral counseling for substance use disorder during the year after enactment.

CHBRP projects drops in copayments or coinsurance rates due to moving to tier 1, and also projects an increase in utilization of medication treatments for opioid use disorder, alcohol use disorder, and tobacco use disorder. For commercial/CalPERS enrollees who had on-formulary coverage for these medications at baseline, out-of-pocket expenses are projected to decrease, due to moving the medications down to tier 1 copayments or coinsurance. For enrollees gaining newly compliant benefit coverage, out-of-pocket expenses for covered benefits will increase, as previously they did not have compliant benefit coverage

and did not access coverage for the FDA-approved SUD medications or in-conjunction behavioral counseling.

It is possible that some commercial/CalPERS enrollees incurred expenses related to medication treatments for which on-formulary, tier 1 coverage was unavailable, but CHBRP cannot estimate the frequency with which such situations occur and so cannot offer a calculation of impact.

As seen in Table 1, average annual reductions in out-of-pocket expenses vary among commercial/CalPERS enrollees with alcohol use disorder, opioid use disorder, and tobacco use disorder. This is due to the different combination of utilization of FDA-approved SUD medications, as well as the movement of these medications to tier 1 pricing. Enrollees with alcohol use disorder will have, on average, a reduction in their cost-sharing of \$65.00 annually, while enrollees with opioid use disorder will have an average reduction of \$338.96 annually in their cost sharing. Enrollees with tobacco use disorder will have a smaller average decrease of \$0.21, due to the already low cost sharing burden (Table 1).

Examining out-of-pocket costs and premium increases by market segment, among commercial/CalPERS enrollees with on-formulary benefit coverage at baseline, the number of enrollees who will be impacted ranges from a low of 0.190% for CalPERS HMO to a high of 0.206% for small group DMHC-plans or CDI-regulated policies. For these enrollees, out-of-pocket expenses are expected to decrease by a range of \$118.15 to \$128.75 (Table 11).

Among commercial/CalPERS enrollees who gained on-formulary benefit coverage, the percent of enrollees who would be affected ranges from 0.035% for CalPERS HMO to 0.089% for individual plans. These enrollees are projected to have an increase in out-of-pocket expenses for medications, with or without behavioral counseling, by a range of \$108.14 to \$115.43.

Table 11. Impact of SB 854 on Average Annual Enrollee Out-of-Pocket Expenses

	Large Group	Small Group	Individual	CalPERS HMO	MediCal HMO
Enrollees with Baseline Coverage					
% of Enrollees with Out-of-Pocket Expenses Impact due to SB 854 (a)	0.193%	0.206%	0.198%	0.190%	0.000%
Avg. Annual Out-of-Pocket Expenses Impact for Enrollees	-\$125.46	-\$128.75	-\$128.13	-\$118.15	\$0.00
Enrollees Newly Covered					
% of Enrollees with Out-of-Pocket Expenses Impact due to SB 854 (a)	0.073%	0.084%	0.089%	0.035%	0.000%
Avg. Annual Out-of-Pocket Expenses Impact for Enrollees	\$108.14	\$108.47	\$111.31	\$115.43	\$0.00

Source: California Health Benefits Review Program, 2020.

Notes: Average enrollee out-of-pocket expenses include expenses for both covered and noncovered benefits. (a) Not including impacts on premiums; (b) Benefit coverage for Medi-Cal beneficiaries does not generally include any cost sharing.

It should be noted that Table 11 shows the per-user annual impact in the form of cost sharing savings (for commercial/CalPERS enrollees currently covered, whose medications will be mandated to be covered with Tier-1 cost sharing) and new spending (for enrollees with new access to these medications). These numbers reflect population averages and will vary significantly for individual members. Sources of variation include the specific medications utilized by the enrollee and the cost sharing and utilization

management protocols applicable to their specific plan or policy. An enrollee may experience a mandate impact significantly higher or lower than those included in this Table 11. For example, there would be no change for enrollees with compliant cost-sharing premandate while another enrollee with non-compliant cost-sharing may see their cost sharing decrease by up to \$888 annually (assuming a Standard Silver plan with 12 monthly scripts for a maintenance medication moved from Tier 3 to Tier 1).

Out-of-pocket spending for covered and noncovered expenses

CHBRP estimates that the commercial/CalPERS enrollees with uncovered expenses at baseline would receive a \$3,796,000 reduction in their out-of-pocket spending for covered and noncovered expenses associated with medication and behavioral counseling for opioid use disorder, alcohol use disorder, or tobacco use disorder (Table 1). CHBRP's estimates are based on claims data and may underestimate the cost savings for enrollees due to carriers' ability to negotiate discounted rates that are unavailable to patients and their families.

Potential Cost Offsets or Savings in the First 12 Months After Enactment

As discussed in the above section on benefit coverage and utilization, CHBRP finds that 94% of commercial/CalPERS enrollees currently have coverage that will be altered to become fully compliant with SB 854 postmandate, including reductions in cost sharing and elimination of utilization management procedures, which will result in varying levels of utilization increases for both medications alone and in conjunction with counseling services. According to Mohlman et al. (2016), there are likely to be changes in the utilization of health care services as a result of receiving substance use disorder treatment. Mohlman et al. (2016) found reductions in inpatient, emergency, medical specialist, and imaging services and increases in PCP visits and surgical specialist visits.

The Mohlman et al. (2016) study included data on utilization offsets that would have included additional office visits or services that may have resulted from both minimal side effects (i.e., redness or swelling at injection sites) and larger harms, like increased risk of overdose when patients treated with naltrexone who discontinue treatment may be sensitive to lower doses of opioids, which could increase their risk of overdose (SAMHSA, 2015). In general, the utilization and cost offsets calculated in this report take into consideration added health services use and spending. Please see the *Medical Effectiveness* section for literature on other harms.

Unit cost offsets were estimated using a combination of the Mohlman et al. (2016) estimates and Milliman claims data. CHBRP has assumed no differential in average unit cost per service pre- and postmandate.

Table 12. Selected Offsets: Avoided Inpatient Days, Inpatient Detoxification, and Emergency Department Visits

	Average Utilization Change per SUD Treatment User	Commercial Unit Cost
Opioid Use Disorder Inpatient Days	-1.46	\$8,360
Opioid Use Disorder Detox Days	-1.46	\$1,379
Opioid Use Disorder Emergency Department Visits	-1.04	\$3,723
Alcohol Use Disorder Inpatient Days	-0.436	\$9,285
Alcohol Use Disorder Detox Days	-0.457	\$1,433
Alcohol Use Disorder Emergency Department Visits	-0.044	\$4,225

Source: California Health Benefits Review Program, 2020.

CHBRP used literature focused on utilization change due to opioid use disorder medication treatment to inform its cost model estimates. Generally, the literature suggests that opioid use disorder treatment with methadone, buprenorphine, naloxone, or naltrexone lead to better outcomes and reduced overall spending when compared with no use (McCarty, 2010; Tkacz, 2014). Despite sizeable costs of opioid use disorder medication services, the recipients in the articles mentioned above experienced 43% lower spending on average for inpatient and outpatient services. These studies suggest in aggregate that opioid use disorder medication services are likely to result in short- and long-term savings (see the *Long-Term Impacts* section).

CHBRP applied estimated utilization and cost offsets based on published evidence (Mark et al., 2010; Mohlman et al., 2016) on the impact of opioid use disorder–related medication and counseling treatment on emergency room use, inpatient services, outpatient physician services, inpatient detoxification, and other opioid use disorder–related services. These cost offsets are reflected in Table 1 and the estimates for expenditures and premium changes in 2021.

Postmandate Administrative Expenses and Other Expenses

CHBRP estimates that the increase in administrative costs of DMHC-regulated plans and/or CDI-regulated policies will remain proportional to the increase in premiums. CHBRP assumes that if health care costs increase as a result of increased utilization or changes in unit costs, there is a corresponding proportional increase in administrative costs. CHBRP assumes that the administrative cost portion of premiums is unchanged. All health plans and insurers include a component for administration and profit in their premiums.

Other Considerations for Policymakers

In addition to the impacts a bill may have on benefit coverage, utilization, and cost, related considerations for policymakers are discussed below.

Postmandate Changes in the Number of Uninsured Persons

Because the change in average premiums does not exceed 1% for any market segment (see Table 1, Table 13, and Table 14), CHBRP would expect no measurable change in the number of uninsured persons due to the enactment of SB 854.

Changes in Public Program Enrollment

CHBRP estimates that the mandate would produce no measurable impact on enrollment in publicly funded insurance programs due to the enactment of SB 854.

How Lack of Benefit Coverage Results in Cost Shifts to Other Payers

There exists one medication for opioid use disorder that has a legally separate method of administration outside of normal health services provider networks: methadone. While methadone is allowed to be administered for pain within hospital and other settings, it can only be administered for treatment of opioid use disorder by a state-licensed and funded facility, often called a “methadone clinic.” These clinics are often funded through state or federal funds, and are not associated with health insurance carrier claims. CHBRP is aware of these clinics, but could not quantify their number, caseload, or the impact that SB 854 may have. Methadone clinics are not generally in-network now and are not expected to become so in the first year postmandate.

Table 13. Baseline Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2021

	DMHC-Regulated						CDI-Regulated			Total
	Privately Funded Plans (by Market) (a)			Publicly Funded Plans			Privately Funded Plans (by Market) (a)			
	Large Group	Small Group	Individual	CalPERS HMOs (b)	MCMC (Under 65) (c)	MCMC (65+) (c)	Large Group	Small Group	Individual	
Enrollee counts										
Total enrollees in plans/policies subject to state mandates (d)	7,797,000	2,127,000	1,938,000	522,000	7,481,000	875,000	645,000	174,000	160,000	21,719,000
Total enrollees in plans/policies subject to SB 854	7,797,000	2,127,000	1,938,000	522,000	0	0	645,000	174,000	160,000	13,363,000
Premiums										
Average portion of premium paid by employer	\$421.33	\$387.36	\$0.00	\$521.09	\$262.75	\$536.28	\$493.36	\$435.79	\$0.00	\$86,519,976,000
Average portion of premium paid by employee	\$109.79	\$140.13	\$632.59	\$97.10	\$0.00	\$0.00	\$137.09	\$167.01	\$509.49	\$31,556,986,000
Total premium	\$531.12	\$527.49	\$632.59	\$618.19	\$262.75	\$536.28	\$630.44	\$602.80	\$509.49	\$118,076,962,000
Enrollee expenses										
For covered benefits (deductibles, copays, etc.)	\$41.92	\$115.98	\$170.63	\$51.02	\$0.00	\$0.00	\$123.80	\$161.70	\$161.76	\$12,776,801,000
For noncovered benefits (e)	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0
Total expenditures	\$573.05	\$643.47	\$803.22	\$669.20	\$262.75	\$536.28	\$754.24	\$764.50	\$671.25	\$130,853,763,000

Source: California Health Benefits Review Program, 2020.

Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance acquired outside or through Covered California (the state's health insurance marketplace).

(b) Approximately 57.36% of CalPERS enrollees in DMHC-regulated plans are state retirees, state employees, or their dependents. About one in five (20.5%) of these enrollees has a pharmacy benefit not subject to DMHC. CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).

(c) Medi-Cal Managed Care Plan expenditures for members over 65 include those who are also Medicare beneficiaries. This population does not include enrollees in COHS.

(d) Enrollees in plans and policies regulated by DMHC or CDI aged 0 to 64 years as well as enrollees 65 years or older in employer-sponsored health insurance. This group includes commercial enrollees (including those associated with Covered California or CalPERS) and Medi-Cal beneficiaries enrolled in DMHC-regulated plans.

(e) Includes only those expenses that are paid directly by enrollees or other sources to providers for services related to the mandated benefit that are not currently covered by insurance. This only includes those expenses that will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

Key: CalPERS HMOs = California Public Employees' Retirement System Health Maintenance Organizations; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care; MCMC = Medi-Cal Managed Care.

Table 14. Postmandate Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2021

	DMHC-Regulated						CDI-Regulated			Total
	Privately Funded Plans (by Market) (a)			Publicly Funded Plans			Privately Funded Plans (by Market) (a)			
	Large Group	Small Group	Individual	CalPERS HMOs (b)	MCMC (Under 65) (c)	MCMC (65+) (c)	Large Group	Small Group	Individual	
Enrollee counts										
Total enrollees in plans/policies subject to state mandates (d)	7,797,000	2,127,000	1,938,000	522,000	7,481,000	875,000	645,000	174,000	160,000	21,719,000
Total enrollees in plans/policies subject to SB 854	7,797,000	2,127,000	1,938,000	522,000	0	0	645,000	174,000	160,000	13,363,000
Premiums										
Average portion of premium paid by employer	\$0.0943	\$0.0939	\$0.0000	\$0.0890	\$0.0000	\$0.0000	\$0.0517	\$0.0424	\$0.0000	\$12,269,000
Average portion of premium paid by employee	\$0.0246	\$0.0340	\$0.1013	\$0.0166	\$0.0000	\$0.0000	\$0.0144	\$0.0162	\$0.0998	\$5,963,000
Total premium	\$0.1189	\$0.1279	\$0.1013	\$0.1056	\$0.0000	\$0.0000	\$0.0661	\$0.0586	\$0.0998	\$18,232,000
Enrollee expenses										
For covered benefits (deductibles, copays, etc.)	-\$0.0230	-\$0.0246	-\$0.0254	-\$0.0210	\$0.0000	\$0.0000	-\$0.0234	-\$0.0345	-\$0.0224	-\$3,796,000
For noncovered benefits (e)	\$0.0000	\$0.0000	\$0.0000	\$0.0000	\$0.0000	\$0.0000	\$0.0000	\$0.0000	\$0.0000	\$0
Total expenditures	\$0.0959	\$0.1033	\$0.0760	\$0.0846	\$0.0000	\$0.0000	\$0.0426	\$0.0241	\$0.0773	\$14,436,000
Percent change										
Premiums	0.0224%	0.0242%	0.0160%	0.0171%	0.0000%	0.0000%	0.0105%	0.0097%	0.0196%	0.0154%
Total expenditures	0.0167%	0.0161%	0.0095%	0.0126%	0.0000%	0.0000%	0.0057%	0.0032%	0.0115%	0.0110%

Source: California Health Benefits Review Program, 2020.

- Notes:* (a) Includes enrollees with grandfathered and nongrandfathered health insurance acquired outside or through Covered California (the state's health insurance marketplace).
- (b) Approximately 57.36% of CalPERS enrollees in DMHC-regulated plans are state retirees, state employees, or their dependents. About one in five (20.5%) of these enrollees has a pharmacy benefit not subject to DMHC. CHBRP has projected no impact for those enrollees. However, CalPERS could, postmandate, require equivalent coverage for all its members (which could increase the total impact on CalPERS).
- (c) Medi-Cal Managed Care Plan expenditures for members over 65 include those who are also Medicare beneficiaries. This population does not include enrollees in COHS.
- (d) Enrollees in plans and policies regulated by DMHC or CDI aged 0 to 64 years as well as enrollees 65 years or older in employer-sponsored health insurance. This group includes commercial enrollees (including those associated with Covered California or CalPERS) and Medi-Cal beneficiaries enrolled in DMHC-regulated plans.
- (e) Includes only those expenses that are paid directly by enrollees or other sources to providers for services related to the mandated benefit that are not currently covered by insurance. This only includes those expenses that will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.
- Key:* CalPERS HMOs = California Public Employees' Retirement System Health Maintenance Organizations; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care; MCMC = Medi-Cal Managed Care

PUBLIC HEALTH IMPACTS

As discussed in the *Policy Context* section, SB 854 addresses the benefit coverage of commercial/CalPERS enrollees who have a pharmacy benefit. For these enrollees' health insurance, SB 854 would mandate coverage of all FDA-approved medications for substance use disorders (SUDs). SB 854 would require these medications to be placed on the lowest tier of the formulary and would prohibit use of prior authorization and step therapy protocols for coverage of these medications. SB 854 would also prohibit use of prior authorization protocols for coverage of counseling that accompanies FDA-approved medication treatment for substance use disorders. The insurance of Medi-Cal beneficiaries enrolled in DMHC-regulated plans would be exempt from these requirements. 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 of SB 854 on health outcomes and potential population disparities. See *Long-Term Impacts* for discussion of premature death, economic loss, and social determinants of health.

Estimated Public Health Outcomes

There are FDA-approved prescription medications for three substance use disorders: opioid use disorder, alcohol use disorder, and tobacco use disorder. As presented in the *Medical Effectiveness* section (Figures 1 and 3), there is clear and convincing evidence of effectiveness of methadone and buprenorphine to treat opioid use disorder, acamprosate and naltrexone to treat alcohol use disorder, and all FDA-approved medications to treat tobacco use disorder when compared with placebo or no medication. There is limited evidence suggesting that naltrexone (oral) is not effective at treating opioid use disorder, and limited evidence suggesting that naltrexone (injectable) is effective at treating opioid use disorder. There is a preponderance of evidence that methadone plus counseling is effective at treating opioid use disorder, and limited evidence that buprenorphine, oral naltrexone, and injectable naltrexone plus counseling are effective at treating opioid use disorder. There is inconclusive evidence that medication plus behavioral therapy is more effective than medication alone for opioid use disorder. Limited evidence shows that disulfiram is not effective when used to treat alcohol use disorder.

The opioid use disorder, alcohol use disorder, and tobacco use disorder medications that are effective promote treatment retention, prevent relapse, and improve birth outcomes. Additionally, evidence shows that effective medications used for opioid use disorder and its symptoms reduce illicit use opioid use (misuse of prescription opioids or use of heroin and illicitly manufactured fentanyl); reverse opioid overdose thus reducing associated mortality; and reduce risk behaviors associated with transmission of HIV or Hepatitis C (see the *Long-Term Impacts* section for further discussion about morbidity and mortality). CHBRP's medical effectiveness review found limited evidence regarding the impact of prohibiting utilization management strategies on reducing enrollee barriers to care. There is limited evidence to show that counseling plus medication is more effective than medication alone for tobacco use disorder.

As presented in the *Benefit Coverage, Utilization, and Cost Impacts* section, CHBRP estimates a marginal increase of up to 11,119 people with opioid use disorder, alcohol use disorder, and tobacco use disorder newly accessing FDA-approved medications or medications with counseling to treat their disorders were SB 854 implemented. Please note, concomitant use of medications by some enrollees may occur, and so these enrollee estimates reflect an upper bound.

Opioid Use Disorder

Given the effectiveness of formulations of five opioid use medications (buprenorphine [-naloxone], methadone, and intramuscular naltrexone for maintenance treatment; lofexidine for withdrawal; and naloxone for overdose reversal), CHBRP anticipates an increase in opioid overdose reversals and

maintenance treatment for the 5,253 commercial/CalPERS enrollees with opioid use disorder projected to have new access to these FDA-approved medications or medications plus counseling. Corresponding decreases in illicit opioid use, opioid overdose and its associated mortality, poor maternal-infant outcomes, and a reduction in behaviors associated with elevated risk of hepatitis B and C, and HIV (unprotected sex and shared injection drug equipment) are expected.

Improving access to opioid use disorder treatment is especially important for reducing risk of hepatitis B and C and HIV. A minority of people with opioid use disorder become injection drug users (IDU) either to improve the high from misused prescription opioids or because they have turned to heroin, which is cheaper and easier to obtain than prescription opioids (NIDA, 2018). National estimates of hepatitis C infection rates among IDU ranges from 60% to 90% (Tsui et al., 2014) indicating a high likelihood of transmitting the infection when sharing contaminated drug equipment. In 2015, about 18% of California females with HIV contracted the infection through IDU (opioid and other drugs) compared with 5% of HIV+ males (although males comprise 88% of the HIV population) (CHDP, 2015). Based on the evidence, injection drug users who take medications to treat opioid use disorder could avert contracting HIV and/or hepatitis C and prevent transmission to others.

In addition to the preventable health burdens, effective FDA-approved medications for opioid use disorder also reduces use of health services. The *Background on Substance Use Disorders and Benefit Coverage, Utilization, and Cost Impacts* sections describe research showing decreased emergency room use and hospitalizations for patients being treated for opioid use disorder as compared with patients with untreated opioid use disorder (Mohlman et al., 2016). In the case of SB 854, CHBRP estimates that in the first year postmandate, there would be cost offsets attributable to fewer opioid use disorder-related services per opioid use disorder patient. Specifically, 1.46 fewer days in both inpatient days and detox days, plus 1.04 fewer opioid use disorder-related ED visits per user (see Table 12 in the *Benefit Coverage, Utilization, and Cost Impacts* section for estimated changes).

The public health impact of SB 854 within a year postmandate may be limited for several reasons. In addition to a relapse rate of 40% to 60% (see *Background on Substance Use Disorders* section), other significant attitudinal and structural barriers contribute to lower opioid use disorder treatment rates than opioid use disorder treatment needs. As discussed in the *Background on Substance Use Disorders* section, patient attitudinal barriers are strong deterrents to seeking treatment. Namely, the nature of addiction precludes some people with opioid use disorder from recognizing their need for help, with an estimated 11% seeking treatment in the first year after onset of the disorder and 24% within 10 years of onset (Blanco et al., 2013). Opioid use disorder stigma from family, friends, and employers produces another significant barrier, as does provider willingness to prescribe and treat. Moreover, structural barriers prevent some who seek medication treatment from obtaining it due to a mismatch between the supply of trained providers and health care settings, and patient demand (Clemens-Cope et al., 2018; Knudsen et al., 2017).

In the first year postmandate, CHBRP estimates that about 5,253 commercial/CalPERS enrollees³⁶ with newly compliant benefit coverage would take FDA-approved prescription medications or prescription medications plus counseling for the treatment of opioid use disorder, 40% to 60% of whom may experience relapse. As supported by clear and convincing evidence, outcomes of such treatment would include reducing illicit opioid use, opioid overdose and associated mortality, acquisition and transmission of hepatitis C and HIV, and poor maternal-infant outcomes. Among those new users, SB 854 would also increase maintenance treatment retention and increase overdose reversals (through the use of naloxone). There is a preponderance of evidence that methadone plus counseling is effective for the treatment of opioid use disorder, and limited evidence that buprenorphine, oral naltrexone, and injectable naltrexone plus counseling are effective for the treatment of opioid use disorder.

³⁶ The number of persons, postmandate, taking FDA-approved opioid use disorder medications is greater than in CHBRP's report on an earlier bill (CHBRP, 2019). The difference is due to inclusion in this analysis of additional medications: naltrexone IM, which is generally not covered through a pharmacy benefit, and lofexidine, which was not available when the prior report was released.

Impact on disparities

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 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 among whites and Native Americans); age cohorts (highest among those aged 25-35); and by gender (males have two times the mortality rate of females). The LGBT population is twice as likely as the heterosexual population to report misusing prescription opioids.

The demographic composition of the estimated 5,253 commercial/CalPERS enrollees projected to start opioid use disorder treatment medication(s) or medications plus counseling is undefined; therefore, the impact of SB 854 on existing disparities in opioid use, mortality, and related health services use is unknown.

Alcohol Use Disorder

As presented in the *Medical Effectiveness* section, there is clear and convincing evidence that two of the three³⁷ FDA-approved alcohol use disorder medications (acamprosate and naltrexone) are effective in reducing alcohol consumption or supporting abstinence from alcohol. There is insufficient evidence of effectiveness for outcomes related to quality of life, injury, and mortality (Jones et al., 2014). As presented in the *Benefit Coverage, Utilization, and Cost Impacts* section, CHBRP estimates about 2,995 commercial/CalPERS enrollees with newly SB 854-compliant benefit coverage will take FDA-approved medications or medications plus counseling for the treatment of alcohol use disorder.

There is well-established evidence of a causal link between alcohol misuse/abuse and higher rates of injury, cancers, fetal alcohol spectrum disorder, stroke, cardiovascular disease, liver cirrhosis, high risk behaviors, and other physical and mental health conditions (Rehm et al., 2010; NIAAA, 2019). Although longitudinal studies on the effectiveness of these medications improving health outcomes is lacking, epidemiologic evidence indicates that reductions in alcohol consumption would translate to lower rates of acute and chronic conditions such as fetal alcohol spectrum disorder; miscarriage; alcohol use disorder-associated injury and mortality (e.g., motor vehicle accidents, falls, suicides, sexual assault); and risky sexual behavior leading to unintended pregnancy or sexually transmitted infections (CDC, 2018) (see the *Long-Term Impacts* section for discussion of cardiovascular and liver disease and cancer).

Two examples of the negative health effects of untreated alcohol use disorder include poor pregnancy outcomes and injuries/accidents:

- Pregnant women who misuse/abuse alcohol increase the risk of poor birth outcomes. Fetal alcohol spectrum disorder (FASD), defined by permanent physical and intellectual disabilities and/or behavioral problems in newborns, is caused exclusively by alcohol. In 2014, SAMHSA showed that, nationally, 2.7% of pregnant women aged 15 to 44 reported binge drinking, and 0.3% reported heavy drinking, which greatly increases the risk of FASD. SAMHSA also reported that about 200,000 cases of FASD occur annually in the U.S. Studies from specific U.S. sites report the prevalence of FASD ranging between 20 to 50 cases per 1,000 births annually (NIAAA, 2018).
- Alcohol misuse/abuse also causes a significant number of injuries/accidents. The CDC hosts the Alcohol-Related Disease Impact database, which reports the number of alcohol-attributable deaths due to excessive alcohol consumption. In California, of the 5,113 acute causes of death,

³⁷ Naltrexone, which helps manage withdrawal symptoms and blocks effects of alcohol and opioids; and acamprosate, which helps reduce cravings, are found to be effective; whereas there is insufficient evidence of the effectiveness of disulfiram.

more than 1,000 motor vehicle deaths, 1,000 homicides, 800 suicides, and 600 falls resulting in death were alcohol related in 2012 (CDC, 2013).

Treating alcohol use disorder with medication may help decrease the incidence of these negative health outcomes. Additionally, treating alcohol use disorder with medication may reduce rates of emergency room use and hospitalizations associated with alcohol use disorder (see the *Background on Substance Use Disorders* section). In the case of SB 854, CHBRP estimates cost offsets associated with reduction in alcohol use disorder related services. Specifically, about a half-day reduction in alcohol use disorder inpatient days and a half-day reduction in alcohol use disorder detox days per alcohol use disorder patient (see Table 12 in the *Benefit Coverage, Utilization, and Cost Impacts* section for estimated changes).

As discussed in the *Background on Substance Use Disorders* section, attitudinal barriers are strong deterrents to seeking treatment. First, the nature of addiction precludes some people with alcohol use disorder from recognizing their need for help. Additionally, stigma from family, friends, and employers may also play a role in patient reluctance to initiating and maintaining a treatment regimen (Fisher et al., 2016; Jones et al., 2015; Verissimo and Grella, 2017). Finally, many providers are reticent to prescribe medication to treat alcohol use disorder, despite more than 10 years of provider education campaigns from government entities and the American Medical Association (Jonas et al., 2014; SAMHSA, 2015). Reasons for provider nonparticipation include prior training to refer to patients with alcohol use disorder to specialty treatment centers, lack of familiarity with medications, systemic division between physical and behavioral health care, and limited referral options to specialty treatment clinics for their patients (provider-of-last resort) (SAMHSA, 2015; Wessell et al., 2014). Wessell et al. found that key facilitators to increasing primary care providers' prescribing alcohol use disorder medication included provider exposure to evidence and case studies, receptive patients, early successful patient outcomes, and low cost (generic oral naltrexone) availability of alcohol use disorder medication (Wessell et al., 2014).

In the first year postmandate, CHBRP estimates that approximately 2,995 commercial/CalPERS enrollees³⁸ with newly compliant benefit coverage would take FDA-approved prescription medications or prescription medications plus counseling for the treatment of alcohol use disorder, of which 50% or more may experience relapse within the first year of treatment. Based on clear and convincing evidence that two of the three FDA-approved alcohol use disorder medications are effective in reducing alcohol consumption, CHBRP projects that these enrollees would experience decreases in negative health outcomes such as injuries/accidents and poor pregnancy outcomes in the first year postmandate to an unknown degree.

Impact on disparities

As described in the *Background on Substance Use Disorders* section, alcohol use disorder–related disparities among racial/ethnic groups exist in California with whites and Native Americans exhibiting the highest rates of heavy drinking, although Hispanics and blacks have higher rates of alcohol-related liver disease and cirrhosis mortality. Similar to other substance use disorders, younger cohorts (aged 18-34 years) report higher rates of heavy drinking as compared with other ages; similarly, the LGBT population reported higher rates of binge drinking than the heterosexual population.

The demographic composition of the estimated 2,995 commercial/CalPERS enrollees projected to start alcohol use disorder treatment medication(s) or medication(s) plus counseling is undefined; therefore, the impact of SB 854 on reducing existing disparities in alcohol use, pregnancy outcomes, injuries/accidents, and related health services use is unknown.

³⁸ The number of persons, postmandate, taking FDA-approved alcohol use disorder is greater than in CHBRP's report on an earlier bill (CHBRP, 2019). The difference is due to inclusion in this analysis of an additional medication: naltrexone IM, which is generally not covered through a pharmacy benefit.

Tobacco Use Disorder

As presented in the *Medical Effectiveness* section, there is clear and convincing evidence that all three FDA-approved tobacco use disorder medications are effective in promoting smoking cessation. As presented in the *Benefit Coverage, Utilization, and Cost Impacts* section, CHBRP estimates that about 2,721 commercial/CalPERS enrollees with newly SB 854 compliant benefit coverage would take FDA-approved medications for the treatment of tobacco use disorder.

Smoking is a known cause of significant morbidity and mortality. A deep and comprehensive literature links smoking to a multitude of conditions and diseases including cancers, cardiopulmonary disease, and poor birth outcomes (HHS, 2014). A comprehensive epidemiological study reported that about 50% of deaths from 12 types of cancer are attributable to smoking, with more than 80% of lung cancer deaths attributable to smoking (Siegel et al., 2015). Despite having the second lowest smoking rate in the U.S. (11.3%), lung cancer remains the leading cause of cancer deaths in California with more than 12,000 deaths occurring in 2014 (ACS, 2017; CDC, 2017). (See the *Long-Term Impacts* section for more discussion of long-term effects of smoking.) Additionally, secondhand smoke increases non-smokers' risk of developing lung cancer, bronchitis, and pneumonia; exacerbating asthma; and causing poor birth outcomes (CDPH, 2018) all of which can lead to an increase in preventable health services utilization. California has the lowest prevalence rate nationally of women who smoke any time during pregnancy (about 2%) according to analysis of 2014 birth certificates (Curtin et al., 2016).

Public health campaigns, smoking policy changes (tobacco taxation, tobacco sales restrictions, workplace restrictions, etc.), and the ACA-requirement for coverage of cessation therapies by many plans and policies have contributed the second lowest state-smoking rate (11.4%) in the U.S. Table 3 shows the prevalence of smoking cessation methods that California smokers reported using (one or more) to quit smoking in the past year (based on the 2016-2017 California Adult Tobacco Survey) (CDPH, 2018). Data from the 2017 California Health Information Survey reports a smaller percentage (55%) of smokers quit for one or more days in the past year (CHIS, 2017). Research has shown that former smokers recalled an average of 4.7 quit attempts before successfully abstaining (CDPH, 2018).

CHBRP estimates that about 2,871 commercial/CalPERS enrollees with newly compliant benefit coverage would take FDA-approved prescription medications or prescription medications plus counseling for the treatment of tobacco use disorder, some of whom will relapse within the first year of treatment initiation. This estimate is supported by clear and convincing evidence that the three FDA-approved medications are effective in increasing quit rates and sustaining abstinence. Thus, some reductions in poor birth outcomes and smoking-exacerbated conditions (e.g., asthma and heart attacks) would be expected in the first year postmandate. (See *Long-Term Impacts* for discussion of premature mortality.)

Impact on disparities

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. As described in the *Background on Substance Use Disorders* section, there are disparities in smoking prevalence by gender, race/ethnicity, age, and sexual orientation.

The demographic composition of the estimated 2,871 commercial/CalPERS enrollees projected to start tobacco use disorder treatment medication(s) or medication(s) plus counseling is undefined; therefore, the impact of SB 854 on reducing existing disparities in tobacco use, and tobacco-related health outcomes is unknown.

Benefit Mandate Structure and Unequal Racial/Ethnic Health Impacts

SB 854 would require compliance from the health insurance of commercial/CalPERS enrollees in DMHC-regulated plans and CDI-regulated policies, but exempts the health insurance of Medi-Cal beneficiaries enrolled in DMHC-regulated plans. Because the distribution of races and ethnicities is different among commercial enrollees than Medi-Cal beneficiaries, CHBRP examined potential unequal racial/ethnic health impacts as a result of benefit mandate structure.

Medications to treat opioid use disorder and alcohol use disorder are “carved out,” covered for Medi-Cal beneficiaries through the fee-for-service (FFS) Medi-Cal program. For Medi-Cal beneficiaries, these medications are generally covered with no cost sharing and without prior authorization or step therapy protocols. The one exception is coverage for the auto-injector version of naloxone, which is currently subject to prior authorization. As stated in the *Medical Effectiveness* section, CHBRP did not identify any evidence of different effectiveness between the auto-injector formulation and the intranasal or intramuscular formulations of naloxone. As the evidence indicates no difference in outcomes due to formulation, SB 854’s resulting increased use of the auto-injector formulation only among commercial/CalPERS enrollees may not alter existing racial/ethnic health disparities as a result of benefit mandate structure.³⁹

Medications for tobacco use disorder are not “carved out” of Medi-Cal Managed Care. They are covered through the DMHC-regulated plan into which the Medi-Cal beneficiary is enrolled. The medications are generally covered without cost sharing, but as noted in Table 15 below, prior authorization protocols and step therapy protocols are applicable to the coverage of these medications for some Medi-Cal beneficiaries enrolled in DMHC-regulated plans.

Table 15. SB 854 Treatment-Specific Baseline Coverage for Medi-Cal Managed Care Plans⁴⁰

Medication	% of enrollees with on-formulary medication coverage	% of enrollees with on-formulary medication coverage that is...	
		...Subject to prior authorization requirements	... Subject to step therapy, or fail-first protocols
Nicotine – Inhaler	100%	21%	8%
Nicotine – Nasal Spray	100%	21%	8%
Varenicline	100%	21%	8%
Bupropion HCL SR	100%	8%	0%

Source: California Health Benefits Review Program, 2020

SB 584 would increase utilization of these effective medications for tobacco use disorder among commercial/CalPERS enrollees, but would not do so among Medi-Cal beneficiaries enrolled in DMHC-regulated plans. As people of people of color are over-represented among Medi-Cal beneficiaries,

³⁹ For more information, see CHBRP’s document *Benefit Mandate Structure and Unequal Racial/Ethnic Health Impacts* under Public Health Impact Analysis at www.chbrp.org/analysis_methodology.

⁴⁰ California law requires coverage of tobacco use disorder medications, but does not place limits on utilization management; W&I 14134.25.

CHBRP would expect to see an increase in disparate health outcomes for some racial/ethnic groups should SB 854 become law.⁴¹

⁴¹ For more information, see CHBRP's document *Benefit Mandate Structure and Unequal Racial/Ethnic Health Impacts* under Public Health Impact Analysis at www.chbrp.org/analysis_methodology.

LONG-TERM IMPACTS

In this section, CHBRP estimates the long-term impact⁴² of SB 854, 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

Utilization Impacts

Long-term utilization of FDA-approved opioid use disorder medications could increase as opioid use disorder prevalence increases in the state. CHBRP estimates that the level of use of FDA-approved medications per user per year predicted in 2021 (see Table 1) would not change over time, but utilization overall would increase if there are more enrollees with opioid use disorder over time.

As new medications approved by the FDA are adopted in clinical practice, shifts in utilization could occur. For example, the new lofexidine for opioid withdrawal symptoms approved in late 2017 could alter the market for buprenorphine administration and increase use of the injectable version over sublingual versions (FDA, 2017). Currently, no paid claims are present to investigate current use, few plans have started covering lofexidine, and CHBRP's content expert suggested physicians are not yet prescribing the medication readily, although it will become widely available late in 2020. CHBRP estimates that providers will switch from an off-label use of generic clonidine to lofexidine over time, which will increase utilization to match the current use of generic clonidine, but that may not happen entirely by Year 2. CHBRP therefore assumes that Year 2 is the same as Year 1, but that eventually clonidine will be replaced entirely by lofexidine.

In the case of alcohol use disorder and tobacco use disorder treatment, there is very low baseline utilization of the FDA-approved prescription medications for the two conditions. Because plans reported few restrictions to obtaining these medications, it appears physicians and patients are not using them frequently to treat alcohol use disorder or tobacco use disorder and therefore CHBRP does not expect long-term changes in prescribing practices of these medications or patient use other than the switches in Year 1 due to the movement of medications to tier 1 and elimination of step therapy and fail-first protocols. SB 854 does not explicitly mention methadone clinics. It is possible that their provision of services mandated by SB 854 (methadone as treatment of opioid use disorder) available only from them may cause some DMHC-regulated plans and CDI-regulated policies to approach them to become in-network as a result of the bill.

Cost Impacts

Maintenance treatment needs with FDA-approved medication would continue and possibly increase if incidence of opioid use disorder, alcohol use disorder, or tobacco use disorder increases over time. After the increases in coverage in Year 1 leading to a different mix of average costs per enrollee with one of these disorders, CHBRP does not project a long-term change in costs over time due to SB 854.

Long-Term Public Health Impacts

Some interventions in proposed mandates provide immediate measurable impacts (e.g., maternity service coverage or acute care treatments) while other interventions may take years to make a measurable

⁴² See also CHBRP's *Criteria and Guidelines for the Analysis of Long-Term Impacts on Healthcare Costs and Public Health*, available at http://www.chbrp.org/analysis_methodology/cost_impact_analysis.php.

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 social determinants of health, premature death, and economic loss.

In the case of SB 854, CHBRP estimates that up to 9,131 enrollees would newly access FDA-approved prescription drug treatments for substance use disorder in the first year of the mandate. For the portion of these and future new users who are able to sustain abstinence, SB 854 would contribute to reductions in substance use-related morbidity and mortality such as cardiovascular disease, cancer, HIV and hepatitis C. (See the *Public Health Impacts* section for discussion of potential reductions in acute conditions such as poor birth outcomes and injuries.)

As discussed in the *Background on Substance Use Disorders* and *Public Health Impacts* sections, a key barrier to abstinence for any substance use disorder is patient interest and readiness to abstain. CHBRP anticipates the demand for treatment of opioid use disorder, alcohol use disorder, and tobacco use disorder would continue as relapsed patients attempt abstinence again and first-time initiators would join the pool of patients seeking care. The SB 854 mandate to place the FDA-approved medications (Table 2) on tier 1 of formularies and remove insurer utilization management tools would continue to facilitate prescription medication treatment for some enrollees whose insurance did not previously offer coverage due to those barriers.

However, limited patient readiness for substance use disorder treatment and the demand-supply mismatch for opioid use disorder and alcohol use disorder treatment remain significant barriers to care. Other policy options to address the (under) supply of properly distributed buprenorphine-waivered and methadone providers may improve in the future as newly funded provider training programs take effect through the California Department of Public Health (Joshi et al., 2017).

For those users who are able to sustain abstinence from substance use, SB 854 would reduce substance use-related morbidity and mortality, but given limited patient readiness for treatment, the effects of SB 854 on long-term public health is uncertain.

Impacts on the Social Determinants of Health⁴³

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 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, substance use disorders can also alter a person's baseline SDoH namely through the consequences of addiction, such as involvement with the criminal justice system, job loss, unstable housing or family situations, and discrimination against those with treated or untreated substance use disorder (Krebs et al., 2016).

Periodically, health insurance mandates may influence SDoH, which can mediate health inequities. The impact of SB 854 on SDoH is unknown; however, it stands to reason that for those enrollees who are adherent to opioid use disorder or alcohol use disorder prescription medication treatment could see reduced interactions with the criminal justice system and/or improvements in family and housing stability.

⁴³ For more information about SDoH, see CHBRP's publication *Incorporating Relevant Social Determinants of Health into CHBRP Benefit Mandate Analyses* at http://chbrp.com/analysis_methodology/public_health_impact_analysis.php.

Impacts on Premature Death

Premature death is often defined as death occurring before the age of 75 years (NCI, 2019).⁴⁴ 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; County Health Rankings, 2019).⁴⁵ Overdose deaths, injuries/accidents, chronic diseases, and violence related to opioid use disorder, alcohol use disorder, and tobacco 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), Tomes 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 U.S. 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 U.S. in 2016 (Tomes, et al., 2018).

Alcohol use disorder: The CDC reported the “average annual alcohol attributable years of life lost” as 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). Blacks had the highest YLL (11.87/1,000), followed by Hispanics (9.15/1,000), whites (8.58/1,000), Alaska Native/American Indian (6.91/1,000), and Asians (3.09/1,000) (Gonzales et al., 2014).

Tobacco use disorder: Max et al. estimated that 17.1 years of potential life were lost per smoker due to smoking-related disease in California with no statistical difference between males and females (Max et al., 2009). Causes of premature death included premature birth, low birthweight, sudden infant death syndrome (SIDS), respiratory stress syndrome, lung cancer, heart disease, and asthma.

There is evidence that smoking cessation can reverse negative health effects from tobacco and can produce similar reductions in morbidity and mortality that would be achieved through pharmaceutical interventions commonly prescribed for heart disease patients (Critchley and Capewell, 2003; Suskin et al., 2001). Other studies show that smoking cessation can boost life expectancy; cessation at age 35 years resulted in a predicted additional 7 to 8 years of life for men and a predicted additional 6 to 7 years of life for women (Jha et al., 2013; Taylor et al., 2002).

The quantitative long-term impact of SB 854 on premature death associated with opioid use disorder, alcohol use disorder, and tobacco use disorder is unknown; however, it stands to reason, based on the effectiveness of FDA-approved medications and the combination of those medications with counseling, that there would be a reduction in premature deaths for those enrollees who undergo treatment for their substance use disorder(s).

Economic Loss

Economic loss associated with disease is generally presented in the literature as an estimation of the value of the YPLL in dollar amounts (i.e., valuation of a population’s lost years of work over a lifetime). In addition, morbidity associated with the disease or condition of interest can also result in lost productivity by causing a worker to miss days of work due to illness or acting as a caregiver for someone else who is ill.

⁴⁴ For more information about CHBRP’s public health methodology, see http://chbrp.com/analysis_methodology/public_health_impact_analysis.php.

⁴⁵ 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).

The National Institute of Drug Abuse reports that substance abuse in the U.S. produces an estimated economic loss of \$740 billion annually. Illicit drugs (including opioids) and misuse of prescription opioids account for \$37 billion, alcohol accounts for \$27 billion, and tobacco accounts for \$168 billion in direct health care costs. The remaining \$507 billion accounts for indirect costs, such as lost work productivity and crime (NIDA, 2017).

CHBRP is unable to estimate the impact of SB 854 on the economic loss associated with substance use disorders in California.

APPENDIX A TEXT OF BILL ANALYZED

On January 15, 2020, the California Senate Committee on Health requested that CHBRP analyze SB 854.

SENATE BILL

NO. 854

Introduced by Senator Beall
(Principal coauthor: Senator Wiener)
(Principal coauthors: Assembly Members Aguiar-Curry, Arambula, and Chiu)
(Coauthors: Senators Glazer and Hill)
(Coauthors: Assembly Members Maienschein and Wicks)

January 14, 2020

An act to add Section 1374.78 to the Health and Safety Code, and to add Section 10144.42 to the Insurance Code, relating to health care coverage.

LEGISLATIVE COUNSEL'S DIGEST

SB 854, as introduced, Beall. Health care coverage: Substance use disorders.

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 provides for the regulation of health insurers by the Department of Insurance. Existing law requires specified health insurance policies that provide coverage for outpatient prescription drugs to cover medically necessary prescription drugs and subjects those policies to certain limitations on cost sharing and the placement of drugs on formularies. Existing law authorizes a health care service plan and a health insurer to utilize formularies, prior authorization, step therapy, or other reasonable medical management practices in the provision of outpatient prescription drug coverage.

This bill would require health care service plans and health insurers that provide prescription drug benefits for the treatment of substance use disorders to place prescription medications approved by the United States Food and Drug Administration (FDA) on the lowest cost-sharing tier of the plan or insurer's prescription drug formulary. The bill would impose various prohibitions on those plans and insurers, including a prohibition on prior authorization requirements on, or any step therapy requirements before authorizing coverage for, a prescription medication approved by the FDA for the treatment of substance use disorders. The bill would require those plans and insurers to make specified disclosures online and in printed provider directories, including which providers provide medication-assisted treatment services,

and would state that these provisions do not apply to health care service plan contracts or health insurance policies for health care services or coverage provided in the Medi-Cal program.

Because a willful violation of the bill's provisions by a health care service plan would be a crime, the 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.

DIGEST KEY

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

BILL TEXT

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

SECTION 1.

Section 1374.78 is added to the Health and Safety Code, to read:

1374.78.

(a) Notwithstanding any other law, a health care service plan that provides prescription drug benefits for the treatment of substance use disorders shall place all prescription medications approved by the United States Food and Drug Administration (FDA) on the lowest cost-sharing tier of the drug formulary developed and maintained by the health care service plan or the pharmacy benefit management company, and shall not do any of the following:

(1) Impose any prior authorization requirements on any prescription medication approved by FDA for the treatment of substance use disorders, or on any behavioral, cognitive, or mental health services prescribed in conjunction with or supplementary to that medication for the purpose of treating a substance use disorder.

(2) Impose any requirement that the enrollee receives coverage at an outpatient facility that exceeds allowable time and distance standards for network adequacy, a specific number of visits, days of coverage, scope, or duration of treatment, or other similar limitations.

(3) Impose any requirement related to an enrollee's prior success or failure with substance use disorder treatment.

(4) Impose any step therapy requirements before authorizing coverage for a prescription medication approved by the FDA for the treatment of substance use disorders.

(5) Exclude coverage for any prescription medication approved by the FDA for the treatment of substance use disorders and any associated counseling or wraparound services on the grounds that those medications and services were court ordered.

(b) A health care service plan shall disclose which providers in each network provide medication-assisted treatment services, and the level of care that those providers render pursuant to the current edition of the ASAM Criteria. The disclosure shall be made in a prominent location in the online and printed provider directories.

(c) This section does not apply to a health care service plan contract issued, sold, renewed, or offered for health care services or coverage provided in the Medi-Cal program (Chapter 7 (commencing with Section 14000) of Part 3 of Division 9 of the Welfare and Institutions Code).

(d) For purposes of this section, the following definitions apply:

(1) "ASAM Criteria" means the national set of criteria for providing outcome-oriented and results-based care in the treatment of addiction, and includes a comprehensive set of guidelines for placement, continued stay, and transfer and discharge of patients with addiction and cooccurring conditions, as published by the American Society of Addiction Medicine.

(2) "Pharmacy benefit management company" means a company that administers a prescription drug plan for a health care service plan.

(3) "Prior authorization" means the process by which a health care service plan or pharmacy benefit management company determines the medical necessity of otherwise covered health care services before those services are rendered. "Prior authorization" includes any health care service plan's or utilization review entity's requirement that an enrollee or health care provider notify the health care service plan or utilization review entity before those services are provided.

(4) "Step therapy" means a protocol or program that establishes the specific sequence that prescription drugs for a medical condition, and which drugs are medically appropriate for a patient, are authorized by a health care service plan or prescription drug management company.

SEC. 2.

Section 10144.42 is added to the Insurance Code, to read:

(a) Notwithstanding any other law, a health insurer that provides prescription drug benefits for the treatment of substance use disorders shall place all prescription medications approved by the United States Food and Drug Administration (FDA) on the lowest cost-sharing tier of the drug formulary developed and maintained by the health insurer, and shall not do any of the following:

(1) Impose any prior authorization requirements on any prescription medication approved by FDA for the treatment of substance use disorders, or on any behavioral, cognitive, or mental health services prescribed in conjunction with or supplementary to that medication for the purpose of treating a substance use disorder.

(2) Impose any requirement that the insured receives coverage at an outpatient facility that exceeds allowable time and distance standards for network adequacy, a specific number of visits, days of coverage, scope, or duration of treatment, or other similar limitations.

(3) Impose any requirement related to an insured's prior success or failure with substance use disorder treatment.

(4) Impose any step therapy requirements before authorizing coverage for a prescription medication approved by the FDA for the treatment of substance use disorders.

(5) Exclude coverage for any prescription medication approved by the FDA for the treatment of substance use disorders and any associated counseling or wraparound services on the grounds that those medications and services were court ordered.

(b) A health insurer shall disclose which providers in each network provide medication-assisted treatment services, and the level of care that those providers render pursuant to the current edition of the ASAM Criteria. The disclosure shall be made in a prominent location in the online and printed provider directories.

(c) This section does not apply to a health insurance policy issued, sold, renewed, or offered for health care services or coverage provided in the Medi-Cal program (Chapter 7 (commencing with Section 14000) of Part 3 of Division 9 of the Welfare and Institutions Code).

(d) For purposes of this section, the following definitions apply:

(1) "ASAM Criteria" means the national set of criteria for providing outcome-oriented and results-based care in the treatment of addiction, and includes a comprehensive set of guidelines for placement, continued stay, and transfer and discharge of patients with addiction and cooccurring conditions, as published by the American Society of Addiction Medicine.

(2) "Pharmacy benefit management company" means a company that administers a prescription drug plan for a health insurer.

(3) "Prior authorization" means the process by which a health insurer or pharmacy benefit management company determines the medical necessity of otherwise covered health care services before those services are rendered. "Prior authorization" includes any health insurer's or utilization review entity's requirement that an insured or health care provider notify the health insurer or utilization review entity before those services are provided.

(4) "Step therapy" means a protocol or program that establishes the specific sequence that prescription drugs for a medical condition, and which drugs are medically appropriate for a patient, are authorized by a health insurer or prescription drug management company.

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

Studies of FDA-approved medications for substance use disorders (SUDs) and relevant behavioral treatments were identified through searches of PubMed, the Cochrane Library, EMBASE, Scopus, and PsycINFO. Websites maintained by the following organizations that produce and/or index meta-analyses and systematic reviews were also searched: the Agency for Healthcare Research and Quality (AHRQ), the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health Service (NHS) Centre for Reviews and Dissemination, the National Institute for Health and Care Excellence (NICE), and the Scottish Intercollegiate Guideline Network. The search was limited to abstracts of studies published in English and current through January 27, 2020, and the search was conducted in the following manner:

- For SUD medications and utilization management, the search only included articles published since January 2019 because CHBRP previously reviewed older literature on medications for these disorders for its report on SB 11, which was issued in 2019.
 - The exception is for injectable naltrexone, which was not covered in the report for SB 11 but was covered in the report for AB 2384 (issued in 2018); the search for articles on injectable naltrexone included articles published since January 2018.
- For combined behavioral therapies and medications for opioid use disorder, the search only included articles published since January 2018 because CHBRP previously reviewed older literature on this treatment approach in its report on AB 2384, which was issued in 2018.
- For combined behavioral therapies and medications for alcohol use disorder, the search was limited to articles published since January 2006 to capture the COMBINE trial.
- For combined behavioral therapies and medications for tobacco use disorder, the search was limited to articles published after January 2015, to account for the most recent USPSTF Tobacco Cessation review.

Of the 558 articles found in the literature review, 94 were reviewed for potential inclusion in this report on SB 854, and a total of 20 studies were included in the medical effectiveness review for this report. The other articles were eliminated because they did not address FDA-approved medications or counseling for SUD, were of poor quality, or did not report findings from clinical research studies.

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*.⁴⁶ 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

⁴⁶ Available at: http://chbrp.com/analysis_methodology/medical_effectiveness_analysis.php.

- 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:

- *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.

Search Terms (* indicates truncation of word stem)

- | | |
|----------------------------------|--------------------------------------|
| 1. Opioid abuse | 21. Cognitive behavioral therapy |
| 2. Opioid use | 22. Motivational interviewing |
| 3. medication assisted treatment | 23. Motivational enhancement therapy |
| 4. methadone | 24. Contingency management |
| 5. buprenorphine | 25. Biofeedback |
| 6. Naloxone | 26. Biomedical risk assessment |
| 7. Lofexidine | 27. Education |
| 8. alcohol abuse disorder | 28. Individual counseling |
| 9. Acamprosate | 29. 12-step programs |
| 10. Naltrexone IM | 30. Peer counseling |
| 11. Disulfiram | 31. Family counseling |
| 12. Tobacco use disorder | 32. Telecounseling/telepsychiatry |
| 13. nicotine addiction | 33. Acupuncture |
| 14. Nicotrol | 34. Acupressure |
| 15. Nicorette | 35. Hypnotherapy |
| 16. Nicoderm CQ | 36. step therapy |
| 17. Varenicline | 37. prior authorization |
| 18. Bupropion HCL ER | |
| 19. Behavioral therapy | |
| 20. Counseling | |

APPENDIX C COST IMPACT ANALYSIS: DATA SOURCES, CAVEATS, AND ASSUMPTIONS

The cost analysis in this report was prepared by the members of the cost team, which consists of CHBRP task force members and contributors from the University of California, Los Angeles, and the University of California, Davis, as well as the contracted actuarial firm, Milliman, Inc.⁴⁷

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.⁴⁸

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

Analysis-Specific Caveats and Assumptions

This subsection discusses the caveats and assumptions relevant to specifically to an analysis SB 854.

SB 854 limits utilization management and cost-sharing requirements for medications approved by the FDA for the treatment of Substance Use Disorders, and behavioral counseling used in conjunction with those medications.

For this analysis, CHBRP identified prescription medications used for the treatment of substance use disorder by combination of a relevant National Drug Code (NDC) and a supporting diagnosis (ICD-10 code) for alcohol use disorder, opioid use disorder, or tobacco use disorder. Exceptions to this methodology were:

- Utilization of naltrexone intramuscular, administered by a clinician as an injection, was identified by HCPCS code J2315.
- Lofexidine is a branded medication that received FDA approval for use in the treatment of opioid use disorder in May 2018. It is chemically equivalent to the generic clonidine, which is used as an off-label treatment for opioid use disorder but is not itself FDA-approved for this use and is therefore not subject to SB 854. CHBRP estimated baseline lofexidine utilization in 2019 as 5% of the clonidine utilization that occurred in conjunction with a diagnosis for opioid use disorder. The baseline cost for this drug was based on the 2019 cost for a 7-day prescription for lofexidine as reported in Bryce (2019).

Table 16 provides a list of the medications included in the analysis.

⁴⁷ CHBRP's authorizing statute, available at http://chbrp.com/CHBRP_authorizing_statute_2018_FINAL.pdf, requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact.

⁴⁸ See method documents posted at http://chbrp.com/analysis_methodology/cost_impact_analysis.php; in particular, see *2019 Cost Analyses: Data Sources, Caveats, and Assumptions*.

Table 16. Outpatient Prescription Medications for SUD and Overdose Reversal Medications

Substance Use Disorder	Category	Drug Name (Generic)	Drug Name (Brand)	Formulation
Opioid Use Disorder	Maintenance	Buprenorphine	Subutex	Sublingual Tablet
Opioid Use Disorder	Maintenance	Buprenorphine	N/A	Sublingual Tablet
Opioid Use Disorder	Maintenance	Buprenorphine	Probuphine	Subdermal Implant
Opioid Use Disorder	Maintenance	Buprenorphine XR	Sublocade	SubQ pre-filled syringe
Opioid Use Disorder	Maintenance	Buprenorphine; Naloxone	N/A	Sublingual Tablet
Opioid Use Disorder	Maintenance	Buprenorphine; Naloxone	Bunavail	Buccal Film
Opioid Use Disorder	Maintenance	Buprenorphine; Naloxone	Suboxone	Sublingual Film
Opioid Use Disorder	Maintenance	Buprenorphine; Naloxone	Zubsolv	Sublingual Tablet
Opioid Use Disorder	Maintenance	Naltrexone	N/A	Tablet
Opioid Use Disorder	Maintenance	Lofexidine	N/A	Tablet
Opioid Use Disorder	Emergency	Naloxone	Narcan	Nasal Spray
Opioid Use Disorder	Emergency	Naloxone	Evzio	Auto-injector Solution
Opioid Use Disorder	Emergency	Naloxone	N/A	Injection Solution
Alcohol Use Disorder	Maintenance	Acamprosate	Campral	Tablet DR
Alcohol Use Disorder	Maintenance	Disulfiram	Antabuse	Tablet
Alcohol Use Disorder	Maintenance	Naltrexone	N/A	Tablet
Tobacco Use Disorder	Maintenance	Nicotine	Nicoderm CQ	Patch 24 Hour
Tobacco Use Disorder	Maintenance	Nicotine	Nicorette	Gum
Tobacco Use Disorder	Maintenance	Nicotine	Nicorette	Lozenge
Tobacco Use Disorder	Maintenance	Nicotine	Nicotrol	Inhaler
Tobacco Use Disorder	Maintenance	Varenicline	Chantix	Tablet
Tobacco Use Disorder	Maintenance	Bupropion HCL SR	Zyban	Tablet SR 12 Hour

Source: California Health Benefits Review Program, 2020.

CHBRP limited the therapy and counseling in this analysis to individual therapy, family therapy, and group therapy provided in conjunction with one of the medications in Table 16. CHBRP determined that more intensive forms of therapy and counseling, such as partial hospitalization and intensive outpatient were not commonly used in conjunction (that is, specifically to support compliant use of the medication) with these medications, although concurrent use was not uncommon. Relevant therapy and counselling utilization was identified by a hierarchical mapping, using the place of service, provider type, revenue codes, and CPT/HCPCS codes.

Table 17. CPT/HCPCS Codes Used for Behavioral Therapy Services for Substance Abuse

CPT/HCPCS Code	Description
99406 – 99407, 4000F - 4004F, G0436 - G0437, G9016, G9458, G9906, D1320, C9801 - C9802, G8402, G8453	Smoking and Tobacco Use Cessation Counseling
4158F, 4320F, G0443, G9621, T1006	Alcohol Use Counseling
4306F	Opioid Use Counseling
H0004	Behavioral Health Counseling
H0005, H0015	Alcohol and/or Drug Counseling

Source: California Health Benefits Review Program, 2020.

CHBRP used the Substance Use Disorder diagnosis codes to identify the Substance Use Disorder Outpatient Drug users in Milliman’s proprietary 2017 Consolidated Health Cost Guidelines Sources Database (CHSD). Only commercial claims were included in this analysis, as SB 854 does not impact Medi-Cal plans.

CHBRP identified all individuals with SUD diagnosis codes throughout the year to establish a baseline estimate of the number of diagnosed individuals with an SUD. CHBRP relied upon the NDC codes to establish the utilization levels for each medication dosage and formulation prescribed for treatment of an SUD. CHBRP used the CPT/HCPCS codes to identify SUD counseling for members identified as using one or more of the specified SUD medications.

The supporting diagnosis codes are shown in Table 18.

Table 18. Diagnosis Codes Used for Substance Use Disorder

Diagnosis Code (ICD-10)	Description
F10.10-F10.99	Alcohol Abuse/Dependence/Use
F11.10-F11.99	Opioid Abuse/Dependence/Use
F17.200-F17.2999	Nicotine Dependence

Source: California Health Benefits Review Program, 2020.

Baseline medication unit costs were trended at an annual rate 7.5% per year from 2017 to 2020 (Milliman 2019 Commercial Health Cost Guidelines™). The 7.5% trend represents the 2019 drug trends for the commercial enrollees represented within the report. As the increase in utilization seems unlikely to impact it, the unit cost per script is expected to be unchanged by SB 854, postmandate. Based on the same source, behavioral therapy unit costs were trended at an annual rate of 4.5% from 2017 to 2020.

Table 19. SB 854 Utilization Impact Factors

Medication	Cost Sharing Reduction (a)	Utilization Management Prohibitions (b), (c)	Offsets (d)	Switch (e)
Acamprosate	1.07	1.10		

Naltrexone – Oral Aud	1.03	1.05		
Naltrexone – IM Aud	1.27	1.05		
Disulfiram	1.00	1.00	No offsets see ME, not effective	
Buprenorphine – IM	1.27	1.25		
Buprenorphine – other	1.08	1.10		
Methadone	1.00	1.00(f)		
Naloxone	1.27	1.25		More auto injector formulation
Naltrexone – Oral Oud	1.03	1.05	No offsets see ME, not effective	
Naltrexone – IM Oud	1.03	1.05		
Buprenorphine-Naloxone	1.19	1.10		
Lofexidine	1.27	1.00	No offsets, parallel decrease in off-label	Less off-label generic clonidine
Nicotine – Inhaler	1.00	1.10		
Varenicline	1.00	1.10		
Bupropion HCL ER	1.00	1.10		

Notes: (a) Developed from 2019 Milliman Health Cost Guidelines Commercial

(b) CHBRP estimates; these are applied only to the membership subject to prohibited utilization management

(c) UM applied to BH therapy is 5% factor

(d) See Offsets table

(e) No current assumptions

(f) Methadone as a treatment for opioid use disorder can only be had from federally certified Opioid Treatment Programs (OTPs, often called methadone clinics). Therefore, the benefit coverage change is not expected to increase utilization in the initial year, postmandate.

Individual, Group and Family Therapy are projected to increase less than the overall increase in medication utilization. Medications indicated for overdose reversal (Naloxone) and treatment of withdrawal symptoms (Lofexidine) are not used in conjunction with therapeutic counseling, for instance. The survey responses provided indicate that there were no coverage gaps or utilization management protocols utilized to restrict access to Individual, Group or Family Therapy when used in conjunction with the medications included in this mandate.

Postmandate Offset Services – Inpatient, Outpatient, and Professional

There are likely to be changes in the utilization of health services as a result of receiving SUD treatment. Mohlman et al. (2016) indicated reductions in inpatient days and emergency department visits associated with treatment of opioid use disorder. Mark et al. (2010) provided estimated reductions in detoxification days, inpatient days and emergency department visits associated with use of medications to treat alcohol use disorder.

Unit costs were estimated using a combination of the Mohlman et al. (2016) estimates, Milliman’s proprietary CHSD data, and relationships between commercial and Medi-Cal unit costs. CHBRP relied upon CHSD data for commercial and Medi-Cal utilization and cost estimate. SB 854 will not cause a significant change in average cost per service postmandate.

Table 20. Offset Assumptions

	Average Utilization Change per SUD Treatment User	Commercial Unit Cost (2021)
Opioid Use Disorder Inpatient Days	-1.46	\$8,862
Opioid Use Disorder ED Visits	-1.04	\$3,983
Alcohol Use Disorder Inpatient Days	-0.436	\$9,842
Alcohol Use Disorder Detox Days	-0.457	\$1,519
Alcohol Use Disorder ED Visits	-0.044	\$4,521

Source: California Health Benefits Review Program, 2020.

Key: ED = Emergency department; SUD = substance use disorder.

Postmandate Offset Services – Inpatient, Outpatient, and Professional

There are likely to be changes in the utilization of non-SUD-related services as a result of receiving SUD treatment. Mohlman et al. (2016) indicated reductions in inpatient days and emergency department visits associated with treatment of opioid use disorder. Mark et al. (2010) provided estimated reductions in detoxification days, inpatient days, and emergency department visits associated with use of medications to treat alcohol use disorder.

Unit costs were estimated using a combination of the Mohlman et al. (2016) estimates, CHSD data, and relationships between commercial and Medi-Cal unit costs. CHBRP relied upon CHSD data for commercial and Medi-Cal utilization and cost estimate. SB 11 will not cause a significant change in average cost per service postmandate.

Determining Public Demand for the Proposed Mandate

This subsection discusses public demand for the benefits SB 854 would mandate. Considering the criteria specified by CHBRP’s authorizing statute, CHBRP reviews public demand for benefits relevant to a proposed mandate in two ways. CHBRP:

- Considers the bargaining history of organized labor; and
- Compares the benefits provided by self-insured health plans or policies (which are not regulated by 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.

On the basis of conversations with the largest collective bargaining agents in California, CHBRP concluded that unions currently do not include cost-sharing arrangements for description treatment or service. In general, unions negotiate for broader contract provisions such as coverage for dependents, premiums, deductibles, and broad coinsurance levels.

Among publicly funded self-insured health insurance policies, the preferred provider organization (PPO) plans offered by CalPERS currently have the largest number of enrollees. The CalPERS PPOs currently provide benefit coverage similar to what is available through group health insurance plans and policies that would be subject to the mandate.

To further investigate public demand, CHBRP used the bill-specific coverage survey to ask carriers 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.

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 SB 854 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 SB 854 would be substantially the same as the impacts in the first year (see Table 1). Minor changes to utilization and expenditures are due to population changes between the first year postmandate and the second year postmandate.

APPENDIX D INFORMATION SUBMITTED BY OUTSIDE PARTIES

In accordance with the California Health Benefits Review Program (CHBRP) policy to analyze information submitted by outside parties during the first 2 weeks of the CHBRP review, the following parties chose to submit information.

The following information was submitted by Maria Sullivan, Senior Medical Director, Medical Affairs, Alkermes, Inc, in January 2020, which offered the following citations:

Sullivan, M. Personal communication regarding Alkermes product Vivitrol. Letter by e-mail. January 23, 2020.

Alkermes Inc. VIVITROL* (Prescribing Information). Waltham, MA:2019.

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The following information was submitted by Ryan Hampton, Director and Advocate, the Voices Project, in February 2020.

Hamilton, R. Personal communication regarding SB 854. Letter by e-mail. February 4, 2020.

The following information was submitted by Alice Hayes, in February 2020.

Hayes, A. Personal communication regarding SB 854. E-mail. February 4, 2020, which offered the following citations:

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National Quality Forum. Enhancing Access to Medication-Assisted Treatment, 2019. *The National Quality Forum.*

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United States Government Accountability Office. OPIOID USE DISORDER: Barriers to Medicaid Beneficiaries' Access to Treatment Medications, 2020. *United States Government Accountability Office.* GAO-20-233.

Submitted information is available upon request. For information on the processes for submitting information to CHBRP for review and consideration, please visit www.chbrp.org/requests.html.

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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.

Faculty Task Force

Janet Coffman, MA, MPP, PhD, Vice Chair for Medical Effectiveness, University of California, San Francisco

Sylvia Guendelman, PhD, LCSW, University of California, Berkeley

Gerald Kominski, PhD, University of California, Los Angeles

Sara McMenamin, PhD, *Vice Chair for Medical Effectiveness and Public Health*, University of California, San Diego

Joy Melnikow, MD, MPH, *Vice Chair for Public Health*, University of California, Davis

Jack Needleman, PhD, University of California, Los Angeles

Nadereh Pourat, PhD, *Vice Chair for Cost*, University of California, Los Angeles

Marilyn Stebbins, PharmD, University of California, San Francisco

Task Force Contributors

Danielle Casteel, MA, University of California, San Diego

Shana Charles, PhD, MPP, University of California, Los Angeles, and California State University, Fullerton

Shauna Durbin, MPH, University of California, Davis

Margaret Fix, MPH, University of California, San Francisco

Sarah Hiller, MA, University of California, San Diego

Naomi Hillery, MPH, University of California, San Diego

Jeffrey Hoch, PhD, University of California, Davis

Michelle Ko, MD, PhD, University of California, Davis

Elizabeth Magnan, MD, PhD, University of California, Davis

Jacqueline Miller, University of California, San Francisco

Marykate Miller, MS, University of California, Davis

Dominique Ritley, MPH, University of California, Davis

Dylan Roby, PhD, University of California, Los Angeles, and University of Maryland, College Park

Riti Shimkhada, PhD, University of California, Los Angeles

Meghan Soulsby Weyrich, MPH, University of California, Davis

Steven Tally, PhD, University of California, San Diego

Marissa Vismara, MA, University of California, Davis

Sara Yoeun, University of California, San Diego

National Advisory Council

Lauren LeRoy, PhD, Strategic Advisor, L. LeRoy Strategies, Chair
Stuart H. Altman, PhD, Professor of National Health Policy, Brandeis University, Waltham, MA
Deborah Chollet, PhD, Senior Fellow, Mathematica Policy Research, Washington, DC
Allen D. Feezor, Fmr. Deputy Secretary for Health Services, North Carolina Department of Health and Human Services, Raleigh, NC
Charles “Chip” Kahn, MPH, President and CEO, Federation of American Hospitals, Washington, DC
Jeffrey Lerner, PhD, President and CEO, ECRI Institute Headquarters, Plymouth Meeting, PA
Donald E. Metz, Executive Editor, *Health Affairs*, Bethesda, MD
Dolores Mitchell, (Retired) Executive Director, Group Insurance Commission, Boston, MA
Marilyn Moon, PhD, Vice President and Director, Health Program, American Institutes for Research, Silver Spring, MD
Carolyn Pare, (Retired) President and CEO, Minnesota Health Action Group, Bloomington, MN
Richard Roberts, MD, JD, Professor of Family Medicine, University of Wisconsin-Madison, Madison, WI
Alan Weil, JD, MPP, Editor-in-Chief, *Health Affairs*, Bethesda, MD

CHBRP Staff

Garen Corbett, MS, Director
John Lewis, MPA, Associate Director
Adara Citron, MPH, Principal Policy Analyst
Ana Ashby, MPP, Policy Analyst
Karen Shore, PhD, Contractor*

<p>California Health Benefits Review Program MC 3116 Berkeley, CA 94720-3116</p>

*Karen Shore, PhD, is an Independent Contractor who works with CHBRP to support legislative analyses and other special projects on a contractual basis.

CHBRP is an independent program administered and housed by the University of California, Berkeley, in the Office of the Vice Chancellor for Research.

ACKNOWLEDGMENTS

CHBRP gratefully acknowledges the efforts of the team contributing to this analysis:

Shauna Durbin, MPH, Elizabeth Magnan, MD, PhD, and Meghan Soulsby Weyrich, MPH, all of the University of California, Davis, prepared the medical effectiveness analysis. Shana Charles, PhD, MPP of the University of California, Los Angeles, and California State University, Fullerton, prepared the cost impact analysis. Daniel Henry, FSA, MAAA of Milliman provided actuarial analysis. Content expert Scott Steiger, MD, University of California, San Francisco, provided technical assistance with the literature review and expert input on the analytic approach. John Lewis, MPA, and Ana Ashby, MPP, of CHBRP staff prepared the Policy Context, Background, and Public Health sections and synthesized the individual sections into a single report. A subcommittee of CHBRP's National Advisory Council (see previous page of this report) and members of the CHBRP Faculty Task Force, Janet Coffman, MA, MPP, PhD, of the University of California, San Francisco, Sara McMenam, PhD, of the University of California, San Diego, Nadereh Pourat, PhD, of the University of California, Los Angeles, and Marilyn Stebbins, PharmD, of the University of California, San Francisco, reviewed the analysis for its accuracy, completeness, clarity, and responsiveness to the Legislature's request.

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.

Garen Corbett, MS
Director

Please direct any questions concerning this document to: California Health Benefits Review Program; MC 3116; Berkeley, CA 94720-3116, info@chbrp.org, or www.chbrp.org