California Health Benefits Review Program

Analysis of California Assembly Bill AB 623 Abuse-Deterrent Opioid Analgesics

A Report to the 2015–2016 California State Legislature

May 20, 2015

CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

Key Findings:

Analysis of California Assembly Bill AB 623 Abuse Deterrent Opioid Analgesics

Summary to the 2015-2016 California State Legislature, May 2015

CALIFORNIA HEALTH BENEFITS REVIEW PROGRAM

AT A GLANCE

Assembly Bill AB 623 as amended March 2015, would require compliant utilization management protocols for coverage of opioid analgesics and opioid analgesics labeled by the Food and Drug Administration as abuse-deterrent (FDA-ADOAs).

- **Enrollees covered.** In 2016, approximately 24.6 million Californians will have state-regulated health insurance subject to AB 623.
- **EHBs.** AB 623 would not exceed essential health benefits, because the mandate is applicable to terms and conditions but does not require new benefit coverage.
- **Background.** National recommendations regarding abuse prevention focus on broad policy interventions, including education; tracking and monitoring; enforcement, regulation, and oversight. Oral (including swallowing unaltered pills) is the most common form of abuse.
- **Medical effectiveness.** The impact of ADOAs on abuse is *ambiguous*. Some studies suggest abuse-deterrent formulations reduce some forms of abuse (particularly those related to inhaling or injecting) of the reformalated drug, but other studies suggest ADOAs shift abuse to other opioid analgesics and/or to illicit drugs (such as heroin).
- **Utilization and expenditures.** Total utilization of opioid analgesics would not change, but use of FDA-ADOAs may increase as much as 38%, resulting in a 13% average unit cost increase (FDA-ADOAs cost more) and a 0.0058% total expenditures increase. These estimates are an "upper bound", as not all patients associated with changing protocols may shift to FDA-ADOAs.
- **Public health.** As the impact of ADOAs on abuse is ambiguous and it is unclear how many patients would shift to FDA-ADOAs, it is unlikely that AB 623 would affect overdoses, associated use of emergency rooms and/or hospitals, or deaths.
- **Long-term impacts.** Long-term reduction in abuse may be more associated with broad policy intervention and with prescriber behavior than with changes in health plan and health insurer utilization management protocols.

BACKGROUND

Opioid analgesics are drugs prescribed to alleviate pain. Prescribed opioid analgesics are increasingly abused. Oral (including swallowing of unaltered pills) is the most common form of abuse. Methods of abuse include crushing, cutting, or dissolving pills (for inhalation or injection) to achieve a more intense and immediate effect. Many opioids are available as extended-release (ER) formulations, which deliver the drug steadily over a long period of time. Altering ER opioids for inhalation or injection effectively increases the dose, which increases the euphoric effect. Nearly half of young users report abusing prescription opioid analgesics before starting heroin. In order to combat the increase in abuse, the White House Administration's *National Drug Control Strategy* and the Centers for Disease Control and Prevention (CDC) recommend implementation of state-level policies addressing three broad areas – education; tracking and monitoring; and enforcement, regulation, and oversight activities. Actions recommended within these broad areas focus on influencing prescriber and patient behavior.

MEDICAL EFFECTIVENESS

Abuse-deterrent opioid analgesics (ADOAs) are intended to deter some forms of abuse (especially abuse related to inhalation or injection) by establishing physical or chemical barriers to the more intense or immediate highs achieved by altering the drug (through crushing, chewing, cutting, or dissolving). However, abuse-deterrent formulations do not reduce or eliminate the addictive properties of opioids or prevent abuse related to swallowing pills. The FDA reviews inclusion of physical and/or chemical deterrents in drug formulation and labels drugs as FDA-ADOAs, but notes that the technologies have not yet proven successful at deterring the most common form of abuse – swallowing intact pills. As of May 2015, CHBRP is aware of three available FDA-ADOAs on the market: Embeda, Hysingla ER, and OxyContin.

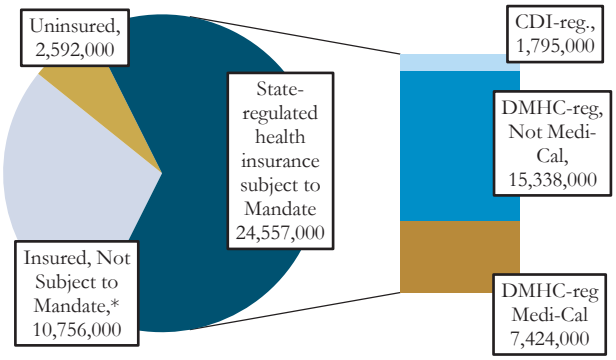
CHBRP reviewed the literature and determined that the impact of ADOAs on abuse is *ambiguous*. Although some studies suggest that abuse-deterrent formulations can

reduce some forms of abuse (particularly those related to inhalation or injection) of a reformulated drug, other studies suggest the presence of ADOAs shifts abuse to other opioid analgesics and/or to illicit drugs (such as heroin).

BILL SUMMARY

In 2016, as noted in Figure 1, AB 623 would apply to the health insurance of 24.6 million Californians (all enrollees with health insurance potentially subject to state-level benefit mandates).

Figure 1. Health Insurance in CA and AB 623



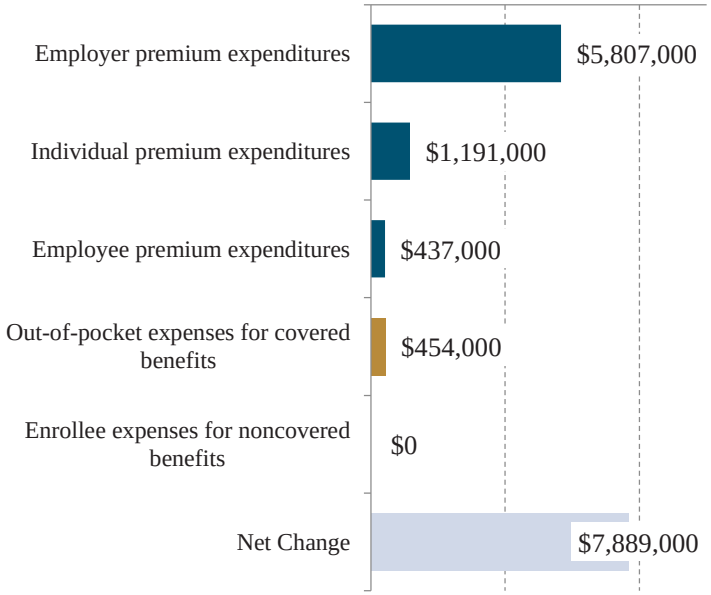
*Federally regulated health insurance, such as Medicare, veterans, or self-insured plans.
Source: California Health Benefit Review Program, 2015.

AB 623 would place requirements on the terms and conditions of outpatient prescription drug (OPD) benefits covered by health plans regulated by the Department of Managed Health Care (DMHC) and by health insurers regulated by the California Department of Insurance (CDI). AB 623 would: (1) prohibit utilization management protocols requiring use of other opioid analgesics before covering opioid analgesics labeled by the Food and Drug Administration as abuse-deterrent (FDA-ADOAs); (2) require that prior authorization protocols for a drug be the same whether the drug is in regular formulation or abuse-deterrent formulation; and (3) require coverage for less than 30-day prescriptions of opioid analgesics.

UTILIZATION AND COST IMPACTS

AB 623 would not alter benefit coverage, but it would require changes in utilization management protocols for approximately 58% of enrollees in DMHC-regulated plans and CDI-regulated policies. The changed protocols would not impact the total number of filled opioid analgesic prescriptions, but would increase the portion of filled prescriptions represented by FDA-ADOAs. AB 623 could increase utilization of FDA-ADOAs by 38%. Such an increase would raise the average unit cost by 13% because FDA-ADOAs cost more (on average) than other opioid analgesics. The increased unit cost would impact total expenditures (premiums and cost sharing), resulting in an increase of 0.0058% across all market segments. Details of the expenditure impacts are presented in Figure 2. These impacts represent a likely upper bound, because CHBRP modeled the replacement of other opioid analgesics with some abuse-deterrent properties, most of which are extended release (ER) drugs, with FDA-ADOAs for all enrollees with utilization management protocols that would change to be compliant with AB 623. The estimate is an upper bound, because not all providers are aware of or interested in prescribing FDA-ADOAs, and not all enrollees would want FDA-ADOAs to be prescribed for them.

Figure 2. Expenditure Impacts of AB 623



PUBLIC HEALTH IMPACTS

In the first postmandate year, AB 623 would have an unknown public health impact due to both the ambiguous evidence of effectiveness of ADOAs in deterring overall abuse and the unknown magnitude of changes in prescriber and patient behavior in response to changing utilization management protocols. However, CHBRP posits that it is unlikely AB 623 would have a measurable impact on abuse, overdose, or premature death for the following reasons:

- Addictive properties are still present in FDA-ADOAs.
- Initial abuse frequently begins with oral abuse (swallowing pills), which is not affected by abuse-deterrent formulation.
- Many continuing abusers prefer to orally abuse.
- Continuing abusers are also able to choose oral abuse when faced with abuse-deterrent formulations.
- Only three FDA-ADOAs are available in the marketplace as of April 2015, so substitution with non-abuse-deterrent formulation opioid analgesics will still occur for some portion of the population.
- Substitution with heroin, which is reportedly cheaper and easier to obtain, will occur for some abusers.

For these reasons, AB 623 is unlikely to materially affect the number of opioid analgesic overdoses and associated emergency department use, hospitalizations, or deaths in the first year after passage.

LONG-TERM IMPACTS

AB 623 would have an unknown long-term public health impact because ADOAs are only one of many population-based, primary and secondary abuse prevention strategies; changes to insurers' utilization management protocols associated with ADOAs would be a small subset of those prevention strategies. Furthermore, to date ADOAs have yet to demonstrate a statistically significant reduction in *overall* prescription opioid abuse and overdose. ADOAs are a relatively new addition to the collection of strategies and, as more ADOAs are FDA-approved, further epidemiologic surveillance and study is required to ascertain its effectiveness.

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May 20, 2015

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ABOUT CHBRP

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

An analytic staff in the University of California's Office of the President supports a task force of faculty and research staff from several campuses of the University of California 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, and 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, as well as all CHBRP reports and publications are available at www.chbrp.org.

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AB 623 IMPACTS ON BENEFIT COVERAGE, UTILIZATION, AND COST

Table 1. AB 623 Impacts on Benefit Coverage, Utilization, and Cost, 2016

	Premandate	Postmandate	Increase/ Decrease	Postmandate Change
Benefit coverage				
Total enrollees with health insurance subject to state benefit mandates (a)	24,557,000	24,557,000	0%	0%
Total enrollees with health insurance subject to AB 623	24,557,000	24,557,000	0%	0%
Number of enrollees with an outpatient prescription drug benefit fully compliant with AB 623	10,245,000	24,557,000	14,312,000	140%
Percentage of enrollees with an outpatient prescription drug benefit fully compliant with AB 623	42%	100%	58%	140%
Utilization and cost				
Annual use of opioid analgesics associated with changing protocols (not including FDA-ADOA) per 1,000 enrollees	325.80	322.09	-3.70	-1%
Annual use of FDA-ADOA per 1,000 enrollees	9.71	13.41	3.70	38%
Average per-unit cost of opioid analgesics associated with changing protocols	$51.38	$57.95	$6.57	13%
Expenditures				
Premium expenditures by payer				
Private employers for group insurance	$58,393,205,000	$58,394,449,000	$1,244,000	0.0021%
CalPERS HMO employer expenditures (b)	$4,391,552,000	$4,391,687,000	$135,000	0.0031%
Medi-Cal Managed Care Plan expenditures	$17,667,731,000	$17,672,159,000	$4,428,000	0.0251%
Enrollees for individually purchased insurance	$21,319,735,000	$21,320,926,000	$1,191,000	0.0056%
Individually purchased - outside exchange	$8,581,274,000	$8,581,885,000	$611,000	0.0071%
Individually purchased - Covered California	$12,738,461,000	$12,739,041,000	$580,000	0.0046%
Enrollees with group insurance, CalPERS HMOs, Covered California, and Medi-Cal Managed Care (c)	$18,703,917,000	$18,704,354,000	$437,000	0.0023%

Enrollee expenses				
Enrollee out-of-pocket expenses for covered benefits (deductibles, copayments, etc.)	$15,510,004,000	$15,510,458,000	$454,000	0.0029%
Total expenditures	$135,986,144,000	$135,994,033,000	$7,889,000	0.0058%

Source: California Health Benefits Review Program, 2015.

Notes: (a) This population includes persons with privately funded (including Covered California) and publicly funded (e.g., CalPERS HMOs, Medi-Cal Managed Care Plans) health insurance products regulated by DMHC or CDI. Population includes enrollees aged 0 to 64 years and enrollees 65 years or older covered by employer-sponsored health insurance.

(b) Of the increase in CalPERS employer expenditures, about 55.4%, or about $75,000, would be state expenditures for CalPERS members who are state employees, state retirees, or their dependents. This percentage reflects the share of enrollees in CalPERS HMOs as of September 30, 2013. CHBRP assumes the same ratio in 2015.

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

Key: CalPERS HMOs = California Public Employees' Retirement System Health Maintenance Organizations; CDI = California Department of Insurance; DMHC = Department of Managed Health Care.

POLICY CONTEXT

The California Assembly Committee on Health has requested[1] that the California Health Benefits Review Program (CHBRP)[2] conduct an evidence-based assessment of the medical, financial, and public health impacts of AB 623, Abuse-Deterrent Opioid Analgesics.

If enacted, AB 623 would affect the health insurance of approximately 24.6 million enrollees (65% of all Californians). This represents 100% of the 24.6 million Californians who, in 2016, will have health insurance regulated by the state[3] that may be subject to any state health benefit mandate law.[4,5]

It is important to note that CHBRP's analysis of proposed benefit mandate bills typically address the incremental effects of the proposed bills – specifically, how the proposed legislation would impact benefit coverage, utilization, costs, and public health. CHBRP's estimates of these incremental effects are presented in this report.[6]

Bill-Specific Analysis of AB 623, Abuse-Deterrent Opioid Analgesics

AB 623 includes language that addresses the terms and conditions of coverage for opioid analgesics, which are covered as part of an outpatient prescription drug benefit. Opioid analgesics are designed to alleviate moderate-to-severe acute pain, chronic noncancer pain (such as chronic back pain, osteoarthritis, etc.), chronic pain related to cancer, and pain at the end of life (Chou et al., 2009). Despite their legitimate medical use, as further discussed in the *Background* section, opioid analgesics are increasingly abused.

Some opioid analgesics are available in abuse-deterrent formulations. However, as discussed further in the *Medical Effectiveness* section, not all abuse-deterrent opioid analgesics (ADOA) are so labelled by the Food and Drug Administration (FDA). Currently, there are three FDA-labelled abuse-deterrent opioid analgesics (FDA-ADOAs) on the market: Embeda, Hysingla ER, and OxyContin. AB 623 would limit utilization management protocols associated with opioid analgesics.

Bill Language

For DMHC-regulated plans and CDI-regulated policies, AB 623 would:

- Prohibit requiring use of other opioid analgesics prior to covering opioid analgesics labeled as "abuse-deterrent" by the Food and Drug Administration (FDA-ADOAs);
- Require the same prior authorization protocols be applicable to an opioid analgesics whether it is in a standard or an FDA labelled abuse-deterrent formulation; and

[1] March 10, 2015, available at www.chbrp.org.
[2] CHBRP is authorized to review legislation affecting health insurance regulated by the state. CHBRP's authorizing statute is available at www.chbrp.org/docs/authorizing_statute.pdf.
[3] State benefit mandates apply to a subset of health insurance in California, those regulated by one of California's two health insurance regulators: the California Department of Managed Health Care (DMHC) and the California Department of Insurance (CDI).
[4] CHBRP's estimates of the source of health insurance available at: www.chbrp.org/other_publications/index.php.
[5] Of the rest of the state's population, a portion will be uninsured (and therefore will have no health insurance subject to any benefit mandate), and another portion will have health insurance subject to other state laws or only to federal laws.
[6] For CHBRP's technical approach to developing estimates, please see Appendix C.

- For covered opioid analgesics, provide coverage for less than 30-day supplies.

The full text of AB 623 can be found in Appendix A.

Interaction With Existing Requirements

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

State Requirements

California law and regulations

CHBRP is aware of a number of current health insurance benefit mandates that might interact with compliance to AB 623, influencing coverage of particular drugs, even when the drug is not on formulary for the enrollee's plan or policy. Examples are listed by Health and Safety Code (H&S), with Insurance Code (IC) when applicable:

- *H&S1367.21/IC10123.195; prescription drugs: off-label use.* Mandate to cover "off-label" uses of FDA-approved drugs – uses other than the specific FDA-approved use – in life-threatening situations and in cases of chronic and seriously debilitating conditions – when a set of specified provisions regarding evidence are met.
- *H&S 1367.22; prescription drugs: coverage of previously covered drugs.* Mandate to cover prescription drugs if the drug previously had been approved for coverage by the plan for a medical condition of the enrollee and the plan's prescribing provider continues to prescribe the drug for the medical condition, provided that the drug is appropriately prescribed and is considered safe and effective for treating the enrollee's medical condition.
- *H&S 1367.22; prescription drug benefits: medically appropriate alternatives.* Mandate to cover prescription drug for an enrollee if the drug previously had been approved for coverage by the plan for a medical condition of the enrollee and the plan's prescribing provider continues to prescribe the drug for the medical condition, provided that the drug is appropriately prescribed and is considered safe and effective for treating the enrollee's medical condition.
- *H&S 1367.24; authorization for nonformulary prescription drugs.* Mandate to review coverage for nonformulary drugs.

Similar requirements in other states

In 2015, CHBRP is aware of a number of states considering bills related to coverage for opioid analgesics, including: CO, CT, FL, KS, MD, MS, OK, OR, RI, TN, VT, VA.

The Florida bill (SB 728) is similar to SB 623: (1) requiring that prior authorization protocols be applicable to opioid analgesics in standard or abuse-deterrent formulations; and (2) prohibiting utilization management protocols that require use of another opioid analgesic before covering an ADOA.

Federal Requirements

Affordable Care Act

The Affordable Care Act (ACA) has profoundly impacted health insurance, its financing, and regulation in California. As of January 2014, an expansion of the Medi-Cal program, California's Medicaid program,[7] and the availability of subsidized and nonsubsidized health insurance purchased through Covered California,[8] the state's health insurance marketplace,[9] significantly increased the number of people with health insurance in California.

A number of ACA provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how AB 623 may interact with requirements of the ACA, including the requirement for certain health insurance to cover "essential health benefits" (EHBs).[10]

AB 623 and essential health benefits (EHBs)

AB 623 would alter the terms and conditions of benefit coverage for opioid analgesics, but would not alter benefit coverage requirements. Therefore, AB 623 would not exceed EHBs, and would not trigger the ACA requirement that the state defray the cost of additional benefit coverage for enrollees in qualified health plans (QHPs)[11] in Covered California.

[7] The Medicaid expansion, which California will pursue, is to 133% of the federal poverty level (FPL) – 138% with a 5% income disregard.
[8] The California Health Benefits Exchange (Covered California) Authorizing Statute is available here: www.healthexchange.ca.gov/Documents/California%20Codes%20Governing%20the%20Health%20Benefit%20Exchange.pdf.
[9] The ACA requires the establishment of health insurance exchanges in every state, now referred to as health insurance marketplaces.
[10] 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. Resources on EHBs and other ACA impacts are available on the CHBRP website: www.chbrp.org/other_publications/index.php.
[11] In California, QHPs are nongrandfathered small-group and individual market DMHC-regulated plans and CDI-regulated policies sold in Covered California, the state's online marketplace.

BACKGROUND ON PRESCRIPTION OPIOID ABUSE

This *Background* section provides context for CHBRP's analysis of AB 623 by discussing the prevalence of prescription opioid analgesic abuse, sources of abused opioids, methods of abuse, and prescription opioid overdose mortality rates, as well as strategies at the local, state, and federal level to prevent prescription opioid analgesic abuse.

Prescription opioid abuse

Abuse of prescription opioids has become a significant public health problem, attracting attention at the federal and state levels (USDHHS, 2015). Abuse is defined as "the intentional, nontherapeutic use of a drug product or substance, even once, to achieve a desirable psychological or physiological effect" (CDER, 2015).

From 2004 to 2011 in the United States, emergency department (ED) visits attributable to prescription opioid abuse increased by 153% (CBHSQ, 2013). Prescription opioid overdose has surpassed firearms and motor vehicle accidents as the leading cause of unintentional injury or death among 35 to 54 year olds, and is the second leading cause of death overall (behind motor vehicle accidents) (CDC, 2010, 2011b). Prescription opioid abuse is associated with other negative health outcomes, including "transitions to injection drug use with resulting risk for infections such as Hepatitis C and HIV, falls and fractures in older adults, and neonatal opioid withdrawal syndrome" (USDHHS, 2013).

Nationally, health care–related costs due to prescription opioid abuse have been estimated to cost insurers (both public and private) approximately $72.5 billion annually (CDC, 2011). In 2006 to 2007, the estimated total economic burden (which includes health care costs, as well as criminal justice and lost productivity costs) have been estimated between $53 billion and $55.7 billion, which is an increase of over 500% from $8.6 billion in 2001 (Birnbaum et al., 2006, 2011; Hansen et al., 2011).

Sources of Abused Prescription Opioids and Methods of Abuse

Commonly abused prescription opioid analgesics include oxycodone-, hydrocodone-, and morphine-based products, as well as methadone (DAWN, 2013). Persons abusing prescription opioid analgesics acquire their opioids from a variety of sources, but it appears that most users obtain the drugs from their doctor or from a friend or relative who was prescribed the drugs. Specifically, the 2013 National Survey on Drug Use and Health (NSDUH) found that 53% of abusers obtained their opioid analgesics free from a friend or relative, and nearly 15% of abusers purchased or took their opioid analgesics from a friend or relative. Twenty-one percent of abusers received their opioid analgesic using a prescription from their doctor. Of those abusers obtaining the opioid analgesic for free from a friend or family member (53% of all abusers), nearly 84% those persons obtained their opioid analgesic using a prescription from their doctor (SAMHSA, 2014).

Persons abusing prescription opioid analgesics use a number of different routes of administration, with the majority being abused orally (swallowing, chewing, or sublingually) (Budman et al., 2009). Additional methods of abuse include crushing, cutting, or dissolving pills (for inhalation or injection) to achieve a more intense and immediate effect than what is experienced through oral consumption (Budman et al., 2009). Using non-oral routes of administration enables the user to access his or her bloodstream faster than the digestive tract, which results in a more immediate and intense effect (Budman et al., 2009). Additionally, many opioids are extended-release formulations that deliver the medication steadily over a long period of time. Altering extended-release opioids for inhalation or injection effectively increases the

dose, which increases the euphoric effect (Moorman-Li et al., 2012). As shown in Table 2, over half of abusers report oral abuse of hydrocodone, oxycodone, and methadone (Butler et al., 2008).

Table 2. Estimated Prevalence of Abusers Using Different Routes of Administration, 2007–2008

Prescription Opioid Analgesic	Oral	Snort	Inject
Hydrocodone	88%	25%	<10%
Oxycodone	76%	45%	22%
Morphine	40%	29%	66%
Methadone	71%	10%	<10%

Source: CHBRP, based on Butler et al., 2008.

Prevalence of Prescription Opioid Abuse

In 2013, the NSDUH estimated that 13.5% of the U.S. population aged 12 years and older reported ever abusing prescription opioid analgesics, with 4.2% reporting past-year abuse and 1.7% reporting past-month abuse. Abuse among individuals ages 12 years and older in the pacific region (defined by the NSDUH as Alaska, California, Hawaii, Oregon, and Washington) was higher than the national rate of abuse, with 16.1% reporting lifetime use, 4.9% reporting past-year use, and 2.2% reporting past-month use (CBHSQ, 2014a).

An analysis of the 2012–2013 NSDUH found that abuse was higher in California compared to the rest of pacific region, with 5.2% of those aged 12 years and older reporting past year prescription opioid abuse, which translates to 1,643,000 Californians. The prevalence of abuse among Californians aged 12 to 17 years was 5.3% (164,000 persons), 10.3% among Californians aged 18 to 25 (459,000 persons), and 4.3% among Californians aged 26 years and older (1,021,000 persons) (CBHSQ, 2015).

Nationally, abuse tends to be higher among males and non-Hispanics (particularly whites, Native Hawaiian/Pacific Islanders, and American Indian/Alaska Natives) and peaks among adults aged 18 to 25 years.

Mortality

From 2000 to 2008, prescription opioid overdose deaths in the United States increased by over 250% (Warner et al., 2011), and an estimated 100 prescription opioid-related deaths occur daily, which is greater than the number of deaths attributable to heroin and cocaine combined (CDC, 2011a). In 2008, the prescription opioid analgesic overdose mortality rate was 4.8 per 100,000 individuals, accounting for nearly 41% of all drug overdose deaths (Warner et al., 2011). Similarly, with the prevalence of prescription opioid abuse, overdose deaths are higher among males and non-Hispanics. In contrast with the abuse rate, overdose deaths are highest among older adults, peaking among those aged 45 to 54 years (CDC, 2011b).

Policies and Strategies to Prevent Prescription Opioid Abuse

The federal government is working in conjunction with states to implement multidisciplinary, complementary strategies and policies to reduce prescription opioid abuse. One of many strategies in a 2013 report from the Prescription Drug Abuse Subcommittee of the U.S. Department of Health and Human Services encouraged the FDA to support industry efforts to develop abuse-deterrent opioid

analgesic products (USDHHS, 2013). This strategy was a subset of a larger policy strategy cited in the subcommittee report suggesting regulatory and oversight activities at the federal, state, and local level to combat prescription opioid analgesic abuse.

Examples of the primary strategies receiving the most attention include the *National Drug Control Strategy* developed by the White House Administration and the strategies suggested by the CDC, which recommend the implementation of several state-level policies addressing three broad areas: (1) education; (2) tracking and monitoring; and (3) enforcement, regulation, and oversight activities (Table 3). More recently, the CDC sponsored the National Rx Drug Abuse Summit in April 2015, which communicated similar prescription opioid abuse prevention strategies (CDC, 2015).

Table 3. Strategies and Policies Recommended to Prevent Prescription Opioid Analgesic Abuse

Area	Strategies or Policies
Physician, Patient & Public Education	• Educate providers on responsible prescribing and medication disposal • Educate patients and public on appropriate medication use, storage and disposal • Require drug manufacturers to develop educational materials through the Opioid Risk Evaluation and Mitigation Strategy (REMS) • Encourage research on patterns of abuse, development of abuse-deterrent drug formulations and treatments for pain without the potential for abuse

Tracking and Monitoring	• Develop and implement prescription drug monitoring databases (PDMPs)
	  ○ Focus on high-risk patients (high dosage, large numbers of prescriptions, use of multiple prescribers) and prescribers with inappropriate prescribing patterns (large doses or number of prescriptions, large proportion of doctor shoppers among their patients)
	  ○ Integrate PDMP information into health care by linking PDMPs with electronic health record (HER) systems
	  ○ Develop incentives for healthcare programs and providers to use PDMPs when prescribing
	• Implement and evaluate patient review and restriction (PRR) policies
	  ○ Require patients using multiple prescribers and/or pharmacies (without medical justification) to use a single prescriber and/or pharmacy for their prescription opioids
	  ○ State Medicaid and workers' compensation programs should implement PRR programs to monitor inappropriate use of prescription opioids
	  ○ Evaluate the effectiveness of programs requiring high utilizers to use only one doctor and/or pharmacy
	• Evaluate the usefulness of Drug Abuse Warning Network (DAWN) data

Enforcement, Regulation & Oversight	• Enforce regulatory action against prescribers who do not follow accepted medical guidelines for safe prescribing of prescription opioids • Write and disseminate a Model Pain Clinic Regulation Law • Enact, enforce and evaluate state laws to prevent doctor and/or pharmacy shopping, "pill mill" operation, and other methods of abuse and diversion • Increase investigations of trafficking at the federal, state, and local levels

Source: Executive Office of the President of the United States, 2011; CDC, November 2011a.

CHBRP found limited literature addressing the effectiveness of these wide-ranging abuse prevention strategies. Haegerich et al. found weak evidence of effectiveness for many of these kinds of strategies

due a small number of studies and their low quality (Haegerich et al., 2014). Nevertheless, the authors recommended that efforts continue to reduce inappropriate prescribing and patient visits to multiple providers, and improve overdose outcomes through prescription drug monitoring programs, insurer strategies, state legislative oversight of pain clinics, and naloxone distribution programs.

Other researchers found that such strategies are promising. Specifically, Dart et al. report that the diversion and abuse of prescription opioids has flattened or decreased since 2011; they attribute this change, in part, to the "hundreds of programs implemented by local, state, and federal governments (Dart et al., 2015).

Despite the lack of evidence-based consensus, these programs, policies and strategies continue to be recommended, developed, and implemented across the United States. For example, Kolodny et al. recommend a primary abuse prevention strategy that effectively educates prescribers about opioid benefits and risks (including the lack of evidence regarding long-term efficacy of opioid use for non-cancer pain), which could reduce the sheer number of opioid prescriptions dispensed and reduce the resulting negative health outcomes and costs. At least six states have passed mandatory prescriber education laws (Kolodny et al., 2015). Kolodny et al. also recommend more "judicious prescribing" of opioids to decrease the risk of abuse and addiction for the patient, as well as their ability to divert the prescriptions to non-patients. Consistent physician screening for and diagnosis of patients with opioid abuse or addiction problems is also a critical component to preventing negative, cascading health outcomes (Kolodny et al., 2015).

Additionally, secondary prevention strategies include state-based prescription drug monitoring programs, electronic prescribing programs that flag doctor or pharmacy "shoppers"[12], establishing "drug take-back sites," and eliminating prescriber fraud ("pill mills") through pain clinic regulation and oversight, and clinical practice guidelines (Manchikanti et al., 2013; Sessler et al., 2014). Community-based opioid programs using methadone, buprenorphine, or naltrexone also help treat and manage addiction, thereby preventing some opioid overdoses and deaths (Kolodny et al., 2014).

[12] Doctor shoppers are patients who obtain prescriptions from multiple physicians within a defined time period to obtain prescription drugs for abuse or diversion. Pharmacy shoppers are patients who visit multiple pharmacies in a defined time period to fill prescriptions for abuse or diversion (Peirce et al., 2012).

MEDICAL EFFECTIVENESS

The medical effectiveness section focuses on abuse-deterrent opioid analgesics (ADOAs), with a specific emphasis on those labeled by the Food and Drug Administration as an *abuse-deterrent opioid analgesic* (FDA-ADOA). This section addresses the FDA labeling requirements for ADOAs and examines Impact of ADOAs on opioid abuse, including possible shift of abuse to other prescription opioids, other routes of administration, or to illicit drugs (heroin).

Opioid Analgesics and Abuse-Deterrence Formulations

Prescription opioid analgesics are designed to alleviate moderate to severe acute pain, chronic noncancer pain (such as chronic back pain, osteoarthritis, etc.), chronic pain related to cancer, and pain at the end of life (Chou et al., 2009).

Despite their legitimate medical use, prescription opioid analgesics are increasingly abused (SAMHSA, 2007). Nearly half of young people who inject heroin surveyed in three recent studies reported abusing prescription opioids before starting to use heroin. Some individuals reported switching to heroin because it is cheaper and easier to obtain than prescription opioids (Cicero et al., 2012; NIDA, 2012). Prescription opioid pain relievers can be particularly dangerous when snorted, injected, or combined with other drugs or alcohol (NIDA, 2014). Although initially intended to be slowly released over 12 hours, abusers of prescription opioid pain relievers were able to disable the controlled-release mechanism and extract the active ingredient, in order to experience a powerful and immediate effect when ingested, snorted, or injected (Manubay et al., 2011).

Abuse-deterrent opioid analgesics (ADOAs) were developed to reduce some forms (especially non-oral forms) of abuse of potent opioid analgesics by minimizing the potential for tampering, particularly for those opioid analgesics available in an extended-release formulation. These new formulations seek to inhibit abuse by establishing physical or chemical barriers to the more intense or immediate effects achieved by altering the opioid (through crushing, chewing, cutting, or dissolving) . *However, abuse-deterrent formulations do not reduce or eliminate the addictive properties of opioids, and, thus do not prevent or affect addiction* (Kolodny et al., 2015). *Furthermore, they do not prevent abuse related to swallowing pills; they simply reduce some ways to achieving more intense or immediate effects with an altered form of the opioid.*

FDA Labeling Guidance for Abuse-Deterrent Opioid Analgesics

Despite the phrasing of the label, FDA guidance related to ADOAs recommends caution in regards to results, stating “Because opioid products are often manipulated for purposes of abuse by different routes of administration or to defeat extended-release (ER) properties, most abuse-deterrent technologies developed to date are intended to make manipulation more difficult or to make abuse of the manipulated product less attractive or less rewarding. It should be noted that these technologies have not yet proven successful at deterring the most common form of abuse—swallowing a number of intact capsules or tablets to achieve a feeling of euphoria (CDER, 2015)”.

The Food and Drug Administration (FDA) defines ADOAs as having one or more of the following formulations[13] (CDER, 2015):

[13] The FDA’s Guidance for Industry: Abuse-Deterrent Opioids—Evaluation and Labeling (U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research [CDER], 2015), issued

1. Formulations using **physical or chemical barriers** to prevent "chewing, crushing, cutting, grating, or grinding of the dosage (i.e., physical barrier) or to prevent the breakdown of an opioid "using common solvents like water, simulated biological media, alcohol, or other organic solvents (i.e., chemical barriers);

2. Formulations with **Agonist/antagonist combinations** that "interfere with, reduce, or defeat the euphoria associated with abuse";

3. Formulations with **aversion** qualities that "produce an unpleasant effect if the dosage form is manipulated or used at a higher dosage than directed";

4. Formulations that modify the **delivery system** of the opioid, such as using an injectable or implant instead of an oral administration; and

5. Formulations employing **new molecular entities and prodrugs**, such as slowing opioid penetration into the central nervous system.

The FDA's guidance does not address issues with the development of generic formulations of abuse-deterrent opioid products, which The FDA intends to address in the future.

As of April 2015, CHBRP is aware (see Table 4) of three FDA-ADOAs, as well as two opioid analgesics on the market with abuse-deterrent formulations that have not obtained FDA approval for labeling and an additional two drugs with FDA-approved labelling that have yet to be released on the market (CDER, 2015).

in 2015, explains the FDA's current thinking about the studies that should be conducted to demonstrate that a given drug formulation has abuse-deterrent properties. This guide makes recommendations about the rigor of the studies and how they should be performed and evaluated to assist with development of opioid drug products with potentially abuse-deterrent properties; it is not intended to apply to products that are not opioids or opioid products that do not have the potential for abuse.

Table 4. Abuse-Deterrent Opioid Analgesics: FDA Labels and Availability

Brand Name Drug	Generic Equivalent	Abuse-Deterrent Technology (ADOA)	Non-Abuse-Deterrent Version of Drug
FDA-labelled abuse-deterrent opioid analgesics (FDA-ADOA)			
Embeda	Morphine/naltrexone ER	Chemical barrier; agonist/antagonist combination	Morphine ER
Hysingla ER	Hydrocodone ER	Physical barrier	NA
OxyContin	Oxycodone ER	Physical barrier	NA
FDA-labelled abuse-deterrent opioid analgesics (FDA-ADOA), but not on the market			
Oxaydo	Oxycodone IR	Physical & chemical barrier; aversion	Oxycodone IR
Targiniq ER	Oxycodone/Naloxone ER	Chemical barrier; agonist/antagonist combination	NA
Has abuse-deterrent formulation, but not labeled as such by the FDA			
Exalgo ER	Hydromorphone ER	Physical barrier	Oxymorphone ER
Nucynta ER	Hydrocodone ER	Physical barrier	NA
Opana ER	Hydromorphone ER	Physical barrier	NA
Xartemis XR	Oxycodone/acetaminophen ER	Physical barrier	NA
Zohydro ER	Hydrocodone ER	Physical barrier	NA

Source: Based on CDER and content expert review, CHBRP 2015.

Key: ER = extended release; IR = immediate release; NA = not available.

Research Approach and Methods

Studies were identified through searches of PubMed, the Cochrane Library,[14] Web of Science, EconLit, and Business Source Complete, the Cumulative Index of Nursing and Allied Health Literature, 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, the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health

[14] Of the studies CHBRP identified on the impact of ADOAs, there was one Cochrane Review (Michna et al., 2013). This study compared efficacy and safety outcomes for commonly prescribed short-acting opioids and long-acting opioids in abuse deterrent form and traditional non-abuse deterrent form. While this review was the only study that compared the efficacy of an abuse-deterrent drug to non–abuse-deterrent drug for pain management, it had several important limitations. The study did not focus on the three drugs pertinent to this bill, did not include any studies comparing efficacy and safety of abuse deterrent to non-abuse deterrent opioids, and the drugs reviewed are old versions of the drugs and may not have had current FDA labelling.

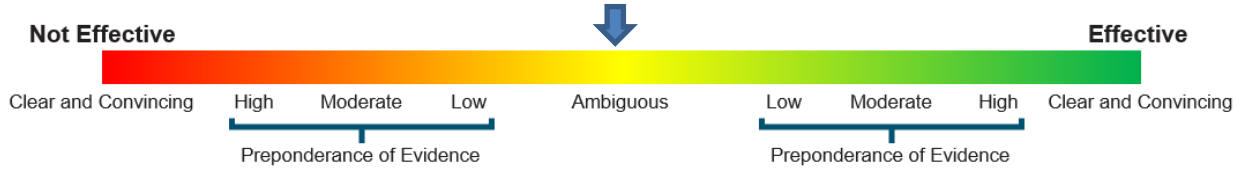
Service (NHS) Centre for Reviews and Dissemination, the National Institute for Health and Clinical Excellence (NICE), and the Scottish Intercollegiate Guideline Network.

The search was limited to abstracts of studies published in English published from 2004 to present. Of the 735 articles found in the literature review, a total of 26 studies were included in the medical effectiveness review for this report. The other articles were eliminated because they did not focus on abuse-deterrent opioid analgesics, were of poor quality as defined by the CHBRP protocol for evaluating the research literature, or did not report findings from clinical research studies.[15] The literature summarized in this report does not address opioid addiction because the abuse-deterrent formulations focus on reducing abuse rather than altering the addictive properties of prescription opioid analgesics. 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: Literature Review Methods.

Overall Study Findings

Figure 3. Summary of Findings

Treatment	Conclusion
ADOAs effect on abuse of opioid analgesics	*Although studies suggest that ADOAs can reduce abuse of the ADOA specific drug, studies also suggest that the presence of ADOAs shifts some abuse to other OAs and/or to illicit drugs (such as heroin). Therefore, the impact on abuse is ambiguous.*



Source: California Health Benefits Review Program.

As noted in Figure 4, the impact of ADOAs on abuse is ambiguous, because ADOAs may reduce the abuse of particular drugs but also result in a shift of some abuse to other opioids (including illicit drugs, such as heroin). The following subsections review the studies that led to this conclusion – first addressing the studies of particular drugs and then addressing the broader issue of cross-drug abuse.

[15] CHBRP classifies research by levels I–V. Level I research includes well-implemented randomized controlled trials (RCTs) and cluster RCTs. Level II research includes RCTs and cluster RCTs with major weaknesses. Level III research consists of nonrandomized studies that include an intervention group and one or more comparison groups, time series analyses, and cross-sectional surveys. Level IV research consists of case series and case reports. Level V represents clinical/ practical guidelines based on consensus or opinion. Using these standards, most of the research related to abuse deterrent opioids would be classified as level III and level II.

Limitations of Available Studies

Many nonrandomized studies on abuse-deterrent opioids are time series analyses. These studies compare before introduction of abuse-deterrent formulations and after these formulas are introduced. These studies compare drug overdose episodes, drug used most often (by subjects) and preferred over all others (by subjects), therapeutic errors, and ADOA-caused mortality. One study was a retrospective cohort study that compared a period before the implementation of prior approval and after. There are several limitations to the studies, including small sample sizes, short study period, inability to identify the source of prescription opioids for individuals who overdosed, and the fact that many individuals who misuse opioids do not obtain them directly from physician prescriptions.

Studies on Particular Drugs, Abuse-Deterrent Formulation, and Abuse

It is widely acknowledged among researchers and clinicians that randomized studies are necessary. However, there are few randomized controlled trials (RCTs) on ADOAs, and most of them are very small and are premarket studies. These studies compared “drug liking,” “drug high,” and “take the drug again” as measurements of abuse-deterrent formulations. Subjects enrolled in the studies were nondependent recreational opioid users and they were asked to rate their “drug liking,” “drug high,” and “take drug again“ experience using a 100-point Visual Analog Scale, where 0 represents maximum disliking, 50 represents a neutral response (neither like nor dislike), and 100 represents maximum liking. Others were nonrandomized studies with comparison groups that compared persons with abuse-deterrent formulas compared to those with traditional formulations.

Labeling information summarized findings from four randomized, double-blind studies on the abuse potential for Embeda when crushed (Pfizer, 2014). Subjects enrolled in the studies were nondependent recreational opioid users and they were asked to rate their “drug liking,” “drug high,” and “take drug again” experience using a 100-point Visual Analog Scale as previously discussed. Two studies, with 32 and 36 subjects, respectively, found that that oral administration of crushed Embeda was associated with statistically significantly lower drug liking and drug high scores compared with crushed morphine (Pfizer, 2014). One study of 36 subjects found the intranasal administration of crushed Embeda was associated with statistically significantly lower drug liking, drug high, and take drug again scores compared with crushed morphine (Pfizer, 2014). Intravenous administration of the combination of morphine sulfate and naltrexone hydrochloride was associated with statistically significantly lower mean and median drug liking and drug high scores compared with morphine (Pfizer, 2014) in one study of 28 subjects.

Labeling information summarized findings from 2 studies that examined the physical properties expected to make abuse difficult by injection and by the intranasal route. Results showed that ADF OxyContin is better able to resist crushing and breaking using a range of tools and solvents, when compared to the original version of OxyContin (which is no longer marketed). When ADF OxyContin is introduced to an aqueous environment, a viscous mass results that cannot pass through a needle. A randomized, double-blind study of 27 recreational opioid users found higher rates of incomplete dosing, due to particles falling from the subject’s nostrils among subjects using finely crushed ADF OxyContin compared to a finely crushed original version of OxyContin. This was associated with a numerically lower mean and median “drug liking” score and a lower mean and median score for “take drug again” compared to finely crushed original OxyContin or powdered oxycodone HCl (Purdue Pharma, 2014). A similar analysis (with this cohort) of drug liking for finely crushed ADF OxyContin relative to finely crushed original OxyContin were comparable. Approximately 43% of subjects had no reduction in drug liking with ADF OxyContin relative to original OxyContin, 57% of subjects had some reduction in drug liking, 36% of subjects had a reduction of at least 30% in drug liking, and 29% of subjects had a reduction (of at least 50%) in drug liking with ADF OxyContin compared to original OxyContin.

Labeling information summarized findings from two randomized, double-blind, placebo and active-controlled clinical studies in nondependent recreational opioid users conducted to characterize the abuse potential of Hysingla ER following physical manipulation and administration via the intranasal and oral routes, that examined the chemical and physical properties expected to make abuse difficult by injection and by the intranasal route (Purdue Pharma, 2015). When subjected to an aqueous environment, Hysingla ER forms a viscous gel that resists passage through a needle. Results showed that Hysingla ER resists crushing, breaking, and dissolution and retains some extended-release properties despite manipulation The intranasal administration of tampered Hysingla ER was associated with statistically significantly lower mean and median scores for drug liking and take drug again ($P < 0.001$ for both), compared with powdered hydrocodone. Eighty percent of subjects had some reduction in drug liking, 69% of subjects had a reduction in drug liking (of at least 30%), 60% of subjects had a reduction in drug liking(of at least 50%), and 20% of subjects had no reduction in drug liking with chewed Hysingla ER relative to hydrocodone solution. The oral administration of chewed and intact Hysingla ER was associated with statistically lower mean and median scores on scales that measure drug liking and desire to take drug again ($P < 0.001$), compared to hydrocodone solution. Eighty percent of subjects had some reduction in drug liking with chewed Hysingla ER, 69% had a reduction of at least 30% in drug liking, and 60% of subjects had a reduction of at least 50% in drug liking, 20% of subjects had no reduction in drug liking with chewed Hysingla ER relative to hydrocodone solution (Purdue Pharma, 2015).

An additional study found in patients whose primary pretrial analgesic was hydrocodone/acetaminophen combination tablets, single-entity Hysingla was effective in reducing pain intensity and in maintaining analgesia over time without need for continued dose increase. Hysingla's safety and tolerability profiles were similar to other opioid analgesics (Bartoli et al., 2015).

It is important to note the small sample sizes for these RCTs.

Studies on the Effects of Abuse-Deterrent Opioid Analgesics on Cross-Drug Abuse and Routes of Administration

Numerous studies have examined the impact of abuse-deterrent opioid analgesics on abuse. In particular, ADOA OxyContin leads to a decrease in the number of prescriptions of that particular drug (Cicero et al., 2012; Cicero and Ellis, 2015; Coplan et al., 2013; Delcher et al., 2015; Havens et al., 2014; Hwang et al., 2015; LaRochelle et al., 2015), a decrease in abuse of that specific drug, or overdose specific to that particular drug (Cicero et al., 2012; Cicero and Ellis, 2015; Coplan et al., 2013; Havens et al., 2014; Sessler et al.,2014). However, studies find a shift in the abuse of alternative prescription opioid analgesics or heroin, or use of alternative routes of administration (Budman et al., 2009; Butler et al., 2013; Cicero et al., 2012; Cicero and Ellis, 2015; Coplan et al., 2013; LaRochelle et al., 2015). Other studies have found that ADOAs lead to reductions in the number of prescriptions filled and decreases in abuse and overdose attributable to OAs but can also lead to increases in abuse of alternative, substituted opioids, including heroin (Budman et al., 2009; Rossiter et al., 2014; Sessler et al., 2014; Twillman and Fudin, 2015). Additionally, oral abuse of ADOAs can also continue (Butler et al., 2013; Manchikanti et al., 2013).

Shifts to cross-drug abuse

One study (Cicero et al., 2012) used self-administered surveys completed anonymously by independent cohorts of patients with opioid dependence who selected a specific prescription opioid as their primary drug of choice (used most often and preferred over all others). Researchers found that when the abuse-deterrent formula for OxyContin was introduced (and production of the original formulation stopped) in 2010, the selection of OxyContin as a primary drug of abuse decreased from 35.6% of respondents before the release of the abuse-deterrent formulation to 12.8% 21 months later ($P < 0.001$).

Simultaneously, selection of other prescription opioid drugs increased slightly, and other prescription opioids (including fentanyl and hydromorphone) rose significantly, from 20.1% to 32.3% ($P = 0.005$). Of all opioids, ADF OxyContin fell from 47.4% of respondents to 30.0% ($P < 0.001$). At the same time, heroin use nearly doubled.

Another study (Cicero and Ellis, 2015) found ADF OxyContin introduction was associated with a significant reduction of past-month abuse from 45.1% (95% confidence interval [CI], 41.2% to 49.1%) in 2009 to 26.0% (95% CI, 23.6% to 28.4%) in 2012; $P < 0.001$; $\chi^2 = 230.83$. However, there was a significant migration to other opioids, especially heroin. Past-month use of heroin in the study population increased steadily and significantly during the 4 years after introduction of ADF ($\chi^2 = 224.98$; $P < 0.001$) (Cicero and Ellis, 2015).

Coplan and colleagues (2013) found that after OxyContin reformulation (ADF OxyContin), there was a significant (36%) decrease in abuse exposures reported to poison centers, a 20% increase for other OA single-entity (SE) oxycodone, and a 42% increase for heroin. Therapeutic errors affecting patients decreased significantly (20%) for ADOA OxyContin and increased 19% for other OA SE oxycodone. Accidental overdoses decreased 39% for ADOA OxyContin, increased 21% for heroin, and remained unchanged for other OA SE oxycodone. A similar study (Cassidy, 2014) found that reformulation of ADF oxycodone hydrochloride controlled-release (CR) tablets shifted abuse to other prescription opioids (such as extended-release [ER] oxymorphone and buprenorphine). Although abuse of ADOA oxycodone product declined by 22% after the abuse-deterrent formula was introduced (RR = 0.78, $P < 0.0001$), OA oxymorphone exhibited a nearly threefold increase (RR = 2.91, $P < 0.0001$), and an approximately twofold increase was noted for OA buprenorphine (RR = 1.85, $P < 0.0001$).

Another study (Delcher et al., 2015) found that oxycodone caused–mortality abruptly declined 25% the month after implementation of Florida's Prescription Drug Monitoring Program (PDMP) ($P = 0.008$) in 2011, 11 months after the introduction of ADF OxyContin. It is important to note that this program also included concurrent law enforcement, policy, and public health actions. PDMPs are designed to detect abnormalities in the prescribing of controlled substances (e.g., higher-than-expected doses per unit time, questionable overlapping prescriptions, “doctor shopping” for multiple prescribers and dispensers), thereby reducing the quantity of pills available from medical sources that could be abused. Readers should note that the federal-, state-, and systems-level policy strategies (discussed in the *Background* section) may confound the findings of some studies that attribute reductions in prescription opioid abuse exclusively to the abuse-deterrent opioid reformulations or to any other specific program (Dart et al., 2015; Haegerich et al., 2014; Sessler et al., 2014).

Shifts in alternative routes of administration

As noted in the *Background* section, the preferred route of administration for those abusing prescription opioids includes oral, inhalation (smoking/snorting), and injection. CHBRP found one study addressing changes in abuse patterns for three opioids 20 months post-reformulation. Butler et al. reported that of the top three preferred routes for ER oxycodone – oral (55%), snorting (53%), and injection (37%) – snorting and injection dropped by 50% (to 25% and 16%, respectively) post-reformulation. Oral abuse remained the top preferred route and increased 40% post-reformulation (to 76% of abusers). There was virtually no difference in preferred routes of administration for ER morphine post reformulation. There was a reduction in oral ER Oxymorphone use (from 38% to 30%), but an increase in snorting (61% to 68%), smoking (0.2% to 2%) and injection (9% to 16%) post-reformulation (Butler et al., 2013).

Conclusion

Although ADOAs may decrease abuse of its non-ADOA counterpart, it may promote shifts to other opioids or other routes of administration. Therefore, the impact of ADOAs on abuse is ambiguous. Furthermore, Budman et al. (affiliated with the pharmaceutical industry) note that although ADOAs might have some impact on rates of abuse, they "will likely have little to no impact on those who prefer to abuse these drugs by taking the drug intact" (Budman et al., 2009).

BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

For DMHC-regulated plans and CDI-regulated policies, AB 623 would:

- Prohibit requiring use of other opioid analgesics prior to covering opioid analgesics labeled as "abuse-deterrent" by the Food and Drug Administration (FDA-ADOAs);
- Require the same prior authorization protocols be applicable to an opioid analgesics whether it is in a standard or an FDA labelled abuse-deterrent formulation; and
- For covered opioid analgesics, provide coverage for less than 30-day supplies.

Compliance with AB 623's requirements would require changes in some utilization management (UM) protocols applicable to outpatient prescription drug (OPD) benefits. This section reports the potential incremental impact of AB 623 on the terms and conditions of baseline benefit coverage, utilization, and overall cost. In performing this analysis, CHBRP assumed that the projected increase in FDA-ADOA prescriptions for enrollees with changing protocols would primarily replace opioid analgesics with some abuse-deterrent properties, generally extended-release (ER) formulations, which are a subset of all of opioid analgesics.[16] CHBRP assumed that the total number of prescriptions for all opioid analgesics would remain constant, postmandate. For further details on the underlying data sources and methods, please see Appendix C.

Benefit Coverage

Premandate (Baseline) Benefit Coverage

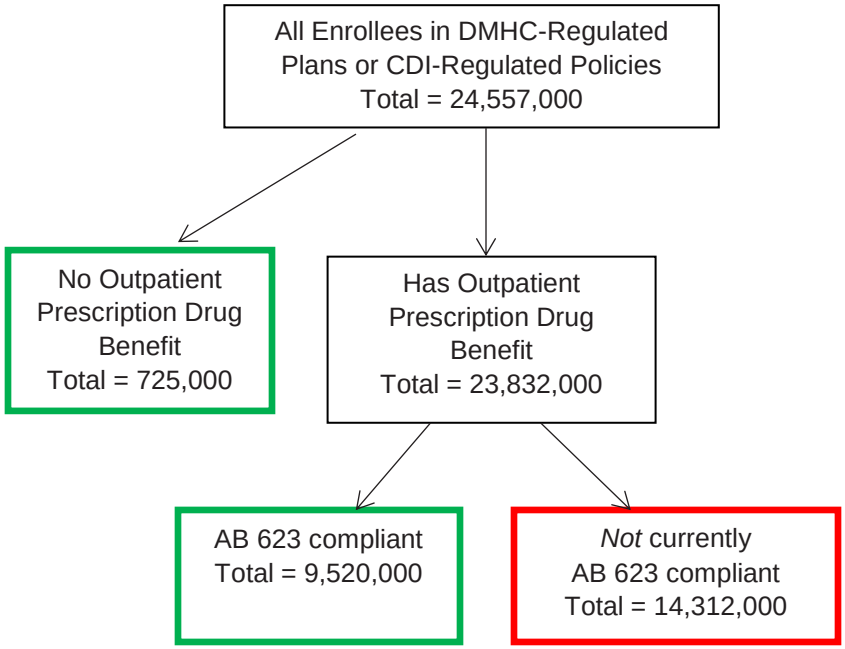
Current benefit coverage and the presence of UM protocols relevant to AB 623 were determined by a survey of the seven largest providers of health insurance in California. Responses to this survey represent:

- 74% of enrollees in the privately funded, DMHC- regulated market;
- 34% of enrollees in the CDI-regulated market; and
- 68% of enrollees in the privately funded market subject to state mandates.

Currently, 42% of enrollees with health insurance that would be subject to AB 623 have mandate-compliant benefit coverage (see Table 1 and Figure 4). The percentage of enrollees with compliant benefit coverage includes enrollees with no outpatient prescription drug (OPD) benefit and enrollees with an OPD benefit that includes no utilization management protocols that would need to change to become compliant with AB 623.

[16] Based on personal communication with content expert Dr. Mark Holtsman, UC Davis, May 4, 2015.

Figure 4. Baseline of Enrollee Benefit Coverage and Status of Mandate Compliance With AB 623



Source: California Health Benefits Review Program, 2015
Note: Numbers may not add to totals due to rounding.

AB 623's prohibition regarding requiring use of another opioid analgesic prior to covering FDA-ADOAs could alter two forms of utilization management. AB 623 could require changes to step therapy protocols and/or to prior authorization protocols. Based on content expert guidance,[17] CHBRP has assumed AB 623 would require such changes only when the change would be clinically appropriate. Clinically inappropriate changes (which CHBRP has not projected for this analysis) would be as follows:

- Because the three currently available FDA-ADOAs are potent drugs, it would be clinically inappropriate to promote their use before use of a significantly less potent opioid analgesic. For this reason, CHBRP has assumed that protocols would not change to promote use of FDA-ADOAs ahead of less potent opioid analgesics (regardless of the less potent drug's formulation).
- Some fast-acting opioid analgesics are intended for persons with extreme pain. In such circumstances, it would be clinically inappropriate to require use of an FDA-ADOA – which are generally extended release (ER) and intended for treatment of chronic pain. For this reason, CHBRP assumes that protocols would not change to promote use of FDA-ADOAs ahead of immediate release (IR) opioid analgesics.

Clinically appropriate changes would include prohibition of requiring use of opioid analgesics with some abuse-deterrent properties, most of which are extended release drugs (ER), prior to covering FDA-ADOAs. See Appendix C for a list of drugs included in this analysis' impact estimates.

[17] Personal Communication, Dr. M. Holtsman, May 4, 2015.

CHBRP examined relevant UM protocols and found that 58% of enrollees have outpatient prescription drug (OPD) benefits that include UM protocols not fully compliant with AB 623. Some step therapy protocols and some prior authorization protocols would require some number of these enrollees to use another, similarly potent opioid analgesic prior to covering an FDA-ADOA. However, the number of changing UM protocols would vary among this group of enrollees depending on how many noncompliant UM protocols were associated with the enrollee's OPD benefit. CHBRP's estimates regarding the variation as to the number AB 623 noncompliant UM protocols among enrollees is presented in Table 5.

Table 5. AB 623 Compliance in Utilization Management Protocols for All Enrollees

AB 623 Compliance and Utilization Management Protocols	Current % of All Enrollees (N = 24,557,000)
Enrollees with no coverage for OPD	3%
Enrollees with coverage for OPD, with no utilization management Protocols or with only compliant utilization management protocols	39%
Enrollees with coverage for OPD, 1–4 noncompliant utilization management protocols	6%
Enrollees with coverage for OPD, 5+ non-compliant utilization management protocols	52%

Source: California Health Benefits Review Program, 2015
Note: Numbers may not add to totals due to rounding.
Key: OPD = Outpatient Drug Benefit

Postmandate Benefit Coverage

Postmandate, 100% of enrollees in DMHC-regulated plans and CDI-regulated policies would have fully mandate-compliant benefit coverage.

To be compliant with AB 623's first and second requirements, CHBRP has projected change for a number of UM protocols (as described in Table 5) so that (when clinically appropriate) use of another opioid analgesic would not be required before coverage of an FDA-ADOA and similar prior authorization protocols would be applicable to an FDA-ADOA and its corresponding non-abuse-deterrent formulation.

CHBRP found no examples of UM protocols that would prohibit coverage of a less than 30-day supply of opioid analgesics, and so projects no changes relevant to AB 623's third requirement.

Utilization

Premandate (Baseline) Utilization

Annually, the current use of opioid analgesics (not including FDA-ADOAs) associated with protocols that would change to become AB 623 compliant is 325.8 per 1,000 enrollees, (Table 1). By contrast, the annual utilization of FDA-ADOAs is 9.71 per 1,000 enrollees. See Appendix C for the list of drugs used to produce these estimates.

Postmandate Utilization

Postmandate, CHBRP modeled the increase of the use of FDA-ADOAs (where clinically appropriate) under AB 623 mandate compliant protocols. CHBRP estimates that the annual use of FDA-ADOAs will increase to 13.41 per 1,000 enrollees, which is an increase of 38% (see Table 1). Under the assumption that the total number of opioid analgesic prescriptions will remain constant, there will be a corresponding 3.7 per 1,000 enrollee drop in the use of opioid analgesic prescriptions associated with changing protocols (not including FDA-ADOAs), a decrease of 1%. CHBRP acknowledges that this estimate constitutes an upper boundary, as some providers may not be educated about FDA-ADOAs and may therefore not prescribe them or may seek to keep their patients on other opioid analgesics. Therefore, the model may overestimate change in utilization to some unquantifiable degree.

Although this model assumes a one-to-one correspondence in the increase of FDA-ADOAs to the decrease in other drug use, there is also the potential for an overall decrease in use of opioid analgesics corresponding to an increase in other types of (potentially illicit) drugs that are commonly abused. Please see the *Background* and *Public Health* sections for in-depth discussions of this potential replacement effect, which is not included in the Cost analysis.

Impact on access and health treatment/service availability

CHBRP anticipates that AB 623 will increase access to FDA-ADOAs, after UM protocols are modified to be AB 623 compliant. However, CHBRP assumes that manufacturers will be able to produce enough to meet the increased demand and that no shortages will occur.

Per-Unit Cost

Premandate (Baseline) and Postmandate Per-Unit Cost

Premandate, CHBRP estimates that the average cost for opioid analgesic prescriptions associated with changing UM protocols is $51.38. Postmandate, the increased utilization of the FDA-ADOA formulations (which are frequently more expensive per prescription than other opioid analgesics) will push the average price of an opioid analgesic prescription associated with changing UM protocols to $57.95. This represents an average per-unit cost increase of $6.57, or 13% (see Table 1).

Premiums and Expenditures

Premandate (Baseline) Premiums and Expenditures

Table 6 presents per member per month (PMPM) premandate estimates for premiums and expenditures by market segment for DMHC-regulated plans and CDI-regulated policies.

PMPM by market segment is as follows for DMHC-regulated plans and CDI-regulated policies, respectively:

- Large group: $537.63 and $646.64;
- Small group: $451.81 and $558.76; and
- Individual market: $422.03 and $334.65.

Total current annual expenditures for all DMHC-regulated plans and CDI-regulated policies is $135,986,114,000.

Postmandate Expenditures

Changes in total expenditures

AB 623 would increase total net annual expenditures by $7,887,000, or 0.0058%, for enrollees with DMHC-regulated plans and CDI-regulated policies. This is due to a $7,434,000 increase in total health insurance premiums paid by employers and enrollees for newly covered benefits, added to an increase of $454,000 in enrollee expenditures for covered benefits (deductibles, copays, etc), for an overall net change of $7,889,000.

Postmandate premium expenditures and PMPM amounts per category of payer

Increases in insurance premiums as a result of AB 623 would vary by market segment. Note that the total population in Table 7 reflects the full 24,557,000 enrollees in DMHC-regulated plans and CDI-regulated policies subject to AB 623.

In DMHC-regulated plans, the premium increases PMPM range from $0.01 (large group) to $0.02 PMPM (individual). In CDI-regulated policies, CHBRP estimates that the premium increases will be $0.04 PMPM for the large group and individual markets and $0.05 for the small group market.

Among publicly funded DMHC-regulated health plans, CHBRP estimates that CalPERS HMOs will increase by $0.02 PMPM. CHBRP estimates that the Medi-Cal managed care plans will have a premium increase of $0.05 PMPM for each of the market segments, both under and over age 65, because Medi-Cal managed care plans have UM protocols that are not currently compliant with AB 623 and would need to change. Because of the changes in Medi-Cal utilization management protocols required under AB 623, CHBRP estimates that these PMPM increases will result in Medi-Cal managed care bearing the largest proportion of the cost increases ($4,428,000; see Table 1).

Enrollee expenses for covered benefits may also increase, from no increase in Medi-Cal managed care plans to a high of $0.01 PMPM in CDI-regulated small-group and individual policies. This is due to some increased cost sharing associated with moving to the higher cost, often nonformulary, FDA-ADOA prescriptions.

Potential cost offsets or savings in the first 12 months after enactment

As mentioned in the *Background* and the *Medical Effectiveness* sections, the evidence is ambiguous as to whether ADOAs reduce medical needs based on opioid abuse. Certainly, persons who abuse opioid analgesics have increased medical costs due to both outpatient and emergency department (ED) visits. The economic damage from opioid analgesic drug addiction and abuse had already been thoroughly discussed in the literature, with 23 articles analyzed in a meta-analysis by Meyer et al. (2014). However, as *Medical Effectiveness* states, there is ambiguous evidence that increased use of ADOAs will reduce these costs. Michna et al. (2014) caution that some patients in their study switched to other forms of non-ADOA drug products when their existing prescription was reformulated to an ADOA. Rates of opioid abuse were higher among these patients, suggesting that patients who are prone to abuse opioid analgesic drug products may seek alternatives when facing an ADOA formulation.

Because of this ambiguity in the connection between use of ADOAs and reduction in costs due to reduced doctor or ED visits, CHBRP cannot quantify any other potential cost offsets or savings under AB 623.

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.

Related Considerations for Policymakers

Postmandate Changes in Uninsured and Public Program Enrollment

Changes in the number of uninsured persons

CHBRP estimates premium increases of less than 1% for each market segment; this premium increase would not have a measurable impact on the number of persons who are uninsured. CHBRP does not anticipate loss of health insurance, changes in availability of the benefit beyond those subject to the mandate, changes in offer rates of health insurance, changes in employer contribution rates, changes in take-up of health insurance by employees, or purchase of individual market policies, due to the small size of the increase in premiums after the mandate.

Changes in public program enrollment

CHBRP estimates that the mandate would produce no measurable impact on enrollment in publicly funded insurance programs or on utilization of covered benefits in the publicly funded insurance market.

How Lack of Coverage Results in Cost Shifts to Other Payers

Currently, 97% of DMHC-regulated plans and CDI-regulated policies include some coverage for FDA-ADOAs, including those for which FDA-ADOAs are nonformulary. AB 623 also does not mandate coverage for ADOAs, but rather reduces UM restrictions that may apply to FDA-ADOAs and other opioid analgesics. Therefore, CHBRP does not estimate any cost shifts to other payers.

Table 6. Baseline (Premandate) Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2015

	DMHC-Regulated						CDI-Regulated			
	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+) (d)*	*Large Group*	*Small Group*	*Individual*	**Total**
Enrollee counts										
Total enrollees in plans/policies subject to state mandates (e)	8,651,000	2,094,000	3,757,000	836,000	6,891,000	533,000	534,000	690,000	571,000	24,557,000
Total enrollees in plans/policies subject to AB 623	8,651,000	2,094,000	3,757,000	836,000	6,891,000	533,000	534,000	690,000	571,000	24,557,000
Premium costs										
Average portion of premium paid by employer	$423.58	$304.59	$0.00	$437.75	$179.24	$445.00	$511.84	$421.06	$0.00	$80,452,488,000
Average portion of premium paid by employee	$114.05	$147.22	$422.03	$109.44	$0.76	$0.00	$134.80	$137.71	$334.65	$40,023,653,000
Total premium	**$537.63**	**$451.81**	**$422.03**	**$547.19**	**$180.00**	**$445.00**	**$646.64**	**$558.76**	**$334.65**	**$120,476,140,000**
Enrollee expenses										
Enrollee expenses for covered benefits (deductibles, copays, etc.)	$36.95	$89.15	$141.84	$29.78	$0.00	$0.00	$99.91	$166.51	$105.38	$15,510,004,000
Enrollee expenses for benefits not covered (f)	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0
Total expenditures	**$574.58**	**$540.97**	**$563.87**	**$576.98**	**$180.00**	**$445.00**	**$746.55**	**$725.28**	**$440.03**	**$135,986,144,000**

Source: California Health Benefits Review Program, 2015.

Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance, inside and outside the exchange.

(b) As of September 30, 2013, 57.5%, or 462,580, CalPERS members were state retirees, state employees, or their dependents. CHBRP assumes the same ratio for 2015.

(c) Includes children formerly in Healthy Families, which was moved into Medi-Cal Managed Care in 2013 as part of the 2012–2013 state budget.

(d) Medi-Cal Managed Care Plan expenditures for members over 65 include those who also have Medicare coverage.

(e) This population includes both persons who obtain health insurance using private funds (group and individual) and through public funds (e.g., CalPERS HMOs, Medi-Cal Managed Care Plans). Only those enrolled in health plans or policies regulated by the DMHC or CDI are included. Population includes all enrollees in state-regulated plans or policies aged 0 to 64 years, and enrollees 65 years or older covered by employer-sponsored health insurance.

(f) 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; DMHC = Department of Managed Health Care; MCMC = Medi-Cal Managed Care.

Table 7. Postmandate Impacts of the Mandate on Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2015

	DMHC-Regulated						CDI-Regulated			
	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+) (d)*	*Large Group*	*Small Group*	*Individual*	**Total**
Enrollee counts										
Total enrollees in plans/policies subject to state mandates (e)	8,651,000	2,094,000	3,757,000	836,000	6,891,000	533,000	534,000	690,000	571,000	24,557,000
Total enrollees in plans/policies subject to AB 623	8,651,000	2,094,000	3,757,000	836,000	6,891,000	533,000	534,000	690,000	571,000	24,557,000
Premium costs										
Average portion of premium paid by employer	$0.01	$0.01	$0.00	$0.01	$0.05	$0.05	$0.03	$0.03	$0.00	$5,807,000
Average portion of premium paid by employee	$0.00	$0.00	$0.02	$0.00	$0.00	$0.00	$0.01	$0.01	$0.04	$1,626,000
Total premium	$0.01	$0.01	$0.02	$0.02	$0.05	$0.05	$0.04	$0.04	$0.04	**$7,434,000**
Enrollee expenses										
Enrollee expenses for covered benefits (deductibles, copays, etc.)	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.01	$0.01	$0.01	$454,000
Total expenditures	$0.01	$0.01	$0.02	$0.02	$0.05	$0.05	$0.04	$0.05	$0.04	**$7,887,000**
Postmandate percent change										
Percent change insured premiums	0.0015%	0.0023%	0.0049%	0.0031%	0.0277%	0.0112%	0.0056%	0.0071%	0.0110%	0.0062%
Percent Change total expenditures	0.0016%	0.0022%	0.0042%	0.0034%	0.0277%	0.0112%	0.0056%	0.0062%	0.0096%	0.0058%

Source: California Health Benefits Review Program, 2015.

Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance, inside and outside the exchange.

(b) As of September 30, 2013, 57.5%, or 462,580 CalPERS members were state retirees, state employees, or their dependents. CHBRP assumes the same ratio for 2015.

(c) Includes children formerly in Healthy Families, which was moved into Medi-Cal Managed Care in 2013 as part of the 2012-13 state budget.

(d) Medi-Cal Managed Care Plan expenditures for members over 65 include those who also have Medicare coverage.

(e) This population includes both persons who obtain health insurance using private funds (group and individual) and through public funds (e.g., CalPERS HMOs, Medi-Cal Managed Care Plans). Only those enrolled in health plans or policies regulated by the DMHC or CDI are included. Population includes all enrollees in state-regulated plans or policies aged 0 to 64 years, and enrollees 65 years or older covered by employer-sponsored health insurance.

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

PUBLIC HEALTH IMPACTS

Most people use extended-release prescription opioid analgesics for clinically appropriate reasons (long term, chronic pain) and adhere to proper administration protocols (Cicero et al., 2013). Nevertheless, approximately 5.2% of Californians over age 12 choose to abuse opioid analgesics (CBHSQ, 2015). Federal and state governments have been struggling to develop and implement numerous abuse prevention strategies to combat this significant public health problem (see the *Background* section).

As presented in the *Medical Effectiveness section*, abuse-deterrent formulations are one method the pharmaceutical industry is pursing to reduce abuse. ADOAs seek to inhibit some forms of abuse by establishing physical or chemical barriers to the more intense or immediate effects achieved by altering the opioid (through crushing, chewing, cutting, or dissolving to inhale, inject, or swallow). *However, these formulations do not reduce the addictive properties of opioids* (Kolodny et al., 2015). Furthermore, they do not prevent abuse based on swallowing unaltered pills. Thus, while there are some documented reductions in the number of prescriptions filled and decreases in abuse and overdose attributable to ADOAs (Rossiter et al., 2014; Sessler et al., 2014), increases in abuse of alternative, substituted opioids, including heroin, do occur and oral abuse of ADOAs can also continue or increase (Manchikanti et al., 2013). (See *Long-Term Impacts*: "Unintended Consequences" for further discussion.)

Additionally, abusers' preferred routes of administration impact the effectiveness of ADOAs in reducing abuse and overdose. Abuse of prescription opioid analgesics occurs through various routes of administration (oral, nasal, or injection) (CBHSQ, 2015). Research shows that of those who abuse prescription opioids, up to 88% favor oral administration; abuse-deterrent opioid analgesics (ADOAs) provide a barrier to the minority who prefer to alter opioid analgesics for inhalation or injection (see the *Background* section, Table 2.

The *Benefit Coverage, Utilization, and Cost Impacts* section reports that AB 623 would have a limited marginal impact on utilization of ADOAs. This is due in part to the 42% of enrollees with premandate compliant, outpatient prescription drug (OPD) benefits and to the variation in utilization management protocols that would have to change for the remaining enrollees with noncompliant benefits. Thus, CHBRP estimates the upper bound of the postmandate marginal change would be about 90,950 additional FDA-ADOA prescriptions (or the equivalent of 7,580 enrollees who would fill ADOA prescriptions[18]) during the first 12 months, postmandate.

Conceptually, AB 623 would eliminate one of many confounders to opioid abuse prevention efforts. By requiring change for some UM protocols, AB 623 may increase the number of FDA-ADOAs in medicine cabinets, thus potentially reducing associated opioid overdose episodes. However, prescribers' (and patient enrollees in consultation with their prescribers) ability to choose preferred prescription opioids remains intact under AB 623. Although CHBRP adopts a simplifying assumption of a 1:1 substitution ratio to demonstrate the mandate's possible magnitude of effect, CHBRP believes that the potential public health impact on the number of FDA-ADOA prescriptions filled would likely be less because some physicians may continue to prescribe the same opioids to stabilized patients and patient requests to continue non-ADOAs may be honored by some prescribers.

[18] CHBRP estimates that the marginal impact of AB 623 would result in 90,950 new 30-day FDA-ADOA prescriptions. According to the literature and CHBRP's content expert, these prescriptions are used continuously to treat chronic pain. CHBRP assumes this number of prescriptions would be the equivalent of about 7,5780 enrollees who would fill ADOA prescriptions throughout the year (90,950/12).

Based on published literature, CHBRP also suggests that those enrollees who are willing to adopt the ADOA formulation are the least likely to abuse the drug (whether for personal use or diversion to others) (Michna et al., 2014). An industry-sponsored observational study found that 31% to 50% of commercially insured patients who were "continuous prescription opioid" users avoided converting their prescriptions to ADOAs. Furthermore, the authors reported that rates of abuse were higher among those who did not convert as compared with those who did adopt the ADOA formulation (Michna et al., 2014).

CHBRP notes that more than 50% of abusers report their source as "friend or family," so to the extent that the FDA-ADOAs prevent diversion from patients to others, and to the extent that the abuser does not simply abuse by swallowing the ADOA pill(s) or substitute an alternative opioid, there may be some benefit on a case-by-case basis. However, due to ambiguous evidence of effectiveness and unknown take-up rates of FDA-ADOA by prescribers and patients, CHBRP finds that AB 623 would have an unknown public health impact.

In the first year postmandate, CHBRP projects AB 623 would have an unknown public health impact due to both the ambiguous evidence of effectiveness of ADOAs deterring overall abuse and the unknown magnitude of changes in prescriber and patient behavior in response to changing utilization management protocols. However, CHBRP posits that it is unlikely AB 623 would have a measurable impact on abuse, overdose, and premature death because:

- Addictive properties are still present in FDA-ADOAs (Kolodny et al., 2015).
- Initial abuse frequently begins with oral abuse (by swallowing pills), which is not affected by abuse-deterrent formulation.
- Many continuing abusers prefer to orally abuse.
- Continuing abusers are able to choose oral abuse when faced with abuse-deterrent formulations.
- Only three FDA-ADOAs are available in the marketplace as of April 2015, so substitution with non-abuse-deterrent formulations will still occur for some portion of the population (Michna et al., 2014).
- Substitution with heroin, which is reportedly cheaper and easier to obtain, will occur for some abusers (Cicero et al., 2012).

See the *Long-Term Impact of AB 623* section for discussion of AB 623 impacts on unintended consequences (e.g., heroin use, contracting HIV, or hepatitis C) beyond the first 12 months of the bill implementation.

Estimated Impact on Financial Burden

For those enrollees who switch to FDA-ADOAs, CHBRP costs would increase by $437,000 in the first year postmandate due to the effects of cost-sharing (deductibles, copays, etc) and the higher unit cost of FDA-ADOAs.

LONG-TERM IMPACT OF AB 623

In this section, CHBRP estimates the long-term impact of AB 623, defined as impacts occurring beyond the first 12 months of 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.

In the long term, the number of Californians enrolled in DMHC-regulated plans or CDI-regulated policies subject to AB 623 would increase with the growth in the population. Abuse-deterrent formulations of opioid analgesics (ADOAs) will likely become more common as the FDA approves labeling for drugs currently in the pipeline and already labeled FDA-ADOAs are brought to market. In July 2014, Targeniq ER[19] was approved but has not yet been marketed. Oxaydo, an instant and therefore short-term release formulation of oxycodone, will be brought to market in the third quarter of 2015. Embeda, a morphine/naltrexone ER product, was voluntarily removed from the market by the manufacturer in 2011 but returned in January 2015. Additionally, Zohydro and Xartemis are in the FDA pipeline for a label change, because they currently have abuse-deterrent properties, but are not labeled as such by the FDA.[20] ADOAs will be a growing proportion of opioid analgesic prescriptions in the future. However, as pointed out in the *Medical Effectiveness* section, the literature is ambiguous as to whether ADOAs lead to reduced abuse of opioid analgesics, because people can abuse ADOAs by swallowing the pills whole and/or switch to replacement drugs (either non-abuse-deterrent formulations or illicit drugs, such as heroin). The increase in ADOAs, therefore, should be not taken to be directly correlated with a corresponding decrease in drug abuse.

Long-Term Utilization and Cost Impacts

Utilization Impacts

In the 12 months following enactment, CHBRP estimates an increase of 3..70 per 1,000 enrollees in the use of FDA-ADOA. In later years, the long-term impact will depend on the increase in utilization as the new FDA-ADOA drug products replace some non-ADOA formulations that are currently available. Although certain populations, such as terminal illness or cancer patients, will not be medically appropriate to move to ADOA drug products, there will likely be some growth in utilization in ADOA.

Hwang, Chang, and Alexander (2015) found that the introduction of an ADOA formulation (OxyContin) was associated with a decrease in the overall usage of the drug oxycodone. Their study found that prior to the ADOA formulation, the annual growth rate in the use of OxyContin was 4.9%, which changed to a -23.8% growth rate after the ADOA formulation.

Cost Impacts

Although ADOA formulations are relatively new (Oxycodone ER was first available in 2010), the research literature has already begun examining the cost savings associated over time of replacing traditional opioid analgesic drug product prescriptions with ADOA drug products, but the results are ambiguous. Ben-Joseph et al. (2014) found with a retrospective study that prior authorization and tier restrictions on

[19] ER = extended release, meaning that the drug is released into the bloodstream over time, limiting the ability of the drug to give an instant high when abused.
[20] Information provided by the content expert, Dr. Mark Holtsman, UC Davis, April 28, 2015.

ADOA drug products increased medical costs because of higher negative health effects from abusing opioids, and had little effect on reducing pharmacy costs. Rossiter et al. (2014) modeled the relative reductions in opioid abuse due to reformulated ER oxycodone, and found that the costs associated with diagnosed opioid abuse were significantly reduced with the introduction of the ADOA. However, Twillman and Fudin (2014) dispute this finding, pointing out that the substitution effect was not adequately taken into account in the models, and the increased costs of heroin or other substance abuse may eliminate any savings from ADOAs.

In time, the increasing number of ADOA formulations should increase pressure to reduce costs to consumers for these drug products. When the patents on these formulations expire, the costs will reduce further, so that the disparity between ADOA and non-ADOA formulations will be minimal. Over the long-term, ADOA formulations will become less expensive to both enrollee and insurance carrier due to these market pressures. However, although it is clear that ADOA will become more available and less costly over time, it is less clear what effect this may have on overall societal health costs, because it is unclear what impact ADOAs will have on cross-drug abuse.

Long-Term Public Health Impacts

The alteration of some utilization management protocols in response to AB 623 is unlikely to measurably impact prescription opioid analgesic abuse. Although ADOAs are one way to reduce the supply of opioids susceptible to certain forms of abuse (but not others, such as swallowing the pills whole), there are many primary and secondary prevention strategies being implemented at the state, federal, and systems levels (see *Background* section). On point, pharmaceutical industry representatives observe that "…it is unlikely that drug formulation alone will be sufficient to address prescription opioid misuse, abuse, and addiction. Educational and preventive interventions for patients and clinicians will continue to play an important role in ultimately lessening the abuse of prescription opioids" (Budman, et al, 2009).

Unintended Consequences of AB 623

ADOAs may help reduce the supply of prescription opioids available for some forms of abuse (particularly inhalation and injection), but some research shows a correlation between the introduction of ADOAs and a shift to alternative opioids, including heroin (Butler et al., 2013; Cicero et al., 2012; Coplan et al., 2013; Dart et al., 2015; Havens et al., 2014; LaRochelle et al., 2015; Michna et al., 2014). Patients at substance abuse treatment centers reported that heroin is more easily obtained and less costly than prescription opioids; heroin also required less extraction effort than what is required to access ADOAs (Cicero et al., 2012). Coplan et al. obtained data on heroin use from poison centers nationally. They noted heroin abuse has been increasing since 2007, however the slope increased significantly after the introduction of abuse-deterrent OxyContin occurred in 2010.

However, authors from the Substance Abuse and Mental Health Administration assert that trend data from the National Survey on Drug Use and Health do not support the belief that prescription opioid users convert to heroin because of prescription opioid abuse prevention strategies (Lipari and Hughes, 2015). They state that the number of heroin initiators has remained fairly constant over the last 10 years (169,000 in 2013) and that heroin use remains uncommon (about 0.3% of the population as compared with 4.2% of the population who misuse prescription opioids) (Lipari and Hughes, 2015). The number of heroin users is higher in 2013 than in 2002 and the number of heroin-related deaths has also increased over the last decade, although this may be more reflective of the steadily increasing use of prescription opioids during the last decade rather than a more recent shift in opioid abuse prevention strategies like ADOAs. More research is required to discern a causal effect.

Nevertheless, reported increases in heroin use have received recent attention in the popular media with reports of increases in HIV and hepatitis C in rural communities due to contaminated needle-sharing for opioid analgesics and heroin. Jordan et al. are conducting a systematic review and meta-analysis regarding prescription opioid misuse and its relation to hepatitis C (research is incomplete and results are unavailable as of this report's publication) (Jordan et al., 2014).

CHBRP estimates AB 623 would have an unknown long-term public health impact because ADOAs are only one of many population-based, primary and secondary abuse prevention strategies; changes to insurers' utilization management protocols associated with ADOAs would be a small subset of those prevention strategies. Furthermore, to date ADOAs have yet to demonstrate a statistically significant reduction in *overall* prescription opioid abuse and overdose. ADOAs are a relatively new addition to the collection of strategies and, as more ADOAs are FDA-approved, further epidemiologic surveillance and study is required to ascertain its effectiveness.

APPENDIX A TEXT OF BILL ANALYZED

On April 10, 2015, the California Assembly Committee on Health requested that CHBRP analyze AB 623.

AMENDED IN ASSEMBLY MARCH 26, 2015

CALIFORNIA LEGISLATURE—2015–16 REGULAR SESSION

ASSEMBLY BILL No. 623

Introduced by Assembly Member Wood

February 24, 2015

An act to *add Section 4069 to the Business and Professions Code, to add Section 1367.217 to* the Health and Safety Code, *and to add Section 10123.203 to the Insurance Code* relating to prescription drugs.

LEGISLATIVE COUNSEL'S DIGEST

AB 623, as amended, Wood. *Abuse-deterrent opioid analgesic drug products.*

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 that act a crime. *Existing law also provides for the regulation of health insurers by the Department of Insurance.* These provisions require specified services and drugs to be covered by the various plans.

This bill would, where an abuse-deterrent opioid analgesic drug product, as defined, is available, prohibit a health care service plan or insurer from requiring the use of opioid analgesic drug products without the abuse-deterrent properties in order to access abuse-deterrent opioid analgesic drug products. The bill would require a health care service plan or insurer to allow a provider to prescribe, and if otherwise covered, to provide coverage for, a less than 30-day supply of an opioid analgesic drug product. Because a willful violation of these requirements with respect to health care service plans would be a crime, this bill would impose a state-mandated local program.

Existing law, the Pharmacy Law, the knowing violation of which is a crime, provides for the licensing and regulation of pharmacists by the California State Board of Pharmacy. Existing regulations require a pharmacist to provide oral consultation to his or her patient or the patient's agent in all care settings upon request or whenever the pharmacist deems it warranted.

This bill would require a pharmacist to inform a patient receiving an opioid analgesic drug product on proper storage and disposal of the drug, and authorizes this information to be included as part of the required oral consultation. Because a violation of this requirement 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.

The people of the State of California do enact as follows:

SECTION 1. The Legislature finds and declares the following:

(a) Prescription and over-the-counter (OTC) drugs are, after marijuana and alcohol, the most commonly abused substances by Americans over 14 years of age.

(b) Over two million people in the United States suffer from substance use disorders related to prescription opioid pain relievers.

(c) More people die from overdoses of prescription opioid pain relievers than from all other drugs combined, including heroin and cocaine.

(d) Prescription opioid pain relievers can have effects similar

to heroin when taken in doses or in ways other than prescribed, and research now suggests that abuse of these drugs may lead to heroin abuse.

(e) Prescription opioid pain relievers can be particularly dangerous when snorted, injected, or combined with other drugs or alcohol.

SEC. 2. Section 4069 is added to the end Business and Professions Code to read:

(a) A pharmacist shall inform a patient receiving an opioid analgesic drug product on proper storage and disposal of the drug. This information may be included as part of the oral consultation required under Section 1707.2 of Title 17 of the California Code of Regulations.

(b) For purposes of this section, "opioid analgesic drug product" has the same meaning as defined in Section 1367.217 of the Health and Safety Code.

SEC. 3.Section 1367.217 is added to the Health and Safety Code to read:

(a) Where an abuse-deterrent opioid analgesic drug product is available, a health care service plan shall not require the use of opioid analgesic drug products without the

abuse-deterrent properties in order to access abuse-deterrent opioid analgesic drug products.

(b) This section shall not be construed to prevent a health care service plan from applying prior authorization requirements to abuse-deterrent opioid analgesic drug products, provided that those same requirements are applied to versions of those opioid analgesic drug products without the abuse-deterrent properties.

(c) A health care service plan shall allow a provider to prescribe, and if otherwise covered, shall provide coverage for, a less than 30-day supply of an opioid analgesic drug product.

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

(1) "Abuse-deterrent opioid analgesic drug product" means a brand or generic opioid analgesic drug product approved by the federal Food and Drug Administration with abuse-deterrence labeling claims that indicate the drug product is expected to result in a meaningful reduction in abuse.

(2) "Opioid analgesic drug product" means a drug product in the opioid analgesic drug class that is prescribed to treat moderate to severe pain or other conditions, whether in immediate release or extended release or long-acting form and whether or not combined with other drug substances to form a single drug product or dosage form.

SEC. 4.Section 10123.203 is added to the Insurance Code to read

(a) Where an abuse-deterrent opioid analgesic drug product is available, an insurer shall not require the use of opioid analgesic drug products without the abuse-deterrent properties in order to access abuse-deterrent opioid analgesic drug products.

(b) This section shall not be construed to prevent an insurer from applying prior authorization requirements to abuse-deterrent opioid analgesic drug products, provided that those same requirements are applied to versions of those opioid analgesic drug products without the abuse-deterrent properties.

(c) An insurer shall allow a provider to prescribe, and if otherwise covered, shall provide coverage for, a less than 30-day supply of an opioid analgesic drug product.

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

(1) "Abuse-deterrent opioid analgesic drug product" means a brand or generic opioid analgesic drug product approved by the federal Food and Drug Administration with abuse-deterrence labeling claims that indicate the drug product is expected to result in a meaningful reduction in abuse.

(2) "Opioid analgesic drug product" means a drug product in the opioid analgesic drug class that is prescribed to treat moderate to severe pain or other conditions, whether in immediate release or extended release or long-acting form and whether or not combined with other drug substances to form a single drug product or dosage form.

SEC. 5

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

Appendix C describes methods used in the medical effectiveness literature review for AB 623. AB 623 would prohibit requiring use of opioid analgesics prior to covering ADF, require that prior authorization protocols applied to ADF be the same as prior authorization protocols applied to other opioid analgesics, and for covered opioid analgesics, provide coverage for less than 30-day supplies. The Medical Effectiveness review examined the impact of abuse-deterrent opioid analgesics on opioid abuse and opioid related health outcomes; the impact of step therapy protocol for abuse-deterrent opioid analgesics on opioid related health outcomes; the impact of coverage for less than 30-day supplies of opioid analgesics on opioid related health outcomes; and the impact of prior authorization of opioid analgesics on opioid related health outcomes.

The medical effectiveness review does not address the effectiveness of all prescription medications because it is not feasible for CHBRP to review the literature on effectiveness of all medications subject to the provisions in AB 623 within the 60-day timeframe allotted for this analysis. In addition, the Food and Drug Administration assesses the effectiveness of all medications available in the United States and sets forth approved uses for them.

CHBRP's medical effectiveness review for a previous bill on step therapy, AB 889, focused on the impact of step therapy protocols for prescription medications in 2013. For the part of AB 623 that paralleled AB 889, the literature search was limited to abstracts of studies published in English from January 2013 to present. For the analysis of AB 623, CHBRP expanded the literature review to include the impact of abuse-deterrent opioids analgesics on opioid abuse, addiction, and opioid related health outcomes; the impact of step therapy protocol for abuse-deterrent opioid analgesics on opioid related health outcomes; the impact of coverage for less than 30-day supplies of opioid analgesics on opioid related health outcomes; and the impact of prior authorization of opioid analgesics on opioid related health outcomes.

The literature search on abuse-deterrent opioids included abstracts of studies published in English from 2000 to present. Studies were identified through searches of PubMed, the Cochrane Library, Web of Science, EconLit, and Business Source Complete. Of the 518 articles found in the literature review, 42 xx were reviewed for potential inclusion in this report on AB 623, and 26 studies were included in the medical effectiveness review for this report. The medical effectiveness review also presents findings from the 13 studies that were previously identified in the 2013 CHBRP AB 899 report.

The medical effectiveness review for step therapy was limited to studies of protocols under which persons were required to try and fail at least one medication before obtaining a prescription for the initially prescribed medication, or a generic version of the same medication. Studies of prior authorization for abuse-deterrent opioids were included only if they required persons to try and fail at least one medication before prior authorization would be granted for the initially prescribed medication.

A systematic review of studies of the impact of industry sponsorship on research findings concluded that sponsorship of studies of medications or medical devices by manufacturers is associated with results and conclusions that are more favorable to their products (Lundh et al., 2012). Sponsorship may also affect findings from studies of step therapy protocols aimed at reducing use of a manufacturer's products.

Two reviewers screened the title and abstract of each citation retrieved by the literature search to determine eligibility for inclusion. The reviewers acquired the full text of articles that were deemed eligible for inclusion in the review and reapplied the initial eligibility criteria. Of the 735 articles found in the literature review, 42 were reviewed for potential inclusion in this report on AB 623, and 26 studies were included in the medical effectiveness review for this report. The medical effectiveness review relied

heavily on information from the pharmaceutical labeling. The other articles were eliminated because the studies they presented did not focus on abuse-deterrent opioids, were not well-designed (that is, not ranked as highly in CHBRP's hierarchy of research designs as those CHBRP did include), did not report findings from clinical research studies, or did not address outcomes of ADF on opioid abuse, addiction, and opioid related health outcomes. In making a "call" for each outcome measure, the team 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.*[21]

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.*[22] To grade the evidence for each outcome measured, the team uses a grading system that has the following categories:

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

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

- Clear and convincing evidence;
- Preponderance of evidence;
- Ambiguous/conflicting 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. This can be further subdivided into preponderance of evidence from high-quality studies and preponderance of evidence from low-quality studies.

[21] Available at: www.chbrp.org/analysis_methodology/docs/medeffect_methods_detail.pdf.
[22] Available at: www.chbrp.org/analysis_methodology/docs/medeffect_methods_detail.pdf.

A grade of *ambiguous/conflicting 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

The search terms used to locate studies relevant to AB 889 were as follows:

Major MeSH terms used to search PubMed

- Naltrexone
- Morphine
- OxyContin
- Oxycodone
- Zohydro
- Hydrocodone
- Hysingla
- Targiniq
- opioid-effectiveness of tamper resistant formulation
- abuse deterrent opioid
- tamper resistant opioid
- Analgesics, opioid, and drug compounding
- Prescription Drug Misuse
- abuse deter
- opioid
- opiate
- narcotic

Keywords used to search PubMed, Cochrane Library, EconLit, Web of Science, and relevant websites

- Naltrexone
- Morphine
- OxyContin
- Oxycodone
- Zohydro
- Hydrocodone
- Hysingla
- Targiniq
- opioid-effectiveness of tamper resistant formulation
- abuse deterrent opioid
- tamper resistant opioid
- Analgesics, opioid, and drug compounding
- Prescription Drug Misuse
- abuse deter
- opioid
- opiate
- narcotic
- Step Therapy
- Step Edit
- Step Therapy Override
- Override
- Step-Therapy
- Prior Authorization
- Drug
- Drugs
- Fail First
- Generics
- Medication
- Prescription
- Prescriptions

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

This appendix describes data sources, estimation methodology, as well as general and mandate-specific caveats and assumptions used in conducting the cost impact analysis. For additional information on the cost model and underlying methodology, please refer to the CHBRP website at: www.chbrp.org/analysis_methodology/cost_impact_analysis.php.

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.[23]

Data Sources

This subsection discusses the variety of data sources CHBRP uses. Key sources and data items are listed below, in Table 8.

Table 8. Data for 2016 Projections

Data Source	Items
California DHCS administrative data for the Medi-Cal program, data available as of end of December 2014	Distribution of enrollees by managed care or FFS distribution by age: 0–17; 18–64; 65+ Medi-Cal Managed Care premiums
California Department of Managed Health Care (DMHC) data from the interactive website "Health Plan Financial Summary Report," August–October, 2014	Distribution of DMHC-regulated plans by market segment*
California Department of Insurance (CDI) Statistical Analysis Division data; data as of December 31, 2013	Distribution of CDI-regulated policies by market segment
California Health Benefits Review Program (CHBRP) Annual Enrollment and Premium Survey of California's largest (by enrollment) health care service plans and health insurers; data as of September 30, 2014; responders' data represent approximately 97.3% of persons not associated with CalPERS or Medi-Cal with health insurance subject to state mandates – 98.0% of full-service (nonspecialty) DMHC-regulated plan enrollees and 97.0% of full-service (nonspecialty) CDI-regulated policy enrollees.	Enrollment by: • Size of firm (2–50 as small group and 51+ as large group) • DMHC vs. CDI regulated • Grandfathered vs. nongrandfathered Premiums for individual policies by: • DMHC vs. CDI regulated • Grandfathered vs. nongrandfathered

[23] CHBRP's authorizing legislation requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact (www.chbrp.org/docs/authorizing_statute.pdf).

Data Source	Items
California Employer Health Benefits Survey, 2014 (conducted by NORC and funded by CHCF)	Enrollment by HMO/POS, PPO/indemnity self-insured, fully insured, Premiums (not self-insured) by: • Size of firm (3–25 as small group and 25+ as large group) • Family vs. single • HMO/POS vs. PPO/indemnity vs. HDHP employer vs. employer premium share
California Health Interview Survey (CHIS) 2012/2013/T7 ("T7" representing the first 6 months of 2014)	Uninsured, age: 65+ Medi-Cal (non-Medicare), age: 65+ Other public, age: 65+ Employer-sponsored insurance, age: 65+
California Public Employees' Retirement System (CalPERS) data, enrollment as of October 1, 2014	CalPERS HMO and PPO enrollment • Age: 0–17; 18–64; 65+ HMO premiums
California Simulation of Insurance Markets (CalSIM) Version 1.9.1 (projections for 2016)	Uninsured, age: 0–17; 18–64 Medi-Cal (non-Medicare) (a), age: 0–17; 18–64 Other public (b), age: 0–64 Individual market, age: 0–17; 18–64 Small group, age: 0–17; 18–64 Large group, age: 0–17; 18–64
Centers for Medicare & Medicaid (CMS) administrative data for the Medicare program, annually (if available) as of end of September	HMO vs. FFS distribution for those 65+ (noninstitutionalized)
Milliman estimate	Medical trend influencing annual premium increases

Notes: (*) CHBRP assumes DMHC-regulated PPO group enrollees and POS enrollees are in the large-group segment.
Key: CDI = California Department of Insurance; CHCF = California HealthCare Foundation; CHIS = California Health Interview Survey; CMS = Centers for Medicare & Medicaid Services; DHCS = Department of Health Care Services; DMHC = Department of Managed Health Care; FFS = fee-for-service; HMO = health maintenance organization; HDHP = high-deductible health plan; NORC = National Opinion Research Center; POS = point of service; PPO = preferred provider organization.

Further discussion of external and internal data follows.

Internal data

1. CHBRP's Annual Enrollment and Premium Survey collects data from the seven largest providers of health insurance in California (including Aetna, Anthem Blue Cross of California, Blue Shield of California, CIGNA, Health Net, Kaiser Foundation Health Plan, and United Healthcare/PacifiCare) to obtain estimates of enrollment not associated with CalPERS or Medi-Cal by purchaser (i.e., large and small group and individual), state regulator (DMHC or CDI), grandfathered and nongrandfathered status, and average premiums. CalSIM and market trends were applied to project 2016 health insurance enrollment in DMHC-regulated plans and CDI-regulated policies.

2. CHBRP's other surveys of the largest plans/insurers collect information on benefit coverage relevant to proposed benefit mandates CHBRP has been asked to analyze. In each report, CHBRP indicates the proportion of enrollees – statewide and by market segment – represented

by responses to CHBRP's bill-specific coverage surveys. The proportions are derived from data provided by CDI and DMHC.

3. External sources.

4. California Department of Health Care Services (DHCS) data are used to estimate enrollment in Medi-Cal Managed Care (beneficiaries enrolled in Two-Plan Model, Geographic Managed Care, and County Operated Health System plans), which may be subject to state benefit mandates, as well as enrollment in Medi-Cal Fee For Service (FFS), which is not. The data are available at: www.dhcs.ca.gov/dataandstats/statistics/Pages/Monthly_Trend_Report.aspx. Medi-Cal enrollment is projected to 2016 based on CalSIM's estimate of the continuing impact of the Medi-Cal expansion implemented in 2014.

5. California Employer Health Benefits Survey data are used to make a number of estimates, including: premiums for employment-based enrollment in DMHC-regulated health care service plans (primarily health maintenance organizations [HMOs] and point of service [POS] plans) and premiums for employment-based enrollment in CDI-regulated health insurance policies regulated by the (primarily preferred provider organizations [PPOs]). Premiums for fee-for-service (FFS) policies are no longer available due to scarcity of these policies in California. This annual survey is currently released by the California Health Care Foundation/National Opinion Research Center (CHCF/NORC) and is similar to the national employer survey released annually by the Kaiser Family Foundation and the Health Research and Educational Trust. More information on the CHCF/NORC data is available at: www.chcf.org/publications/2014/01/employer-health-benefits.

6. California Health Interview Survey (CHIS) data are used to estimate the number of Californians aged 65 and older, and the number of Californians dually eligible for both Medi-Cal and Medicare coverage. CHIS data are also used to determine the number of Californians with incomes below 400% of the federal poverty level. CHIS is a continuous survey that provides detailed information on demographics, health insurance coverage, health status, and access to care. More information on CHIS is available at: www.chis.ucla.edu.

7. California Public Employees Retirement System (CalPERS) data are used to estimate premiums and enrollment in DMHC-regulated plans, which may be subject to state benefit mandates, as well as enrollment in CalPERS' self-insured plans, which is not. CalPERS does not currently offer enrollment in CDI-regulated policies. Data are provided for DMHC-regulated plans enrolling non-Medicare beneficiaries. In addition, CHBRP obtains information on current scope of benefits from evidence of coverage (EOC) documents publicly available at: www.calpers.ca.gov. CHBRP assumes CalPERS's enrollment in 2016 will not be affected by continuing shifts in the health insurance market as a result of the ACA.

8. California Simulation of Insurance Markets (CalSIM) estimates are used to project health insurance status of Californians aged 64 and under. CalSIM is a microsimulation model that projects the effects of the Affordable Care Act on firms and individuals. More information on CalSIM is available at: http://healthpolicy.ucla.edu/programs/health-economics/projects/CalSIM/Pages/default.aspx.

9. Milliman data sources are relied on to estimate the premium impact of mandates. Milliman's projections derive from the Milliman Health Cost Guidelines (HCGs). The HCGs are a health care pricing tool used by many of the major health plans in the United States. Most of the data sources underlying the HCGs are claims databases from commercial health insurance plans. The data are supplied by health insurance companies, HMOs, self-funded employers, and private data vendors. The data are mostly from loosely managed health care plans, generally those characterized as PPO plans. More information on the Milliman HCGs is available at:

http://us.milliman.com/Solutions/Products/Resources/Health-Cost-Guidelines/Health-Cost-Guidelines---Commercial/.

10. The MarketScan databases, which reflect the health care claims experience of employees and dependents covered by the health benefit programs of large employers. These claims data are collected from insurance companies, Blue Cross Blue Shield plans, and third party administrators. These data represent the medical experience of insured employees and their dependents for active employees, early retirees, individuals with COBRA continuation coverage, and Medicare-eligible retirees with employer-provided Medicare Supplemental plans. No Medicaid or Workers Compensation data are included.

11. Ingenix MDR Charge Payment System, which includes information about professional fees paid for health care services, based upon claims from commercial insurance companies, HMOs, and self-insured health plans.

Projecting 2016

This subsection discusses adjustments made to CHBRP's Cost and Coverage Model to project 2016, the period when mandates proposed in 2015 would, if enacted, generally take effect. It is important to emphasize that CHBRP's analysis of specific mandate bills typically addresses the incremental effects of a mandate – specifically, how the proposed mandate would impact benefit coverage, utilization, costs, and public health, *holding all other factors constant*. CHBRP's estimates of these incremental effects are presented in the *Benefit Coverage, Utilization, and Cost Impacts* section of this report.

Baseline premium rate development methodology

The key components of the baseline model for utilization and expenditures are estimates of the per member per month (PMPM) values for each of the following:

- Insurance premiums PMPM;
- Gross claims costs PMPM;
- Member cost sharing PMPM; and
- Health care costs paid by the health plan or insurer.

For each market segment, we first obtained an estimate of the insurance premium PMPM by taking the 2014 reported premium from the abovementioned data sources and trending that value to 2016. CHBRP uses trend rates published in the Milliman HCGs to estimate the health care costs for each market segment in 2016.

The large-group market segments for each regulator (CDI and DMHC) are split into grandfathered and nongrandfathered status. For the small-group and individual markets, further splits are made to indicate association with Covered California, the state's health insurance marketplace. Doing so allows CHBRP to separately calculate the impact of ACA and of specific mandates, both of which may apply differently among these subgroups. The premium rate data received from the CHCF/NORC California Employer Health Benefits survey did not split the premiums based on grandfathered or exchange status. However, CHBRP's Annual Enrollment and Premium (AEP) survey asked California's largest health care service plans and health insurers to provide their average premium rates separately for grandfathered and nongrandfathered plans. The ratios from the CHBRP survey data were then applied to the CHCH/NORC aggregate premium rates for large and small group, to estimate premium rates for grandfathered and

nongrandfathered plans that were consistent with the NORC results. For the individual market, the premium rates received from CHBRP's AEP survey were used directly.

The remaining three values were then estimated by the following formulas:

- Health care costs paid by the health plan = insurance premiums PMPM × (1 − profit/administration load);
- Gross claims costs PMPM = health care costs paid by the health plan ÷ percentage paid by health plan; and
- Member cost sharing PMPM = gross claims costs × (1 − percentage paid by health plan).

In the above formulas, the quantity "profit/administration load" is the assumed percentage of a typical premium that is allocated to the health plan/insurer's administration and profit. These values vary by insurance category, and under the ACA, are limited by the minimum medical loss ratio requirement. CHBRP estimated these values based on actuarial expertise at Milliman, and their associated expertise in health care.

In the above formulas, the quantity "percentage paid by health plan" is the assumed percentage of gross health care costs that are paid by the health plan, as opposed to the amount paid by member cost sharing (deductibles, copays, etc.). In ACA terminology, this quantity is known as the plan's "actuarial value." These values vary by insurance category. For each insurance category, Milliman estimated the member cost sharing for the average or typical plan in that category. Milliman then priced these plans using the Milliman Health Cost Guidelines to estimate the percentage of gross health care costs that are paid by the carrier.

General Caveats and Assumptions

This subsection discusses the general caveats and assumptions relevant to all CHBRP reports. The projected costs are estimates of costs that would result if a certain set of assumptions were exactly realized. Actual costs will differ from these estimates for a wide variety of reasons, including:

- Prevalence of mandated benefits before and after the mandate may be different from CHBRP assumptions.
- Utilization of mandated benefits (and, therefore, the services covered by the benefit) before and after the mandate may be different from CHBRP assumptions.
- Random fluctuations in the utilization and cost of health care services may occur.

Additional assumptions that underlie the cost estimates presented in this report are:

- Cost impacts are shown only for plans and policies subject to state benefit mandate laws.
- Cost impacts are only for the first year after enactment of the proposed mandate.
- Employers and employees will share proportionately (on a percentage basis) in premium rate increases resulting from the mandate. In other words, the distribution of the premium paid by the subscriber (or employee) and the employer will be unaffected by the mandate.
- For state-sponsored programs for the uninsured, the state share will continue to be equal to the absolute dollar amount of funds dedicated to the program.

- When cost savings are estimated, they reflect savings realized for 1 year. Potential long-term cost savings or impacts are estimated if existing data and literature sources are available and provide adequate detail for estimating long-term impacts. For more information on CHBRP's criteria for estimating long-term impacts, please see: www.chbrp.org/analysis_methodology/docs/longterm_impacts08.pdf.

- Several studies have examined the effect of private insurance premium increases on the number of uninsured (Chernew et al., 2005; Glied and Jack, 2003; Hadley, 2006). Chernew et al. (2005) estimate that a 10% increase in private premiums results in a 0.74 to 0.92 percentage point decrease in the number of insured, whereas Hadley (2006) and Glied and Jack (2003) estimate that a 10% increase in private premiums produces a 0.88 and a 0.84 percentage point decrease in the number of insured, respectively. Because each of these studies reported results for the large-group, small-group, and individual insurance markets combined, CHBRP employs the simplifying assumption that the elasticity is the same across different types of markets. For more information on CHBRP's criteria for estimating impacts on the uninsured, please see *Criteria and Methods for Estimating the Impact of Mandates on the Number of Individuals Who Become Uninsured in Response to Premium Increases*, available at: www.chbrp.org/analysis_methodology/cost_impact_analysis.php.

There are other variables that may affect costs, but which CHBRP did not consider in the estimates presented in this report. Such variables include, but are not limited to:

- Population shifts by type of health insurance: If a mandate increases health insurance costs, some employer groups and individuals may elect to drop their health insurance. Employers may also switch to self-funding to avoid having to comply with the mandate.

- Changes in benefits: To help offset the premium increase resulting from a mandate, deductibles or copayments may be increased. Such changes would have a direct impact on the distribution of costs between health plans/insurers and enrollees, and may also result in utilization reductions (i.e., high levels of cost sharing result in lower utilization of health care services). CHBRP did not include the effects of such potential benefit changes in its analysis.

- Adverse selection: Theoretically, persons or employer groups who had previously foregone health insurance may elect, postmandate, to enroll in a health plan or policy because they perceive that it is now to their economic benefit to do so.

- Medical management: Health plans/insurers may react to the mandate by tightening medical management of the mandated benefit. This would tend to dampen the CHBRP cost estimates. The dampening would be more pronounced on the plan/policy types that previously had the least effective medical management (i.e., PPO plans).

- Geographic and delivery systems variation: Variation exists in existing utilization and costs, and in the impact of the mandate, by geographic area and by delivery system models. Even within the health insurance plan/policy types CHBRP modeled (HMO, including HMO and POS plans, and non-HMO, including PPO and FFS policies), there are likely variations in utilization and costs. Utilization also differs within California due to differences in the health status of the local population, provider practice patterns, and the level of managed care available in each community. The average cost per service would also vary due to different underlying cost levels experienced by providers throughout California and the market dynamic in negotiations between providers and health plans/insurers. Both the baseline costs prior to the mandate and the estimated cost impact of the mandate could vary within the state due to geographic and delivery system differences. For purposes of this analysis, however, CHBRP has estimated the impact on a statewide level.

- Compliance with the mandate: For estimating the postmandate impacts, CHBRP typically assumes that plans and policies subject to the mandate will be in compliance with the benefit coverage requirements of the bill. Therefore, the typical postmandate coverage rates for persons enrolled in health insurance plans/policies subject to the mandate are assumed to be 100%.

Analysis-Specific Caveats and Assumptions

This subsection discusses the caveats and assumptions relevant specifically to an analysis of AB 623.

AB 623 would impose requirements on outpatient prescription drug (OPD) benefit utilization management protocols. CHBRP identified both step therapy protocols and prior authorization protocols that would change to become AB 623 compliant. CHBRP's analysis focused (see Table 9) on the impact of these restrictions on utilization of the three FDA-labeled ADOAs currently available in the market and clinically appropriate substitutes (opioid analgesics with some abuse-deterrent properties).

Table 9. Opioid Analgesics with Abuse-Deterrent Properties

Brand Name Drug	Generic Equivalent	Non-Abuse-Deterrent version
FDA-labeled as ADOA		
Embeda	Morphine/naltrexone ER	Morphine Extended Release
Hysingla ER	Hydrocodone ER	
OxyContin	Oxycodone ER	
Not FDA-labeled, with abuse-deterrent properties		
Exalgo	Hydromorphone ER	
Farginiq ER	Oxycodone/naloxone ER	
Nucynta ER	Tapentadol ER	
Opana ER	Oxymorphone ER	Oxymorphone ER
Oxaydo	Oxycodone IR	Oxycodone IR
Xartemis XR	Oxycodone/acetaminophen ER	
Zohydro ER	Hydrocodone ER	

Source: California Health Benefits Review Program, 2015.

Note: Other drugs that may be included in step therapy or prior authorization protocols relating to opioid analgesics include hydrocodone/acetaminophen, Hydromorphone IR, Oxycodone IR/acetaminophen, oxycodone/aspirin, Abstral SL, Fentora Buccal, Subsys.
Key: ADOA = abuse-deterrent opioid analgesic; ER = extended release; IR = immediate release

CHBRP relied on content expert review to determine the compliance of utilization management protocols associated with opioid analgesics. Based on this review, CHBRP estimated the utilization per 1,000 enrollees and average allowed charge for drugs associated with changing protocols. Estimates were derived from data in the the Milliman Consolidated Health Cost Guidelines Sources Database (2012) and supplemented by data in the Milliman Health Cost Guidelines (2015). Because abuse-deterrent formulations of opioid analgesics are recent innovations, of the FDA-ADOAs, only OxyContin appears in the 2012 data.

CHBRP assumed that increased access to ADOAs would have no net impact on the utilization of opioid analgesics, but would shift some utilization to FDA-ADOAs.

Determining Public Demand for the Proposed Mandate

This subsection discusses public demand for the benefits AB 623 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 the DMHC or CDI and therefore not subject to state-level mandates) with the benefits that are provided by plans or policies that would be subject to the mandate.

On the basis of conversations with the largest collective bargaining agents in California, CHBRP concluded that unions currently do not generally include issues related to formulation-specific terms and conditions of outpatient prescription drug benefits in their health insurance negotiations. 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.

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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.

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CHBRP staff coordinates the efforts of the Faculty Task Force, works with Task Force members in preparing parts of the analysis, and coordinates all external communications, including those with the California Legislature.

CHBRP is also grateful for the valuable assistance of its National Advisory Council, who provide expert reviews of draft analyses and offer general guidance on the program. CHBRP is administered by the Division of UC Health at the University of California, Office of the President, led by John D. Stobo, MD, Senior Vice President.

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

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