
Abuse Deterrent Formulations of Opioids: Comparative Value Draft Results

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INSTITUTE FOR CLINICAL
AND ECONOMIC REVIEW

NOTE: Based on initial draft report, subject to change

Introduction

- The Institute for Clinical and Economic Review (ICER)
- The New England Comparative Effectiveness Public Advisory Council (New England CEPAC)

How was the ICER draft report on ADF opioids developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- Internal ICER economic modeling
- Clinical expert report reviewers
- NEXT: Public comment and revision
- Draft Evidence Report is available at:
<https://icer-review.org/material/adf-draft-report/>

Comparative Value: Draft Results

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Disclosures

- I have no conflicts of interest to report.

DRAFT

Objective

To estimate and compare the costs and benefits of using ADF opioids or non-ADF opioids for chronic pain

- Benefits defined as reduction in abuse-related outcomes
 - Number of incident cases of abuse
 - Number of opioid overdose-related deaths
 - Subsequent health care resource use
- Key research questions:
 - 1) What are the potential net costs and outcomes of using ADFs compared to non-ADF?
 - 2) What levels of effectiveness in abuse reduction and in price difference would be needed for ADF opioids to achieve cost neutrality or net savings relative to non-ADF opioids?

Methods in Brief

Overall Approach

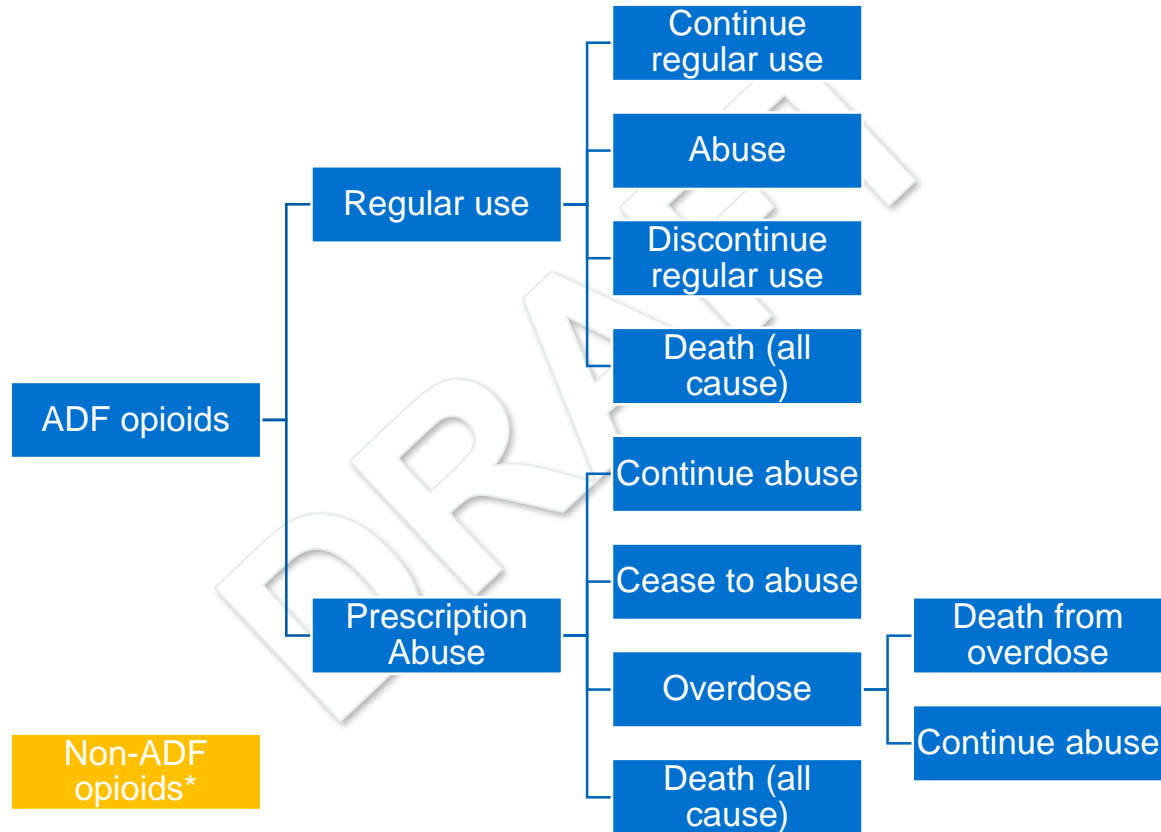
- Compared a hypothetical cohort of 100,000 adult non-cancer chronic pain patients who were newly prescribed either:
 - a) extended-release (ER) ADF opioids, or
 - b) ER non-ADF opioids
- Time horizon: 5 years (with 1 year cycle length)
- Perspective: third-party payer covering commercially-insured population

Overall Approach

- NOTE: Did not include costs of externalities such as diversion or switching to heroin and other non-ADF opioids that may occur in reaction to the abuse-deterrent properties of ADFs.
 - Tested as scenario analysis using various assumed estimates for the level of diversion and the relative risk (RR) of diversion with ADF opioids.
- Also conducted state-specific policy analysis of all non-ADF ER opioid prescription users being converted to ADF, for Massachusetts and Vermont (not presented here)

Model Structure

Representing One Cycle for the ADF Opioid Cohort



Key Model Assumptions

- Base case used incidence of abuse pre- and post-Oxycontin® reformulation for abuse-deterrent effectiveness of ADF relative to non-ADF cohorts*
- Incidence of abuse differs between ADF and non-ADF cohorts, but abuse episodes assumed to have same costs
- Diversion and effects on heroin/other opioid use that might result from receiving ADF opioid not included, as considering only new opioid prescriptions
- Daily dosage assumed to be 90mg MED, split over three doses daily
- Cost estimates sourced from a commercial claims study by Rice et al. that included opioid users from January 2006 to March 2012**

Discontinuation Rates

- Rate of discontinuation of regular use of opioids assumed to be same for ADF and non-ADF cohorts
 - Ranged from 17.8% in year 1 to 40.4% in year 5 after initiating ER opioid use
- Annual rate of cessation of opioid abuse assumed to be 10% in both cohorts
 - In year of cessation, patient assumed to incur 50% of abuse-related costs prior to dropping out of model

Clinical Inputs

Input	Value	Source
Incidence of non-ADF ER opioid abuse	3.647%	Rossiter et al., 2014
Incidence of ADF ER opioid abuse (Oxycontin®)	2.542%	Rossiter et al., 2014
Annual percentage of discontinuation of prescription opioid use	Year 1 – 17.8% Year 2 – 28.4% Year 3 -- 34.6% Year 4 – 38.2% Year 5 – 40.4%	Martin et al., 2011

Drug Costs

- Costs for a typical ADF and non-ADF opioid calculated as weighted average of market share, based on number of incident users of opioids in Massachusetts in 2016
 - Used Federal Supply Schedule (FSS) to calculate discounted prices of all opioids
 - List of opioids and their market share within the ADF and non-ADF groups available in ICER's report
 - Opioids with ADF properties but without an FDA-approved ADF label fell into the non-ADF opioid category in our analysis.
- Costs (both drug and non-drug) were calculated annually and inflated to 2016 dollars using medical care component of US Consumer Price Index.

Cost Inputs

Input	Value		Source
ADF Opioids – 90mg MED			
Cost per daily dose*	\$11.60		FSS, 2017
Annual cost	\$4,234		Calculation
Non-ADF Opioids – 90mg MED			
Cost per daily dose*	\$5.82		FSS, 2017
Annual cost	\$2,124		Calculation
Mean Annual Health Care Costs			
	Regular use	Abuse	
Hospitalization	\$2,643	\$6,586	Rice et al., 2014
Outpatient visits	\$4,505	\$6,160	
ER	\$982	\$3,565	
Rehabilitation	\$55	\$2,053	
Other visits	\$460	\$1,383	
Prescription drug fills**	\$2,305	\$3,186	

Model Results

Results

Burden of Abuse for ADF and Non-ADF Opioids after 5 Years

Outcome (at 5 years)	ADF opioids	Non-ADF opioids	Increment (ADF – Non-ADF)
Incident abuse	7,450	10,532	-3,082
Person-years of abuse	21,091	29,943	-8,852
Overdose deaths	1.25	1.77	-0.52

Total Estimated Health-Care Costs of ADF and Non-ADF Opioids at 5 Years

	ADF opioids	Non-ADF opioids	Difference (ADF – non-ADF)
Regular use*	\$3,123,262,001	\$3,042,279,103	\$80,982,898
Abuse*	\$510,590,928	\$724,896,371	-\$214,305,443
Prescription opioid costs (entire cohort)	\$1,301,831,255	\$657,301,870	\$644,529,385
Total	\$4,935,684,184	\$4,424,477,344	\$511,206,840

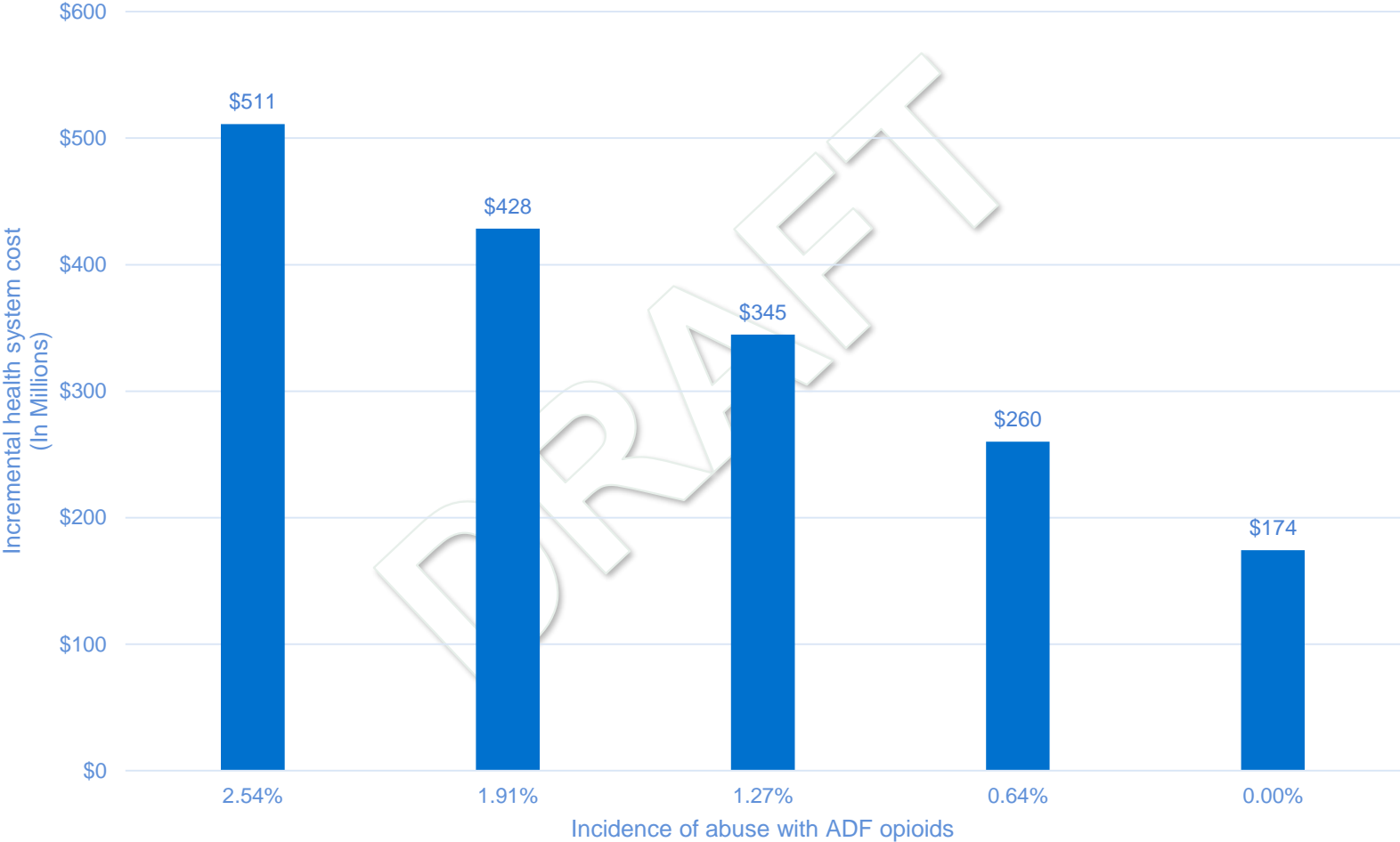
Cost Per Incremental Outcome of ADF Opioids vs. Non-ADF Opioids

Incremental outcome	Cost
Preventing 1 new abuse case	\$165,868
Preventing 1 new abuse year	\$57,749

Results: Cost Neutrality Threshold Analysis

- Increased effectiveness of ADFs in reducing abuse (i.e., decreased incidence of abuse in ADF opioid cohort) to identify point at which cost-neutrality would be achieved.
- Decreasing incidence from base case estimate of 2.54% to 0 (that is, assuming ADF opioids completely eliminate cases of abuse) still resulted in net costs over 5 years of approximately \$174.4 million compared to that of the non-ADF opioid cohort.

Results: Cost Neutrality Threshold Analysis

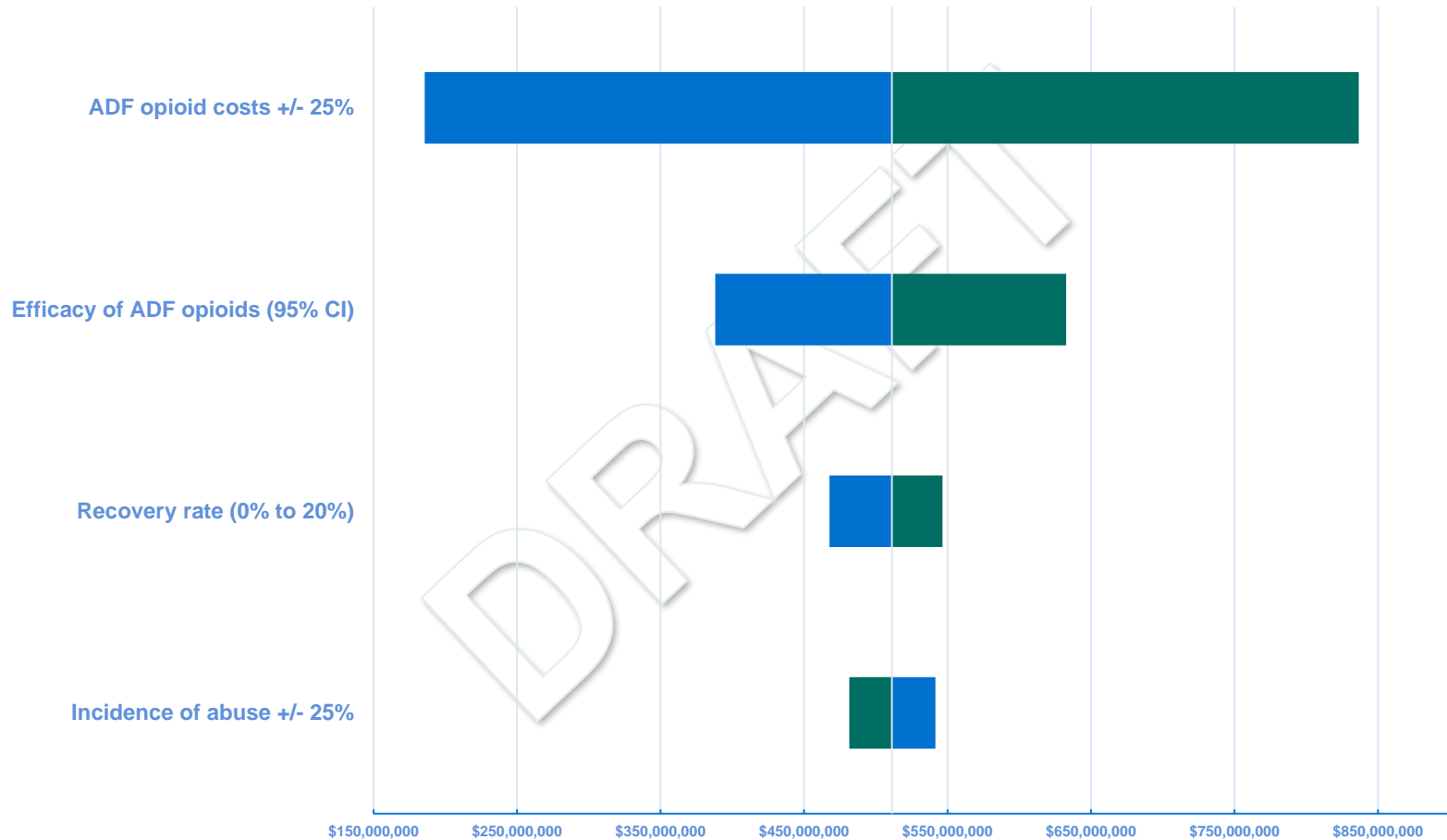


Results: Cost Neutrality Threshold Analysis

- In 2nd threshold analysis, varied ADF opioid drug cost to achieve cost-neutrality
 - Kept base case incidence of abuse in each opioid cohort constant
- Average daily ADF opioid costs would need to be reduced from \$11.60 to \$7.04 at 90mg MED per day to achieve cost neutrality
 - 39% discount from current pricing

	Base-case cost	Cost to attain cost-neutrality	Percentage difference
ADF opioid average daily drug cost*	\$11.60	\$7.04	-39.3%

One-Way Sensitivity Analyses

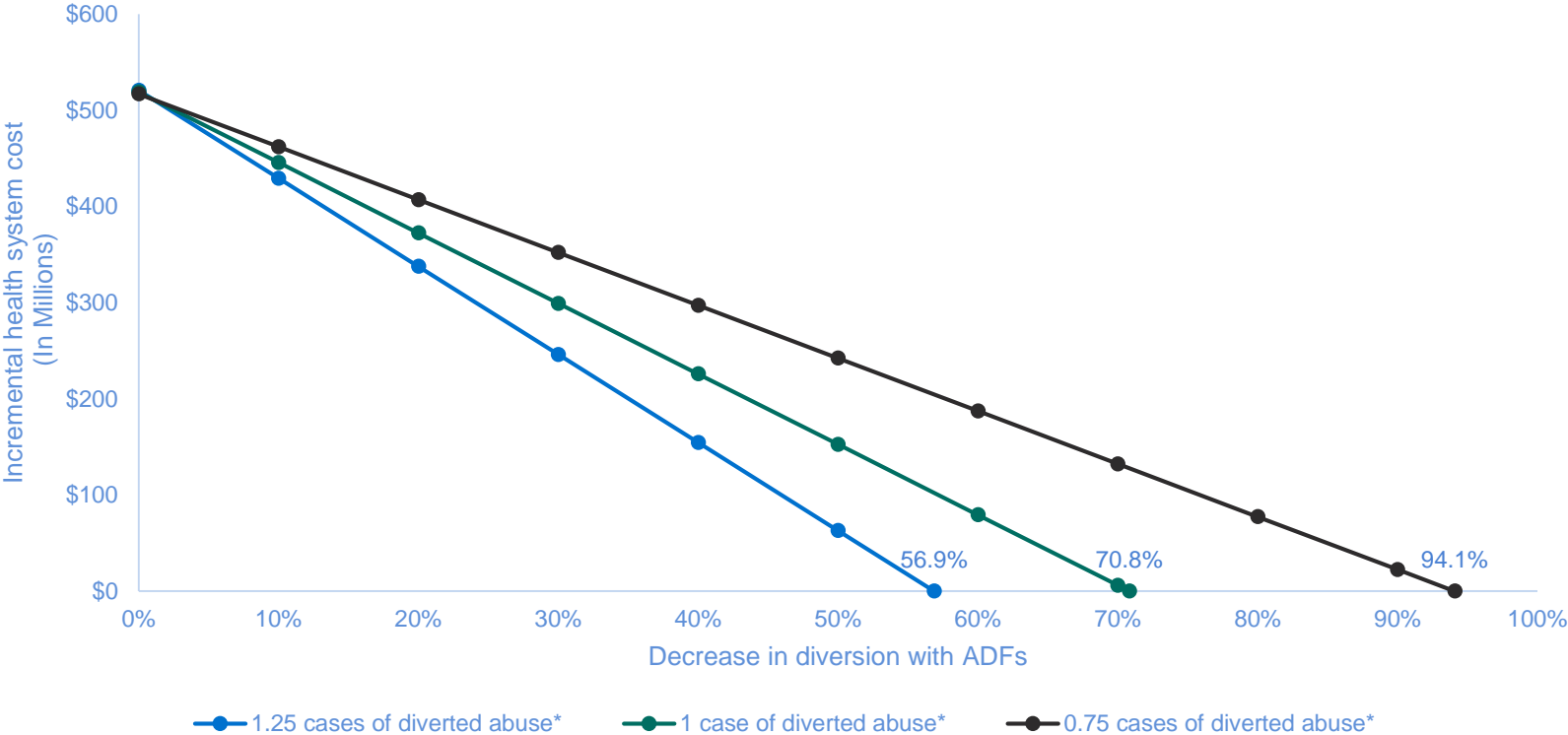


Scenario Analysis: Diversion

- Using estimate of 1.25 cases of diverted abuse for every case of prescription opioid abuse, ADF cohort has additional spending of ~\$521 million over 5 years.
- To achieve cost-neutrality, diversion in the ADF cohort would need to decrease by approximately 57% relative to the non-ADF cohort.
- Reducing the rate of diversion to 1:1 and 0.75:1 ratios required greater reductions in diversion risk to achieve cost neutrality.

Scenario Analysis Results: Diversion

Incremental Costs of Diversion and Percentage Decrease In ADF Opioid Diversion Required to Achieve Cost-Neutrality



*For every case of prescription abuse with non-ADF opioids

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Model Feedback and Validation

- Preliminary results of model presented to manufacturers, and feedback resulted in model revision
 - Inclusion of different data sources for inputs
 - Added scenario analysis to assess diversion
- Internal validity assessed by stress-testing the model through variations in inputs across a wide range of estimates
- Reviewed other published, ADF-related economic models to assess external validity
- Draft report underwent external peer review

Limitations

- Assumed static estimate for incidence of opioid abuse that does not change over time
- Assumed death from overdose occurs only in abuse population and not in regular use population (i.e., excludes risk of accidental overdose)
- Only includes overdose deaths, not incidence of overdose generally
- Market-basket of ADF and non-ADF opioids used to calculate weighted average opioid drug costs derived from Massachusetts data
- Source for annual rates of ER opioid discontinuation based on data for both IR and ER opioids
- Annual costs for regular use and abuse assumed the same each year

Limitations

- Primary model analyses do not include diversion to a population outside the existing cohort, which may represent a cost to the health system
- Costs of switching to other opioids or heroin among individuals frustrated by ADF properties are also not included in this model due to a lack of robust data
- Conducted scenario analysis examining different assumed levels and relative risks of diversion of ADF and non-ADF opioids, but focused only on reduced costs associated with preventing diversion of medication used to treat chronic pain in the cohort, and not on any increased use of legal or illicit opioids.

Summary

- Our results suggest ADF opioids substantially reduce incidence of opioid abuse relative to non-ADF formulations among patients initially prescribed these drugs for therapeutic purposes, but with increased costs to the health system.
- Further research is required to ascertain how the balance of reduced diversion of prescribed opioids versus increased use of other legal and illicit opioids affects clinical and economic outcomes in these populations.