Abuse Deterrent Formulations of Opioids: Comparative Value Draft Results

RADARS System Annual Scientific Meeting
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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.
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-ADFs?
  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

ADF opioids

Regular use

- Continue regular use
- Abuse
- Discontinue regular use
- Death (all cause)

Prescription Abuse

- Continue abuse
- Cease to abuse
- Overdose
- Death (all cause)

Non-ADF opioids*

- Death from overdose
- Continue abuse

*Similar decision tree for non-ADF opioids

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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**

*Rossiter et al., 2014 **Rice et al., 2014
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

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

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

*Market-share based weighted average cost of drugs within each category. Drugs are listed in Appendix table D1.

**Assumed to include only non-opioid prescription fills.

NOTE: Based on initial draft report, subject to change
Model Results
# Results

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

<table>
<thead>
<tr>
<th>Outcome (at 5 years)</th>
<th>ADF opioids</th>
<th>Non-ADF opioids</th>
<th>Increment (ADF – Non-ADF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident abuse</td>
<td>7,450</td>
<td>10,532</td>
<td>-3,082</td>
</tr>
<tr>
<td>Person-years of abuse</td>
<td>21,091</td>
<td>29,943</td>
<td>-8,852</td>
</tr>
<tr>
<td>Overdose deaths</td>
<td>1.25</td>
<td>1.77</td>
<td>-0.52</td>
</tr>
</tbody>
</table>

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

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

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

<table>
<thead>
<tr>
<th>Incremental outcome</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventing 1 new abuse case</td>
<td>$165,868</td>
</tr>
<tr>
<td>Preventing 1 new abuse year</td>
<td>$57,749</td>
</tr>
</tbody>
</table>
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

Incremental health system cost (in Millions)

- Incidence of abuse with ADF opioids
  - 2.54%: $511
  - 1.91%: $428
  - 1.27%: $345
  - 0.64%: $260
  - 0.00%: $174

NOTE: Based on initial draft report, subject to change
Results: Cost Neutrality Threshold Analysis

• In 2\textsuperscript{nd} 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

<table>
<thead>
<tr>
<th></th>
<th>Base-case cost</th>
<th>Cost to attain cost-neutrality</th>
<th>Percentage difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADF opioid average daily drug cost*</td>
<td>$11.60</td>
<td>$7.04</td>
<td>-39.3%</td>
</tr>
</tbody>
</table>

*Indicates drug cost per day at 90mg MED daily dose
One-Way Sensitivity Analyses

- **ADF opioid costs +/- 25%**
- **Efficacy of ADF opioids (95% CI)**
- **Recovery rate (0% to 20%)**
- **Incidence of abuse +/- 25%**

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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

NOTE: Based on initial draft report, subject to change
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.