Considerations for Studying the Impact of OA REMS CE on Practice Behavior and Patient Outcomes

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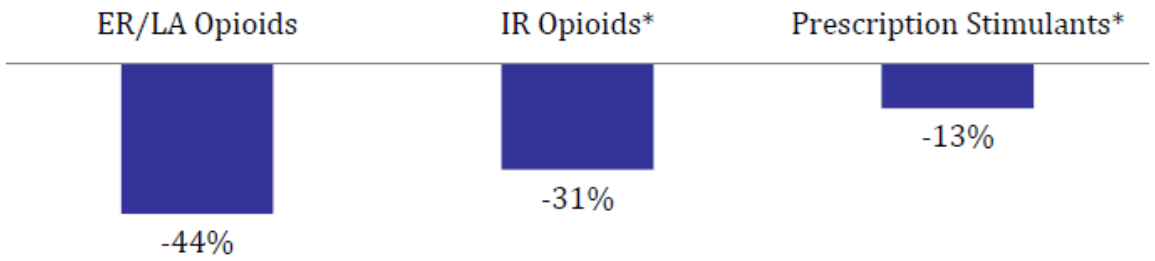
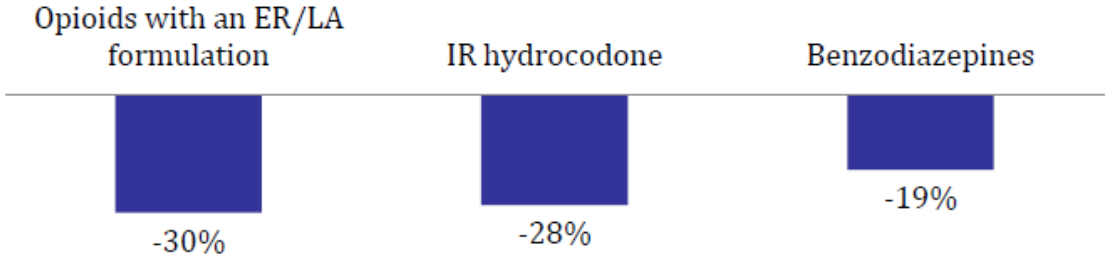
Prior RPC work to evaluate impact of REMS on prescriber behavior and patient outcomes

36-month ER/LA REMS Assessment: Pre vs. post -- rates of abuse and overdose

Change in intentional abuse call rates, Pre- vs. Active REMS period (RADARS® Poison Center Program study)



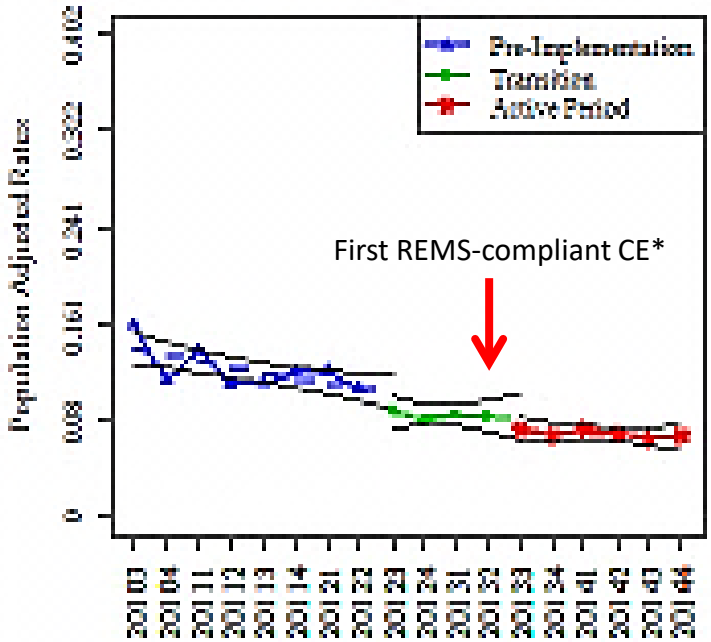
Change in overdose death rates in state of Washington, Pre- vs. Active REMS period (WA State Medical Examiner Study)



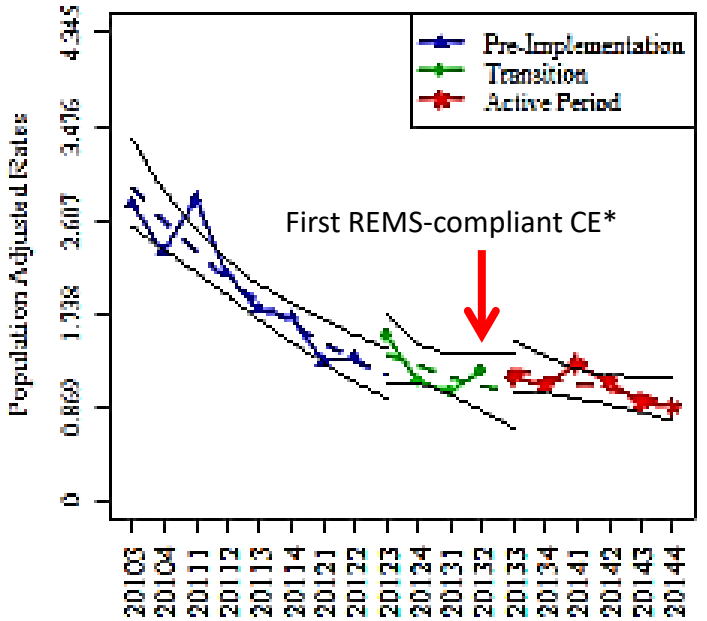
* % change significantly different from ER/LA opioids

36-month ER/LA REMS Assessment: Trends in ER/LA opioid abuse and overdose rates

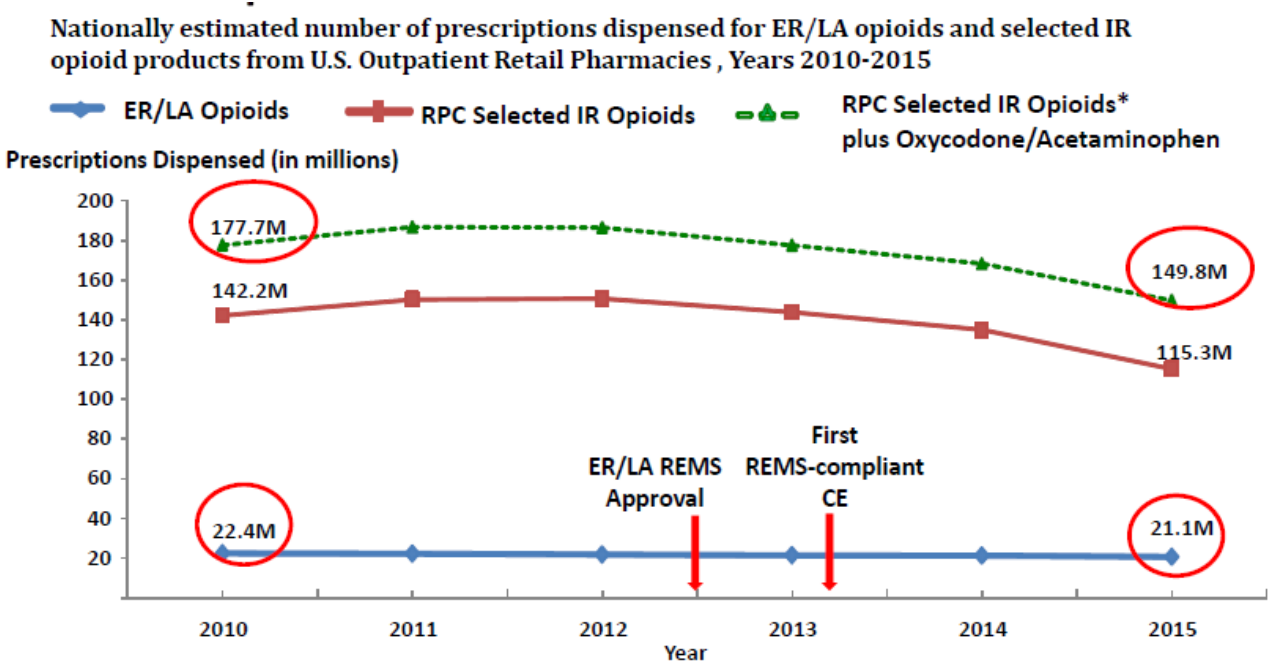
ER/LA opioid abuse poison center calls



Recent ER/LA opioid abuse in people entering OUD treatment

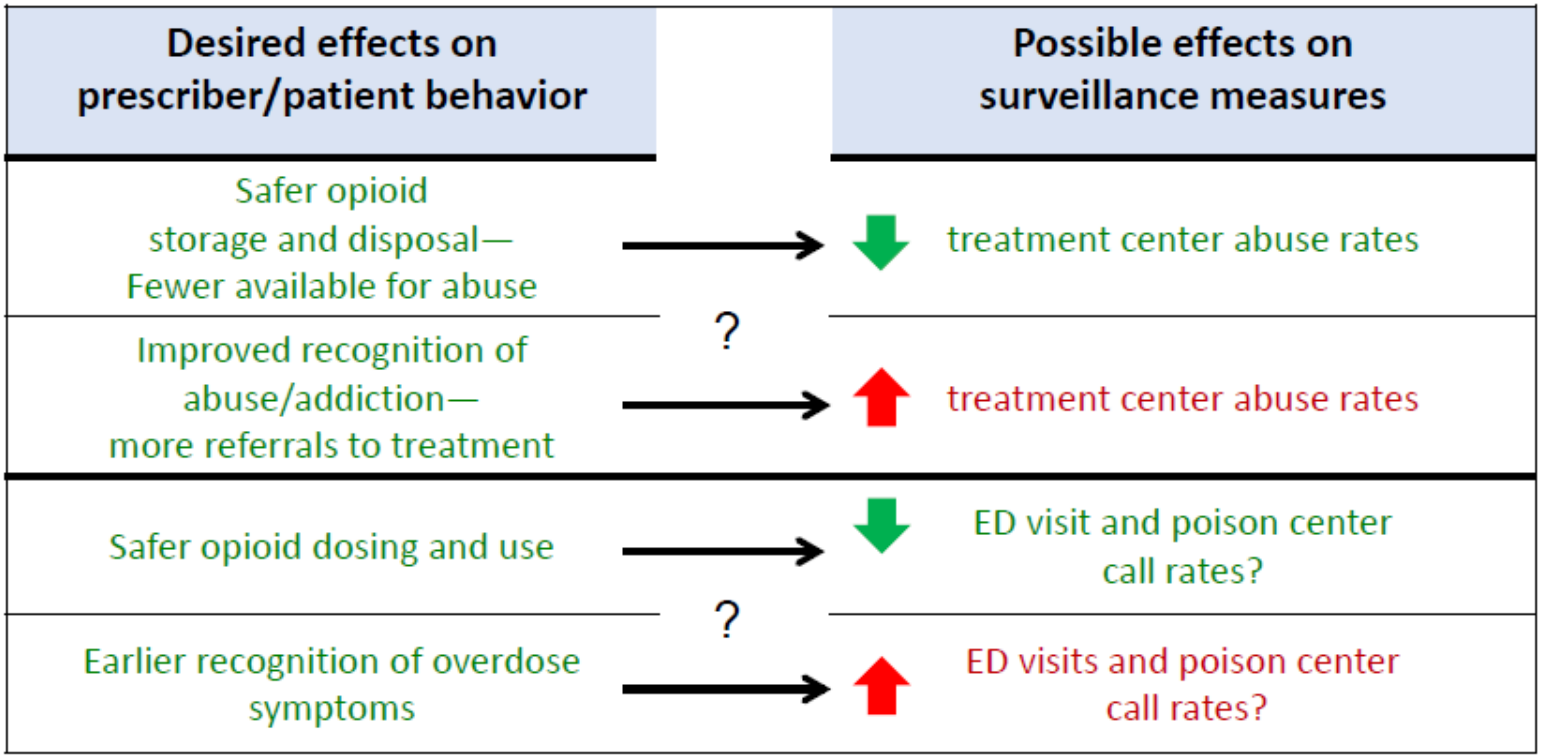


36-month ER/LA REMS Assessment: Prescription Volume

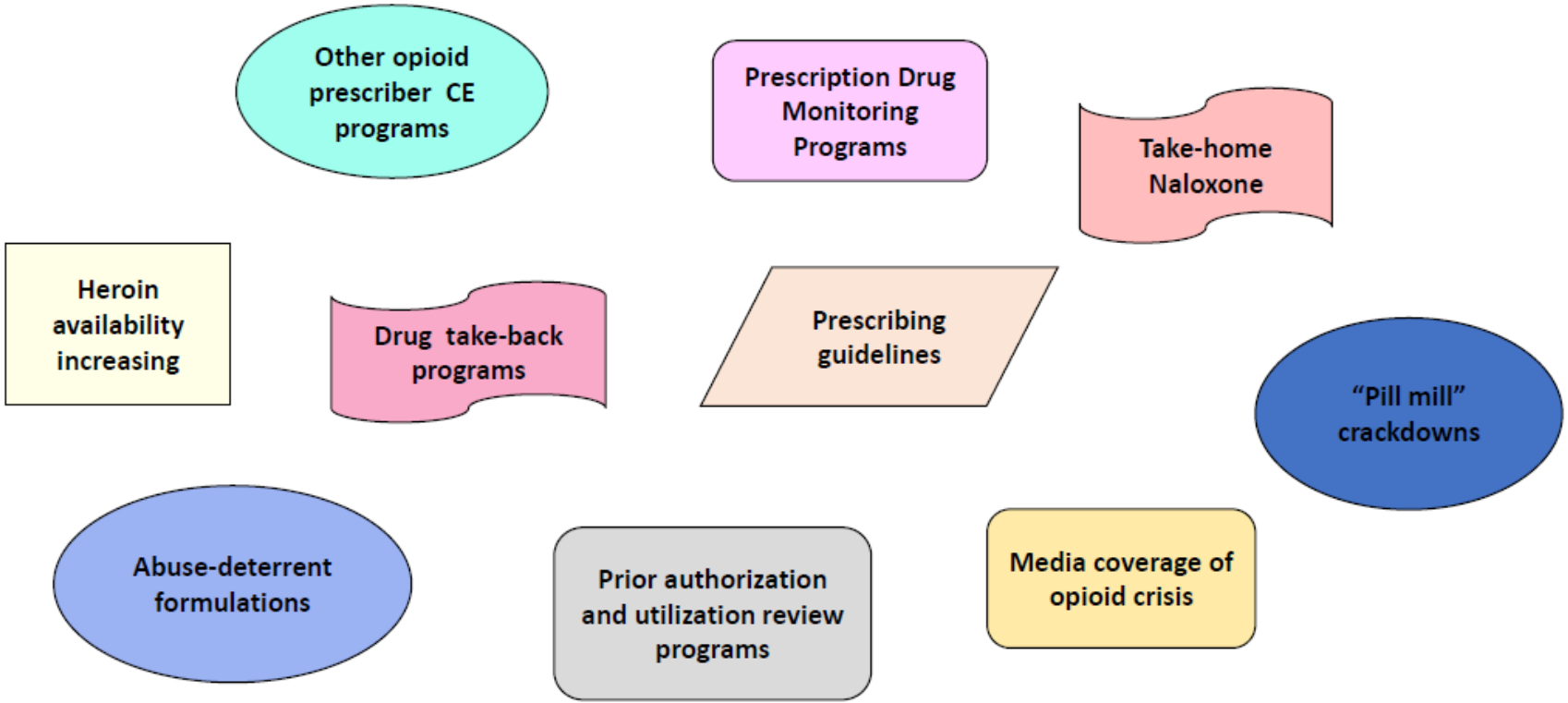


* IR opioid prescription data provided by the RPC, shown in red, did not include oxycodone/acetaminophen products.
Above analyses conducted by FDA using IMS Health, National Prescription Audit™, extracted January 2016.

36-month ER/LA REMS Assessment: Causal pathway not straightforward



36-month ER/LA REMS Assessment: Other efforts and secular trends



36-month ER/LA REMS Assessment: Conclusions

- Decreases in opioid prescribing and adverse outcomes **encouraging, but unable to isolate effect of REMS**
- **National trend data useful for *surveillance*, but need alternative designs to evaluate REMS impact**
  - Link CE completion to changes in behavior/outcomes
  - Outcomes more directly related to the CE
  - Selection bias, confounding by secular trends
  - Feasible???

48-month ER/LA REMS Assessment: Concept Paper

- RPC submitted concept paper for a study using NPI# to link EHR data to prescriber participation in one large REMS training program (Pri-med).
  - Compare trends in prescribing and patient outcomes pre vs. post training completion
  - Matched non-completer control group
- FDA provided comments
  - Requested further detail on linkage capability, sample size, proposed metrics, etc.

72-month ER/LA REMS Assessment: Feasibility assessment and revised concept paper

- Feasibility assessment
  - Linked prescriber participation in large REMS training program to two large *claims databases*
  - Suggested enough subjects to assess the impact of training on patient outcomes (e.g., overdose, OUD diagnosis, death)
- Proposed difference-in-differences analysis
  - Pre vs. post CE rates of patient outcomes for trained compared to matched untrained providers

72-month (Final) ER/LA REMS Assessment: Analysis of CE completion linked to prescribing data

- Used NPI# to link completion of one large REMS CE program to IQVIA prescriber file
  - n=24,428 trained providers, mostly primary care
- Metrics (1 year pre/post training):
  - Opioid analgesic (ER/LA, IR) prescription volume
  - ER/LA to IR opioid switching
  - ER/LA dispensing to opioid non-tolerant patients
  - Concomitant dispensing with CNS depressants
- Two types of comparison
  1. Pre vs. post CE (same prescriber)
  2. Concurrent comparison (matched completer vs non-completer)

72-month ER/LA REMS Assessment: CE completion linked to prescription data

- After CE, slightly lower opioid analgesic prescribing and concomitant BZD
- Opioid analgesic prescribing by trained prescribers > untrained providers
- No meaningful differences in other metrics
- Limitations:
  - Low opioid analgesic prescribing overall
    - Prescription volume ≠ appropriate prescribing
  - Confounding, selection bias
    - No difference-in-difference analysis
    - Few variables available for matching
  - "Untrained" providers could take other opioid CE

OA REMS 12-month Assessment: Proposed pharmacoepidemiologic study (white paper)

- Use NPI# to link CE completion to national dispensing (and potentially other) claims data
- Sophisticated modeling to control for prescriber characteristics, past prescribing behavior, other interventions ("environmental factors")
- After completing landscape analysis of opioid CE and policies, RPC determined that scope and complexity of environmental factors (e.g., required CE, prescribing limits, guidelines,) creates insurmountable challenges
- Dr. Alec Walker will discuss further ideas on use of "big data"

Examples of non-RPC studies evaluating impact of pain management initiatives on prescriber behavior and patient outcomes

Anderson 2016[1]: Evaluating a pain management intervention in a community health center network

Design/Setting	Intervention	Metrics	Findings
• Pre-post comparison • 12 community health centers 25 primary care providers and their patients with chronic pain (n=3,357) • 2010–2014, CT	• Stepped Care Model for Pain Management • Education • EHR templates • Protocols • Dashboard • Consultations • Onsite resources	<u>EHR structured data</u> • Opioid prescribing • Pain scores • Opioid Treatment Agreement • Urine drug testing (UDT) • Functional assessment, reassessment • Referrals <u>Chart review (n=300)</u> • Pain Care Quality extraction tool[2]	<u>Significant improvement</u> • Treatment agreement use • UDT • Documentation of pain, function, treatment plan, reassessment • Referrals <u>No change</u> • Opioid prescribing • Pain scores

1. Anderson et al. Improving pain care through implementation of the Stepped Care Model at a multisite community health center. *Journal of Pain Research*, 2016
2. Dorflinger et al. Development and application of an EHR information extraction tool to assess quality of pain management in primary care. *Transl Behav Med* 2014

Von Korff 2016[1], Thakral 2017[2], Von Korff 2019[3]: Evaluating an opioid risk reduction initiative in a group practice

Design/Setting	Intervention	Metrics	Findings
• Observational cohort (n=22,205 patients) Intervention group: group practice Control group: contracted care • 2006-2014, WA state	• CME on chronic pain management • Practice standards • Practice support tools (e.g., templates, patient ed material,) • Expert consultation • Performance tracking and financial incentives	Structured EHR data • Opioid dose • Excess days supply • Care plan documentation Patient interviews • Pain, enjoyment, and general activity (PEG) scale • Patient Health Questionnaire (PHQ-8) EHR/ state death records • Opioid overdose rate	Intervention group had Larger declines in opioid dose and excess days supply Improved care plan documentation No difference in • Pain or depressive symptoms • Opioid overdose declines

1. Von Korff et al. Impact of opioid risk reduction initiatives on opioid prescribing for chronic opioid therapy patients. *J Pain*, 2016.
2. Thakral et al. Comparing pain and depressive symptoms of chronic opioid therapy patients receiving dose reduction risk mitigation initiatives with usual care. *J Pain*, 2018
3. Von Korff et al. Impact of chronic opioid therapy risk reduction initiatives on opioid overdose. *J Pain*, 2019.

Liebschutz 2017[1]: Randomized trial of an intervention to improve adherence to opioid therapy guidelines

Design/Setting	Intervention	Metrics	Findings
• Cluster-randomized design • 4 safety-net primary care practices 53 primary care clinicians and their patients on chronic opioids (n=985) • 2014–2016, MA	Transforming Opioid Prescribing in Primary Care (TOPCARE) • Academic detailing • Care management • Registry • Electronic decision tools (both groups)	<u>EHR data</u> • Patient-provider Agreement use • UDT • Early refills • Opioid dose (MEDD) • Opioid discontinuation	Intervention group had <u>Increased</u> • use of patient-provider agreements • UDT • Odds of 10% dose reduction or opioid discontinuation <u>No change</u> in early refills *Discontinuation mostly for misuse, had *decreased follow-up care*[2]

1. Liebschutz et al. Improving adherence to long-term opioid therapy guidelines to reduce opioid misuse in primary care; A Cluster-randomized clinical trial. *JAMA Int Med*, 2017.
2. Husain et al. Reasons for opioid discontinuation and unintended consequences following opioid discontinuation within TOPCARE Trail. *Pain Med*, 2019

Considerations for evaluating the impact of OA REMS CE on practice and outcomes

- Is it plausible that a single CE training would confer a measurable effect?
  - What are appropriate metrics?
  - Do other systems/supports need to be in place to see an effect?
- Settings and data source(s):
  - Administrative claims (“big data”)
  - EHR (structured data, chart reviews)
  - Prospectively collected data (e.g., patient interviews, surveys)
- How to address selection bias and confounding?
  - Observational vs randomized design?
- How to address heterogenous CE formats, participant groups, content focus?

Thank you!