Benefits and Harms of Long-term Opioid Dose Reduction or Discontinuation in Patients with Chronic Pain

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Portland VA Medical Center

August 2019
Presentation Outline

• Background on ESP & Evidence Synthesis Products
• Background on Opioid SOTA
• Overview of Topic
• Findings from August 2019 ESP Rapid Review
• Discussion and Questions
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Operational Partners
Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend TEP members; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for report dissemination.

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This report is based on research conducted by the Evidence Synthesis Program (ESP) Coordinating Center located at the Portland VA Medical Center, Portland, OR, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development.

The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs.

No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.
Who We Are

Mission: To make high-quality evidence synthesis available to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans.

“ESP reports are a terrific resource to inform policy decisions. They are methodologically rigorous and available [upon] request.”

https://www.hsrdr.research.va.gov/publications/esp/
ESP Center Locations

Coordinating Center
Portland, OR

ESP Center
Portland, OR

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Minneapolis, MN

HSR&D/QUERI, VACO
Washington, DC

ESP Center
Los Angeles, CA

ESP Center
Durham, NC
Our Reports Help VA With

- Guidelines and performance measures
- Effective services and patient outcomes
- Clinical policies
- Future research
Range of Products for Different Needs

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<th>Speed (product within 4 months)</th>
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* Possible on a case-by-case basis
ESP Products’ Key Characteristics

**Standard Systematic Review** (9-12 months)
Comprehensive synthesis using the most methodologically rigorous process. Reviews several broad, overarching key questions.

**Scoping Review** (4-12 months)
Descriptive overview that identifies gaps and overlap in key concepts and highlights specific and/or unique features of interest.

**Evidence Map** (9-12 months)
User-friendly visual figure or graph and interpretive summary of a broad research field that provides quick access to questions and answers that previous research has addressed and identifies gaps that are important for VHA.

**Rapid Evidence Brief** (2-4 months)
Detailed report that generally follows, but streamlines, accepted systematic review methods and PRISMA reporting guidelines.

**Evidence Assist™** (1-4 months)
Consultative memorandum with flexible format.

**Evidence Compendium** (1-2 months)
Brief summary of key features, data abstraction, and bibliography, organized by key features (eg, key question, study design, population, etc).

**Evidence Inventory** (1-4 weeks)
Bibliography organized by key features (eg, key question, study design, population, etc).
Opioid SOTA Background & Goals

• **Background:** In September 2019, VA HSR&D will hold a State of the Art Conference (SOTA) on *Effective Management of Pain and Addiction: Strategies to Improve Opioid Safety*

• **Goals:**
  - Assess current VA burden and clinical practice
  - Review state of the evidence and relevance to VA population
  - Where evidence is sufficient, define consensus
  - Where evidence is conflicting or limited, define research agenda
  - Make practice or policy recommendations where consensus exists but is at odds with practice
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Workgroup 1: Managing Opioid Use Disorder

Workgroup 2: Long-term Opioid Therapy and Tapering

Workgroup 3: Managing Co-Occurring Pain and Substance Use Disorders
The Problem: A Difficult Balance

• Evolving crisis of morbidity, mortality, and misuse due to opioids

• VA/DoD and CDC guidelines recommend considering LTOT tapers when risks > benefits

• Patients with chronic pain on long-term opioid therapy (LTOT) and the providers who care for them are at the center of a difficult balance

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VA/DoD and CDC Tapering Recommendations

• Emphasize shared decision-making regarding LTOT tapers

• Individualize taper speeds and suggest gradual tapers with pauses in the tapering process as needed

• Similar approaches are recommended by the American Academy of Family Physicians, the Washington State Agency Medical Directors’ Group, and the Oregon Pain Guidance Clinical Advisory Group
Concerns related to LTOT Tapers

Perspective
No Shortcuts to Safer Opioid Prescribing
Deborah Dowell, M.D., M.P.H., Tamara Haegerich, Ph.D., and Roger Chou, M.D.

“Recently, the FDA has received reports of serious harm, including serious withdrawal symptoms, uncontrolled pain and suicide, in patients who are physically dependent on opioid pain medicines when these medicines are suddenly discontinued or when the dose is reduced too quickly, often without adequate patient communication, follow-up or support.”

Existing Evidence


- Included 40 studies of patient outcomes following LTOT tapers
- Most studies fair- or poor-quality
- Inconclusive evidence on the impact of LTOT tapers on pain severity, pain-related function, quality of life, withdrawal symptoms, substance abuse, and adverse effects
Aim of this Review

• Synthesize evidence on LTOT dose reduction and discontinuation for a broader range of outcomes and with an emphasis on evidence most relevant and applicable to VHA populations

• Identify evidence gaps
Evidence Brief:

Benefits and Harms of Long-term Opioid Dose Reduction or Discontinuation in Patients with Chronic Pain

August 2019

Prepared for:
Department of Veterans Affairs
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Washington, DC 20420

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Full-length report available on ESP website:
http://www.hsrd.research.va.gov/publications/esp/reports.cfm
Key Question 1: Among patients prescribed long-term opioid therapy for chronic pain, what are the benefits and harms of opioid dose reduction or discontinuation?

Key Question 2: Do the benefits and harms of opioid dose reduction or discontinuation vary by:
- Patient characteristics
- Patient engagement in tapering
- LTOT regimen
- Tapering characteristics
Eligibility Criteria

**Population:** Adults prescribed long-term opioids (≥ 3 months) for chronic pain (excluding patients receiving palliative care, treatment for cancer-related pain, or undergoing surgery)

**Intervention:** Dose reduction or discontinuation (excluding studies of chronic pain interventions not explicitly designed to lower opioid doses)

**Comparator:** Any

**Outcomes:** Pain severity, pain-related function, quality of life, patient satisfaction, healthcare utilization, opioid withdrawal symptoms, substance use, opioid overdose, suicidal ideation and suicidal self-directed violence

**Timing, Setting, Study Design:** Any
Evidence Brief Methods

- **Search:** MEDLINE, PsycINFO, Cochrane databases and other sources (January 1, 2017 - March 15, 2019) and consulted with experts

- **Study selection:** Based on eligibility criteria

- **Data abstraction:** Study characteristics and results

- **Critical appraisal:** Use of standardized tools

- **Quality control:** Assessments first completed by one reviewer and checked by at least one additional reviewer. Disagreements resolved by consensus.

- **Peer Review:** Topic and methodological experts commented, responses are publicly available
GRADE Criteria to Evaluate Body of Evidence

Methodological Limitations

Precision

Consistency

Directness

HIGH
We are very confident that the true effect lies close to that of the estimate of the effect

MODERATE
We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

LOW
Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

VERY LOW
We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

1539 records identified from database/hand searching after removal of duplicates

1390 titles and abstracts excluded

149 full-text articles assessed for eligibility

104 full-text articles excluded

45 articles met inclusion criteria

1 SR

44 Primary Studies
(34 in previous SR, 10 new)
Prioritization of Evidence

- VHA settings
- Non-VHA but with sufficiently described populations and interventions
- Evaluated serious harms of tapering (e.g., overdose and suicide)
- All other studies
15 Prioritized Studies

- 2 RCTs
- 2 Observational studies with a control group
- 11 Observational studies without a control group
- Remaining studies either had low applicability to VHA patients or care settings or included patients or interventions that were not well-described
Results of 15 Prioritized Studies

- 33% in VHA Setting
- 33% Back Pain Most Common
- 60% Voluntary Tapers
- 47% Fast Taper Speed
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# KQ1: Summary of Results

## Patient Outcomes

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<th>Pain-related Function</th>
<th>Quality of Life</th>
<th>Patient Satisfaction</th>
<th>Healthcare Utilization</th>
<th>Depression or Anxiety</th>
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| Harden, 2015 | ✓ | ✓ | ✓ | = | ✓ | ✓ | ✓ | | |
| Hundley, 2018<sup>73</sup> | ✓ | ✓ | ✓ | ✓ | = | = | ✓ | × | × |
| Kurita, 2018<sup>66</sup> | ✓ | ✓ | ✓ | ✓ | = | ✓ | = | | × |
| Mark, 2019<sup>73</sup> | ✓ | ✓ | ✓ | ✓ | ✓ | × | | | |
| Murphy, 2013 | ✓ | ✓ | ✓ | ✓ | ✓ | | | | |
| Sullivan, 2017<sup>54</sup> | ✓ | ✓ | ✓ | ✓ | ✓ | | | | |
| Von Kottf, 2019<sup>72</sup> | ✓ | ✓ | ✓ | ✓ | ✓ | | | | |
| **Overall Evidence Quality** | Low | Low | Very low | Very low | Very Low | Very Low |

- ✓ Symptoms improved
- = No change in symptoms
- × Unclear effect on symptoms/no comparator

*New since Frank 2017; Bold = VHA study; Abbreviations: SUD = substance use disorder, SSV = suicidal self-directed violence; Blank cells no data reported; No studies reported on opioid-related side effect outcomes.*
**High Intensity Interventions**

### Example of High Intensity Intervention

Description of Cleveland Clinic outpatient Interdisciplinary Chronic Pain Rehabilitation Program:

“Participation from “7:30 AM to 5:00 PM Monday to Friday, and includes daily medical management, individual psychotherapy (2-3 per week), group psychotherapy (7 hours per week), and cognitive behavioral group interventions and psychoeducation, physical and occupational therapy, substance use education, weaning from habituating medications, and optional monthly aftercare.”

Moderate, Low, or Unclear Intensity Interventions

**Moderate Intensity Intervention:**
- 2 RCTs embedded in multidisciplinary pain clinics, 1 with medication optimization prior to a scheduled taper and 1 with enhanced psychosocial supports

**Low Intensity Intervention:**
- 1 uncontrolled observational study of a self-help book paired with individual clinician guidance

**Unclear:**
- 6/15 studies did not describe a specific tapering intervention
Important Caveat Regarding Measures of Pain Severity

• No studies reported the proportions of patients who experienced a clinically significant worsening in pain severity

• Common measures of pain severity:
  o Pain Numerical Rating Scale (NRS)
  o Multidimensional Pain Inventory (MPI)
  o Brief Pain Inventory (BPI)

• A limitation of assessments of mean change is that they do not tell us whether a change in score was clinically meaningful for patients
LTOT Tapers and Substance Use

• Evidence is unclear; studies have not directly examined this outcome

• **Best evidence:** 2019 study by Mark et al of Medicaid claims data in Vermont
  
  o Between 2013-17 opioids were discontinued in 494/694 patients on ≥ 120mg MEDD
  o Prior to discontinuation, 60% of patients had a diagnosis of substance use disorder
    and after almost half (49%) of patients had an ED visit or hospitalization due to opioid
    poisoning or substance use disorder

• Study does not describe LTOT discontinuation reasons or exclude reverse causation

• Evidence is unclear; few studies have examined this outcome

• **Best evidence**: 2019 large retrospective cohort study by Von Korff et al examining opioid overdose rates following different phases of an opioid risk reduction initiative in Washington
  o Overdose rates decreased by 17% per year within the intervention group (patients in Washington’s Group Health practice) after a dose reduction effort (relative annual change 0.83; 95% CI 0.70 to 0.99)
  o Reduction was not significantly different when compared to the control group (patients followed at Group Health’s contracted community clinics)

• Provides inconsistent support that reducing opioid doses leads to lower overdose rates

• Does not capture the potential for reverse causation

• Evidence is unclear; few studies have examined this outcome

• **Best evidence: 2017 retrospective study by Demidenko et al**
  o 509 VA patients *with substance use disorders* and matched controls underwent clinician-initiated tapers due mostly (75%) to aberrant behaviors
  o 47 (9.2%) had new-onset suicidal ideation and 12 patients (2.4%) had suicidal self-directed violence in the year following opioid discontinuation
  o Baseline PTSD (OR = 2.56, 95% CI 1.23 to 5.32) and psychotic disorders (OR = 3.19, 95% CI 1.14 to 8.89) were associated with suicidal ideation and suicidal self-direction violence

• Important limitations: data obtained by chart review only; patients who died in the year after opioid discontinuation were excluded from analysis; excluded patients who had no VHA contact in the year following discontinuation
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KQ2: Variation in Outcomes?

- Very limited evidence is available to address the question of whether benefits and harms of LTOT tapers vary by different patient characteristics or taper approaches

- Important evidence gap
Discussion

• Pain severity and function may improve with voluntary, intensive pain management interventions that incorporate opioid tapering and may not change with less intensive interventions

• Our confidence in these findings is low and additional evidence is needed before drawing stronger conclusions

• Findings for other outcomes are inconclusive

• We know the least about outcomes with clinician-initiated/involuntary tapers including outcomes for patients suspected of opioid misuse
Evidence Gaps: Future Research

- Rates of serious adverse events associated with LTOT tapers, including overdose and suicide
- Rates of newly diagnosed OUD during LTOT tapers
- Specific patient and intervention characteristics associated with improved pain and function following opioid tapers, including how outcomes differ between voluntary/patient-initiated tapers and mandated tapers and by opioid regimen.

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Limitations

- Inherent risk of bias in observational studies
- Lack of control groups
- Unclear fidelity to interventions
- Inadequate reporting or unclear handling of missing data
- Rapid reviews streamline systematic review methods which can result in missing eligible studies or study data
Evidence is inadequate to fully weigh the balance of the benefits and harms of LTOT for chronic pain against the benefits and harms of opioid tapering, primarily due to limited information on tapering harms.
If you have further questions, please feel free to contact:

Kate Mackey, MD, MPP
katherine.mackey@va.gov

Full-length report and cyberseminar available on ESP website:

http://www.hsrdr.research.va.gov/publications/esp/