NOHARM: Nonpharmacological Options in post-operative Hospital-based And Rehabilitation pain Management pragmatic trial

Andrea Cheville, MD, MSCE
Professor of Physical Medicine and Rehabilitation
Mayo Clinic

Jon Tilburt, MD
Professor of Medicine
Mayo Clinic

MAYO CLINIC

NIH National Institute on Aging

NIH NICHD

HEAL NIH · Helping to End Addiction Long-term

NIH PRAGMATIC TRIALS COLLABORATORY
Rethinking Clinical Trials®

P — Patient Population

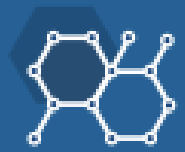
- Enrollment at the level of the surgical procedure
- No patient-level criteria
- Qualifying surgeries:
  - Colorectal
  - Orthopedic
  - Cardiovascular
  - Thoracic,
  - Solid organ transplant,
  - Gynecologic
  - Cesarean delivery

I — Intervention

Multicomponent EHR-based intervention promoting NPPC use:

1. Portal-based *Healing After Surgery* (HAS) guide
2. Provider-directed EHR clinical decision support (CDS)
3. Suite of nonpharmacologic pain care (NPPC) support materials

C — Comparator



- Standard perioperative practices
- No EHR-based
  - Patient education
  - NPPC preference elicitation
  - Clinician-directed CDS

O — Outcome

Co-Primary:
PROMIS physical function & pain interference T scores

Secondary:
Opioid exposure – any and MMEs

PROMIS – anxiety T score

Utilization – ED, hospitalizations, & ICU

T — Time

October 16, 2020 – April 4, 2024

S — Setting

6 high-volume surgical centers (3 quaternary referral centers and 3 community hospitals) in Minnesota, Wisconsin, Florida, and Arizona within the Mayo Clinic Enterprise

Intervention Effects on Patient-Reported Outcomes

Total N = 68,141 surgeries, including 62,892 index procedures in unique patients

Symptom	Adjusted Mean Difference (Intervention vs Control), β (95% CI)	P-value
Pain Interference*	0.090 (-0.176, 0.357)	0.506
Physical Function†	0.149 (-0.114, 0.412)	0.267
Anxiety‡	-0.073 (-0.435, 0.289)	0.692

All models adjusted for baseline symptom score, study site, study step, age, rural status, and (if imbalanced with SMD > 0.1 for that symptom cohort): laparoscopic status, GI/Hip surgery, surgery hours, prior prescription, and study step. Models also include random effects for cluster (care team) and patient (to account for multiple surgeries).

* Sample of Pain Interference PROMIS CAT responders: Intervention N=25981, Usual care N=15807
† Sample of Physical Function PROMIS CAT responders: Intervention N=25563, Usual care N=15520
‡ Sample of Anxiety PROMIS CAT responders: Intervention N=15227, Usual care N=11195

Adjusted Opioid Exposure by Intervention Status:

Any opioid prescribed or administered

Metric	Adjusted UC % (95% CI)	Adjusted Intervention % (95% CI)	Odds Ratio (95% CI)	P-value
Administered in hospital	67.1 (60.7,73.4)	67.6 (61.3,73.8)	1.032 (0.960,1.111)	0.393
Prescribed in hospital**	78.9 (75.8,82.1)	80.7 (77.8,83.7)	1.156 (1.065,1.254)	<0.001
Prescribed or administered in hospital	88.8 (85.6,92.0)	89.8 (86.8,92.7)	1.143 (1.023,1.278)	0.019
Administered post hospital	20.6 (17.2,24.0)	20.2 (16.9,23.6)	0.977 (0.904,1.055)	0.551
Prescribed post hospital	27.4 (23.2,31.5)	26.2 (22.2,30.3)	0.938 (0.876,1.004)	0.065
Prescribed or administered post hospital	36.0 (31.8,40.1)	34.5 (30.4,38.5)	0.930 (0.873,0.991)	0.025

Adjusted Opioid Exposure by Intervention Status:
Morphine milligram equivalents prescribed or administered

Metric	Adjusted UC MME	Adjusted Intervention MME	Adjusted Rate Ratio for Opioid Exposure (95% CI)	P-value
Opioid Total MME	2633.81 (1671.85,3595.77)	2373.56 (1520.99,3226.13)	0.901 (0.822,0.988)	0.027
Administered in hospital	1305.82 (977.61,1634.02)	1220.58 (914.03,1527.13)	0.935 (0.897,0.974)	0.001
Prescribed in hospital	99.87 (51.94,147.81)	88.85 (46.24,131.46)	0.890 (0.844,0.937)	<0.001
Prescribed or administered in hospital	1365.99 (1071.09,1660.88)	1284.50 (1007.55,1561.45)	0.940 (0.903,0.979)	0.003
Administered post hospital‡	160.19 (132.61,187.77)	153.09 (126.88,179.30)	0.956 (0.898,1.017)	0.151
Prescribed post hospital‡	148.49 (113.15,183.83)	156.40 (119.39,193.40)	1.053 (0.946,1.173)	0.344
Prescribed or administered post hospital‡	365.01 (305.83,424.20)	366.46 (307.54,425.37)	1.004 (0.934,1.079)	0.914

Lessons

- Opioid exposure can be reduced during transient periods of elevated risk, including among both opioid-naïve and prior users
- EHR-embedded CDS targeting patients and allied health teams is feasible at scale and can support NPPC engagement
- Intervention intensity requires tradeoffs: lower-burden, low-touch designs may improve clinician acceptance but limit effects on patient-reported outcomes
- Working within a single EHR with dedicated build expertise is a major enabler of scalable implementation
- Informatics-driven interventions introduce opportunities and challenges for implementation fidelity and monitoring

Conclusions

- No difference in patient-reported outcomes (primary and secondar) between intervention and usual care periods.
- Lower total opioid exposure (rate ratio, 0.90 [95% CI…]) during intervention periods, corresponding to an approximately 10% relative reduction without improving (or worsening) patient-reported outcomes.

HEAL-compliant Repository Selection Guide

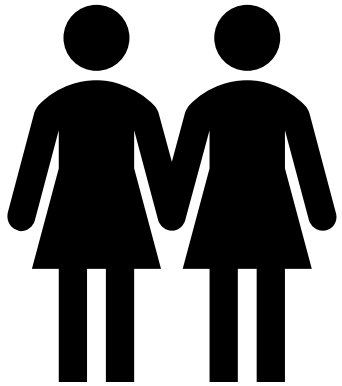
https://www.healdatafair.org/resources/guidance/selection

Repository	Descriptive Tags	Organism	IC/Program	Links
NIMH Data Archive	Human Subjects, Imaging	Human	NIMH	Guidance[1] | Overview
NICHD DASH	Clinical Trial, Biospecimens	Human	NICHD[2]	Guidance | Overview
NAHDAP	Human Subjects	Human	Some NIDA studies	Guidance | Overview
NIDA Data Share	Clinical Trial	Human	NIDA CTN[2]	Guidance | Overview
NIDDK Central Repository	Human Subjects, Biospecimens	Human	NIDDK[2]	Guidance | Overview
SPARC	Brainstem, Spinal Cord, Peripheral Nerv...	Unrestricted	RE-JOIN, PRECISIO...	Guidance | Overview
Pennsieve	Generalist, Imaging, Microphysiology, O...	Unrestricted		Guidance | Overview
ICPSR	Social and behavioral data	Human		Guidance | Overview
Vivli	Clinical Trial, Generalist	Human		Guidance | Overview

1 row selected

Rows per page: 100 1-29 of 29

Leveraging support resources



- Identifying sources of support
  - Email announcements
  - Conferences
    - Annual HEAL meeting
      - HEAL Data Ecosystem
  - Web sites
    - Searchable interfaces, https://www.healdatafair.org/resources/guidance/selection
  - Colleagues
  - Collaboratory
  - Program officers
- Modes of support
  - Email exchange
    - HEAL Data Stewards Webinars
  - Training videos
  - Webinars
  - Telephone & video conference
- Differentiating across resources
  - General vs. niche
  - Commodity specific-, e.g. metadata, dictionary
  - “Step” specific, e.g., form completion, curation, transfer

NIH PRAGMATIC TRIALS COLLABORATORY
Rethinking Clinical Trials®

What and when to share

- CT.gov
  - <= 12 months following
  - Extension possible but challenging to obtain
- Pilot data
  - How much to invest?
  - Harvard Data Verse
- Data dictionary
  - Pilot vs. analytic vs. repository data set
- Meta data
  - HEAL stewards will curate metadata
  - CEDAR, https://metadatacenter.org/
    - Study-level Metadata
    - Variable-level Metadata
    - Common Data Elements
- Pre-/post- publication
  - Staggered approach
    - Primary and secondary outcome reporting
    - Exploratory analyses
  - Data not included in repository

NIH PRAGMATIC TRIALS COLLABORATORY
Rethinking Clinical Trials®