

VA



U.S. Department
of Veterans Affairs

Office of Research and Development

**Pain & Opioid Use Actively
Managed Portfolio (POU AMP)**

Spotlight on Pain Management

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BLUF: ORD PAIN AND OPIOID USE AMP

Pain and Opioid Use (POU) Actively Managed Portfolio (AMP) – **focus** on VHA and Veterans high priority areas

Goal is to provide “evidence” to facilitate translation of results into new lines of treatment, best practices, and implementation into VHA for Veterans.

(https://www.research.va.gov/services/amp/pain_opioid.cfm)

ORD Pain covers a broad range of topics

- Entire translational spectrum from basic science and clinical trials to program evaluation and implementation.
- Co-existing, non-painful conditions (mental health, TBI, SCI, substance use disorder, etc.)
- Main outcome is **NOT** pain, long-term opioid therapy (LTOT) or opioid use disorder (OUD).



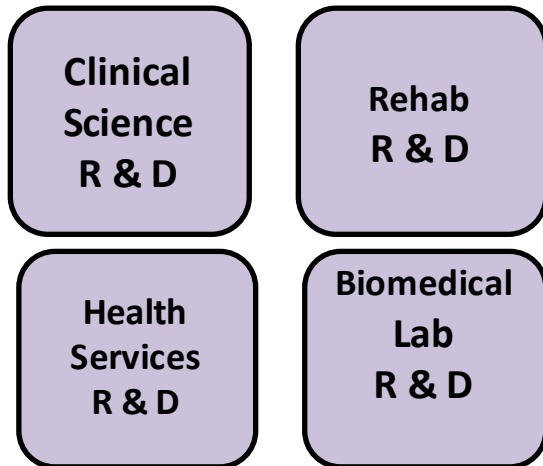
RESEARCH MISSION OF THE VA

- Advance knowledge to improve Veterans' health Care across the research spectrum (basic, translational, health services and rehabilitative science)
- Create, test, compare and implement new treatments, technologies and models of care so that Veterans receive the most effective individualized care.
- Attract, train, retain and nurture the highest quality investigators and staff as leaders in their field and VHA.
- Assure a culture of professionalism, collaboration, accountability, and concern for patient safety.

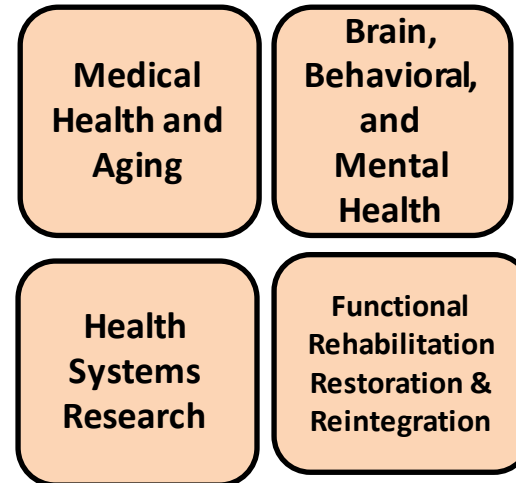


ORGANIZATIONAL TRANSFORMATION IN ORD

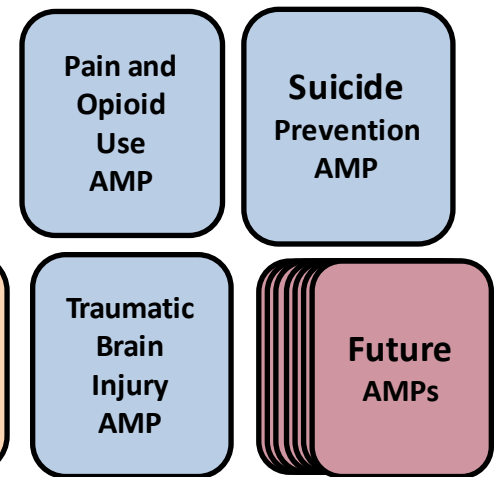
The Four Services of Research Disciplines



Broad Portfolios



Actively Managed Portfolios



Each Portfolio will be developed in a way that encourages collaboration, prevents duplication of research, and improves care to Veterans



KEY CAPABILITIES FOR PAIN OPIOID USE AMP



Team approach – members from all services blending ‘culture’ and expertise



Enable strategic coordination of research projects within the portfolio



Foster greater collaboration between ORD research and VHA clinical partners as well as external collaborators



Set research roadmap and strategic priorities



Establish criteria for rapid review and funding of prioritized research studies



Enhance utilization of existing data and analytical tools to increase coordination and collaboration of research



Team-based AMP model

Current SPMs of pain/opioid panels:

- Carol Fowler – Biomedical Laboratory Research (BLR)
- Cathie Plouzek – Health Systems Research (HSR)
- Jayanthi Sankar – Clinical Science Research (CSR)
- Audrey Kusiak – Rehabilitation Research (RR)



Portfolio Drivers

Office of National Drug Control Policy (ONDCP)

- Annual budget submission
- Harm Reduction, Substance Use Disorder Treatment, and Building a Recovery-Ready Nation

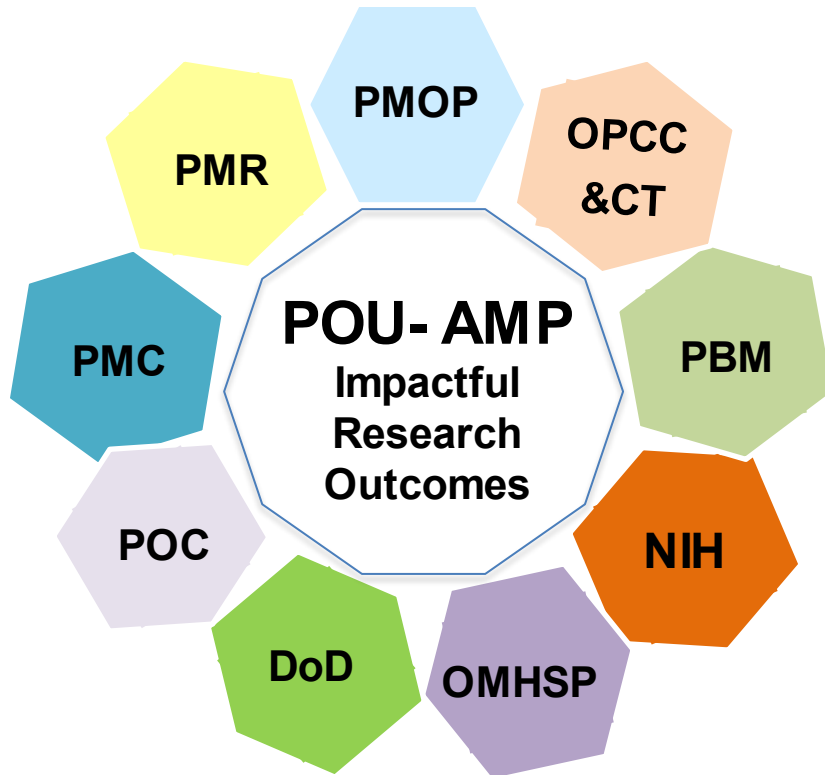
Congressional Acts and Requests

- Comprehensive Addiction and Recovery Act (CARA) – Interagency Pain Research Coordinating Committee (Federal Pain Research Strategy)
- Hannon Act
- Mission Act

Veterans and Clinical need



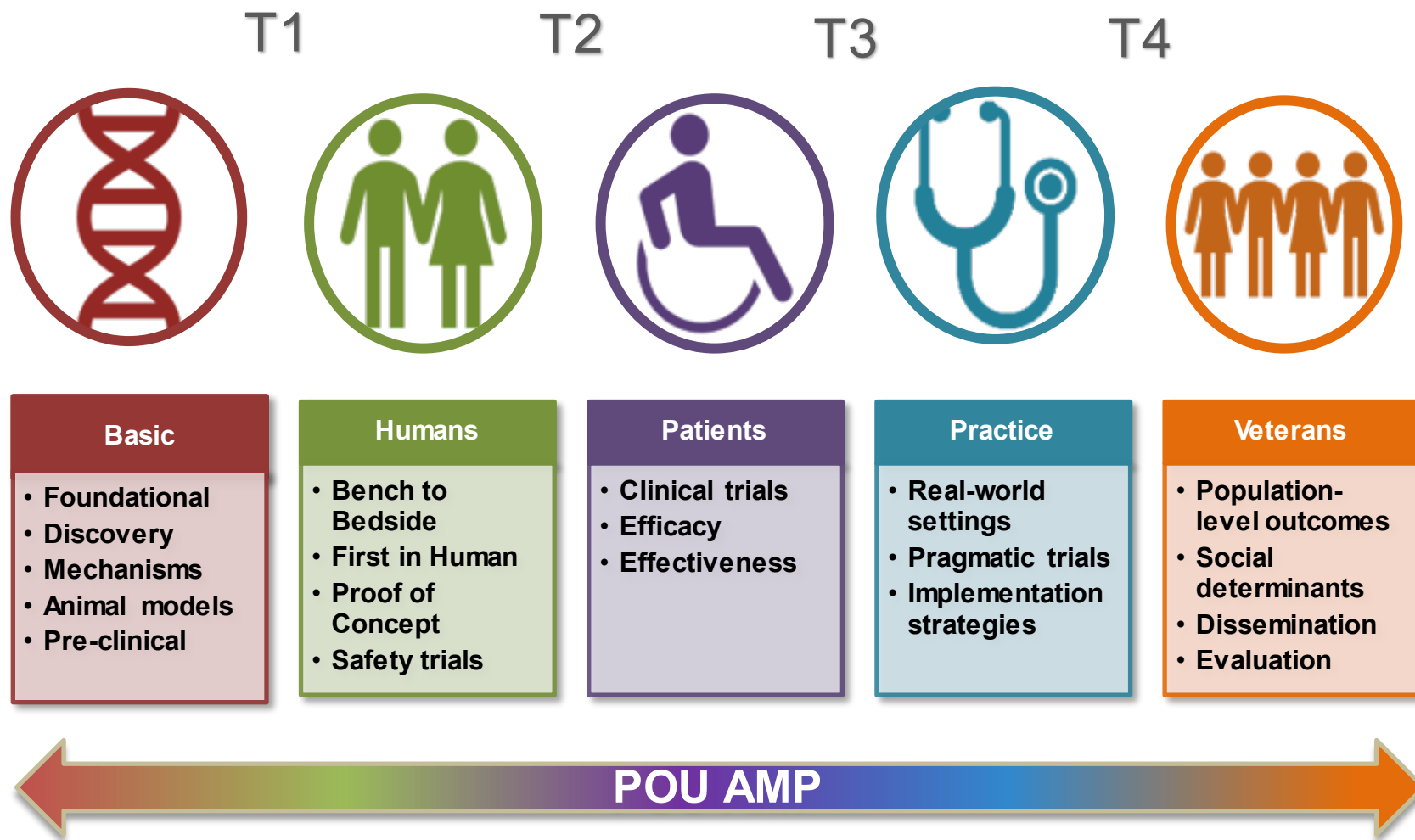
Major Partners and Collaborators



Pain Management Opioid Safety and Prescription Drug Monitoring (PMOP)
Office of Patient Centered Care and Cultural Transformation (OPCC&CT)
Pharmacy Benefits Management (PBM)
Office of Mental Health & Suicide Prevention (OMHSP)
Pain Management Collaboratory (PMC)
Physical Medicine and Rehabilitation (PMR)
HSRD-funded Pain/Opioid Core (POC)
National Institutes of Health (NIH)
Department of Defense (DoD)



Translational Research Spectrum





POU AMP Purview

1. Clinical studies of the genetic, anatomical, and behavioral basis of algesia (pain), or tolerance, addiction, opioid metabolism, and tapering of opioid medication in acute and chronic painful conditions.
2. Clinical treatments emphasizing non-opioid medications and complementary and integrative approaches.
3. Implementation of treatments and approaches across VAMCs, evaluation of methods to enhance pain services, and evaluation of the quality and safety of pain care.
4. Preclinical development and translation of non-opioid therapies; and the accompanying anatomical, molecular, biochemical, behavioral, and genetic mechanism(s).



POU AMP Purview

5. Studies identifying therapeutic targets for algesia (pain), tolerance and/or addiction to opioid medication in acute and chronic painful conditions.
6. Interventional and observational research of interventions to improve outcomes in opioid use disorder, including new models for OUD care, medication and behavioral therapy for OUD, use of overdose rescue medication.
7. Examination of pharmacology, pharmacotherapeutics, pharmacogenomics, and phenotype as well as the use of functional outcomes (e.g., correlating subjective pain measures with objective measures of function such as ADL, gait kinetics and kinematics, range of motion, and QoL or activity measures, etc.).



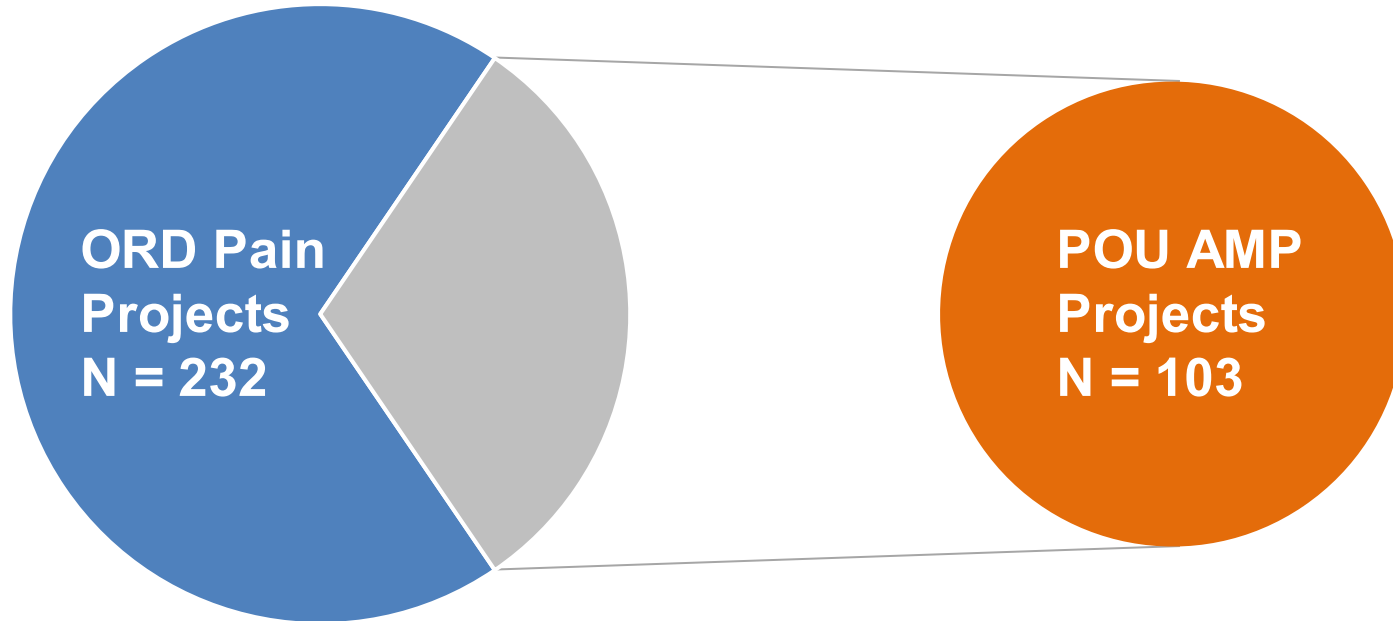
POU AMP PORTFOLIO ANALYSIS



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POU AMP is a Portion of ORD's Portfolio



**ORD's portfolio is based on coding definition for reporting purposes.
All projects measuring pain as an outcome are included.**

POU AMP projects based on purview; primary outcome = pain.



Project and Funding Breakdown

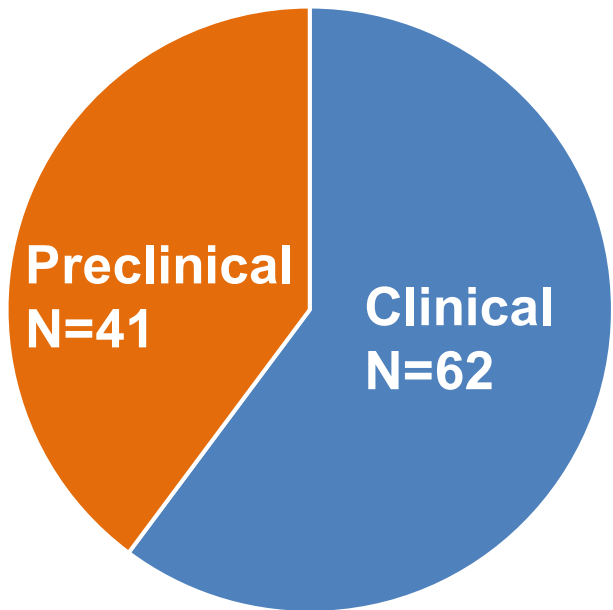
The allocation total below reflect all projects including those on hold as of 4/1/2024.

The # of Projects reflect funding allocated and projects on hold (a total of 4 projects are on hold and clearing JIT).

Service	Allocated Budget	# of Projects
BLR&D	\$4,559,236	26
CSR&D	\$3,706,919	8
CSP	\$4,333,767	1
HSR&D	\$6,403,753	28
RR&D	\$5,115,627	40
Total:	\$24,119,302	103



POU AMP - Portfolio



Total = 103

Funding Type

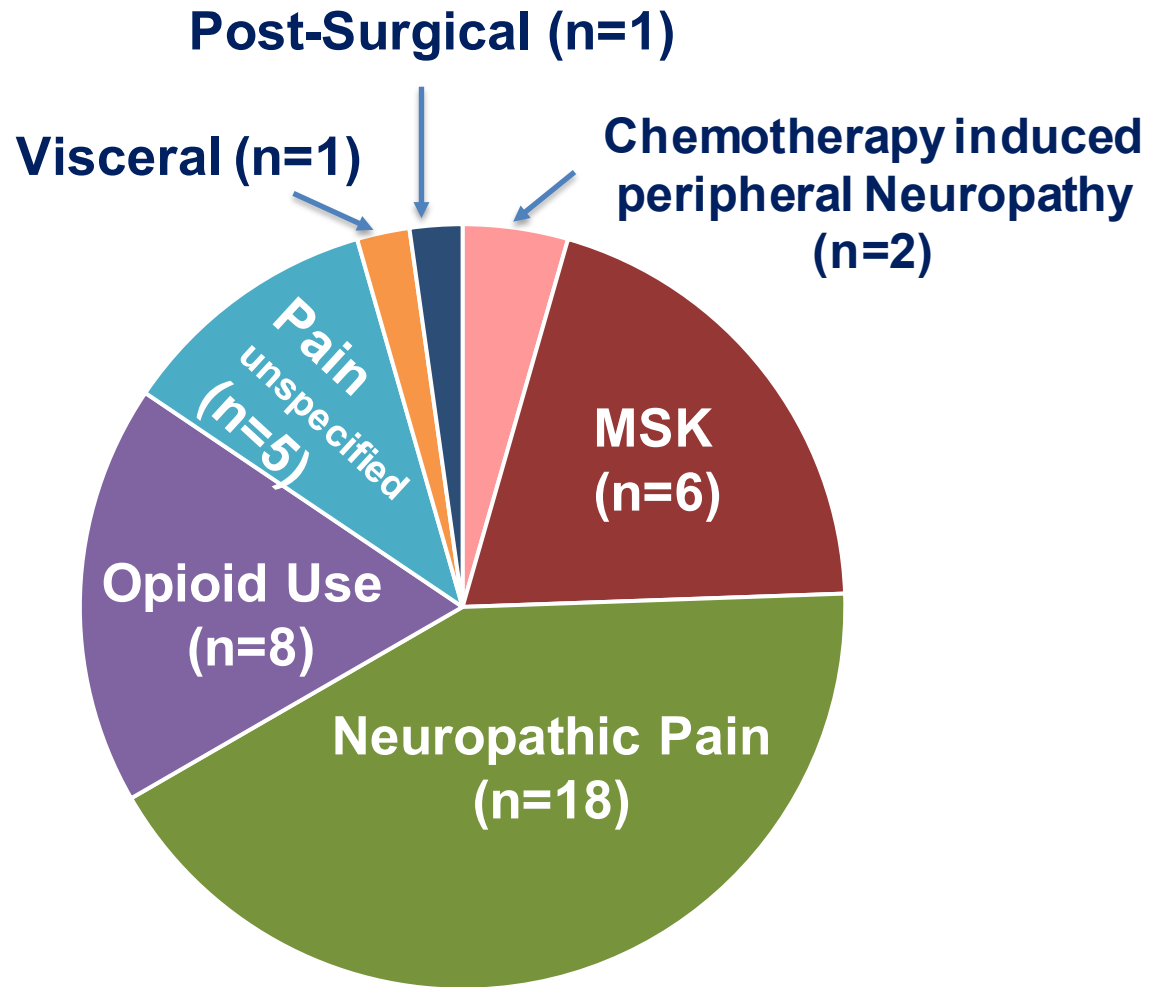
- Merit (n=83)
- SPiRE (n=16)
- Special Projects (n=3)
- CSP (n=1)

Purview

- Preclinical R&D on non-opioid therapies for pain
- CIH and non-pharmacological approaches
- Clinical studies – pain chronification and opioid safety (genetic, anatomical and behavior)
- Implementation and evaluation of pain treatments

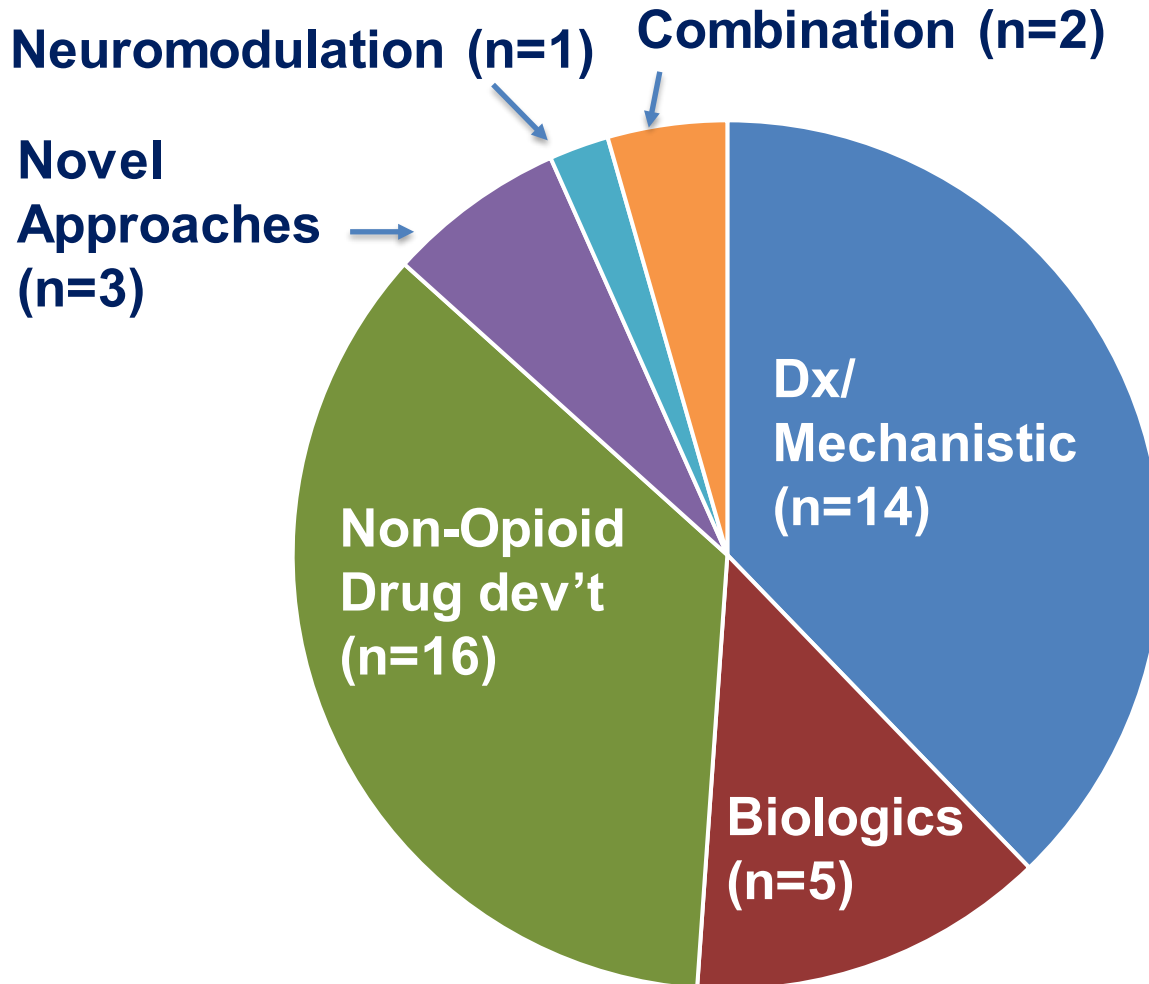


POU AMP - Preclinical Pain Models





POU AMP - Preclinical Therapeutic Approaches



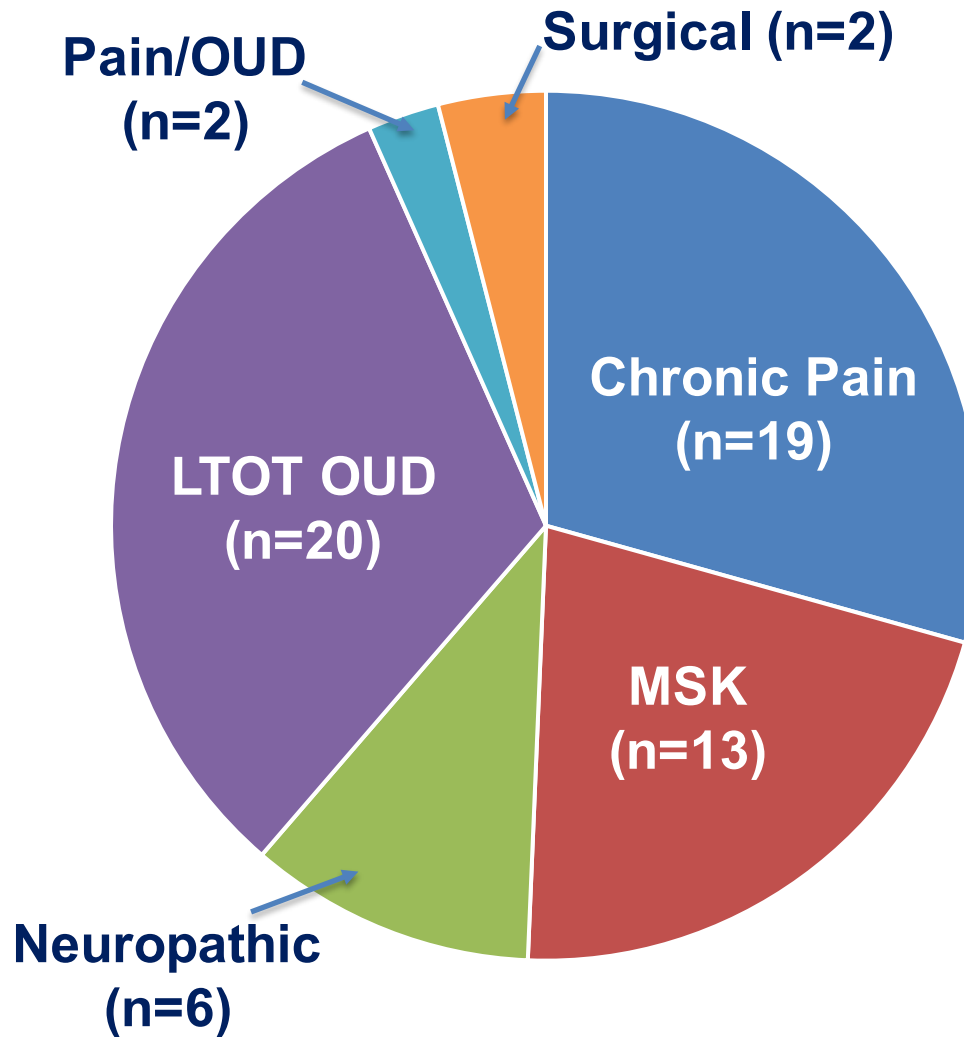


POU AMP - Preclinical Research Summary

- **Majority of studies focus on non-opioid drug development.**
 - Endomorphins
 - Ion channels
- **Studies are also diagnostic/mechanistic in nature examining disease development, identifying brain circuitry underlying painful conditions.**
 - TBI headaches
 - neuroma formation
 - visceral sensitivity
- **Emphasis on neuropathic pain models.**
- **Emerging role of cell therapies to repair damaged tissue alleviate pain.**

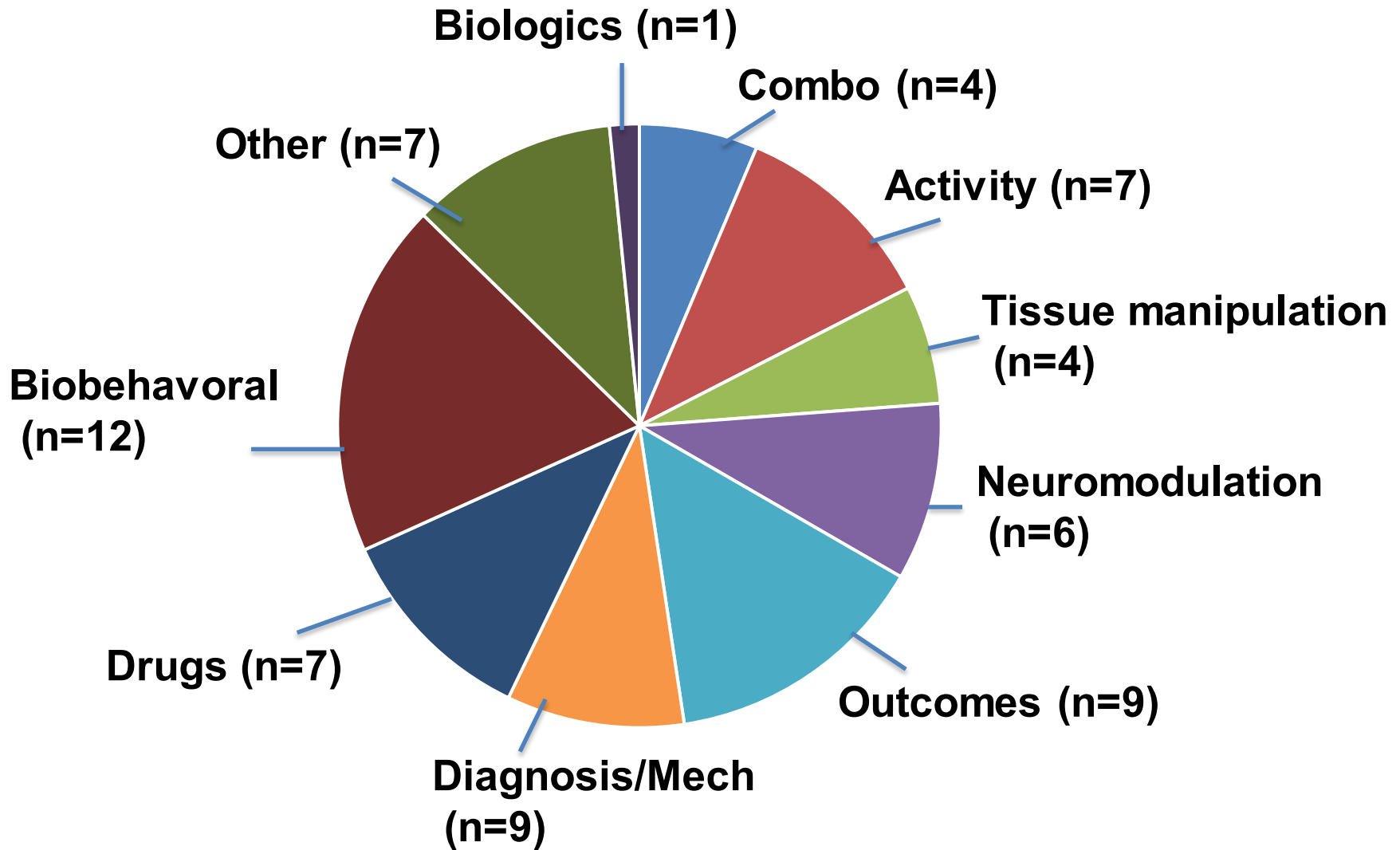


POU AMP - Clinical Conditions





POU AMP - Clinical therapeutic approaches





POU AMP - Clinical Research Summary

- **Studies mainly focus on chronic pain – musculoskeletal.**
- **Prominent focus on LTOT/ODD.**
- **Abundance of treatment approaches tested.**
- **Trend towards technology-based treatment delivery – apps, web-based and telehealth.**
- **Outcomes positive, negative, and adverse being recorded.**
- **Most of portfolio in clinical trial stage.**



Co-occurring Conditions

Mental health

- Depression
- PTSD

Substance Use Disorder

- Cocaine
- Cannabis

CNS disease and disorders

- TBI
- SCI
- Stroke
- Parkinson's disease

Renal disease

Pancreatitis

COPD

Cancer (CIPN)

COVID



POU AMP “Process Steps”

- **Executive Committee** – VHA Clinicians representing pain and opioid use service lines:
 - Pain Management Opioid Safety and Prescription Drug Monitoring (PMOP)
 - Primary Care
 - Office of Patient Centered Care and Cultural Transformation (OPCC&CT)
 - Pharmacy Benefits Management
 - Physical Medicine and Rehabilitation and Office of Mental Health
 - Suicide Prevention (OMHSP)
- **QUERI** – conducted a survey of of stakeholders from VISN Directors, Chiefs of Staff, clinicians, pharmacists, administrators, and Veterans focus groups to identify areas based on purview.
- **SOTA held in July 2023** – discussed, refined and ranked key areas of clinical and Veteran needs.



Clinically Identified High Priority Areas

➤ **Management of Pain or Opioid Use**

- Combination approaches using CIH and/or Biobehavioral (CBT/ACT) +/- pharma for specialty populations.
- Use of functional outcomes as a readout for pain intensity.
- Pragmatic/adaptive.
 - ✓ LTOT/OD
 - ✓ Minorities, aged, sex, aberrant opioid use in pain population, etc.
 - ✓ Overlapping painful conditions

➤ **Pain Management Teams**

- What makes up a high functioning team?
- Roles and responsibilities of team members and communication strategies; identify best practices.

➤ **Pharmacogenomics/Biomarkers to Guide Clinical Care**

- Identifying risk factors including behavioral and genetic to identify individuals with high impact chronic pain.
- Who will be responsive to certain pharmaceuticals.



POU AMP RFAs

Pain and Opioid Use Actively Managed Portfolio, I01

➤ **Parent Merit Review Award**

Development of non-opioid therapies - preclinical

Epidemiology

Genetics and genomics – MVP

Implementation of treatments and evaluation of care services

➤ **Clinical Trials**

➤ **Pharmacogenomics/Biomarker Studies to Guide Clinical Care in Pain and OUD**

Development and validation of predictive analytics and biomarkers to identify Veterans with High Impact Chronic Pain (HICP) or who are at risk of developing HICP or opioid use disorder (OUD), and to guide clinical care for these individuals and those living with chronic pain.



POU AMP RFAs

➤ **Areas of Special Emphasis**

Basic and applied studies of fentanyl adulterated with xylazine use in humans. Proposed studies must be responsive to the Office of National Drug Control Policy (ONDCP) Fentanyl Adulterated or Associated with Xylazine Response Plan

➤ **Pain and Opioid Use AMP Preapplication**

Preapplications for all submissions



POU AMP FUNDING SUMMARY (FY 2024)

PRE-
CLINICAL

BLR

Four applications were responsive to the Parent RFA

• **One application has been funded**

– Pedro Vera “Spinal targets to treat persistent bladder pain”

HSR

Two applications were responsive to the Parent RFA

• **One application has been funded**

– Sara Edmond, Will Becker, Patrick Hammett “EVOLVE: Emulated trial of the VOice study for improving pain and reducing Long-term opioid use for VEterans” starts May 1, 2024

RR

Four applications were responsive to the Parent RFA

• **Two applications were recommended for funding**

– Anna Woodbury “Auricular Neuromodulation in Veterans with Fibromyalgia: A Randomized, Sham-Controlled Study”

– Letitia Travaglini “Exploring the Efficacy of Cognitive Behavioral Therapy for Chronic Pain in Veterans with Serious Mental Illness”

CLINICAL



POU AMP FUNDING SUMMARY (FY 2024)

HSR

NIH/VA Pain Management Collaboratory

CLINICAL

- **One application was funded by VA**
 - Sara Edmond, Will Becker and Karen Seal “Pain Management Teams Using Whole Health to Optimize Function and Safety in Veterans: The TEAMWORK Trial”.



POU AMP SWOT Chart

Strengths:

1. Focused areas of study – pain management and opioid use.
2. Spans translational spectrum.
3. Alignment with Congressional Acts/Requests and ONDCP priority areas.
4. History of collaboration with VHA, NIH and DoD.
5. Clinician investigators and strong health systems research.

Opportunities:

1. MVP and pharmacogenomics.
2. Stronger collaboration with **VHA**, DoD and NIH partners.
3. Better alignment of portfolio to mirror **VHA** clinical needs; reduce overlap.
4. Develop pathways to facilitate translation of products.
5. Leverage VHA organization with ORD research infrastructure, etc.

Weaknesses:

1. Heavy focus on preclinical and Phase 2 clinical trials.
2. Lack of pragmatic trials, translation to Phase 3 trials and implementation to standard of care (QUERI).
3. Fluidity of portfolio to mirror the aging Veteran population, demographics, and health disparities (take-home studies, etc.)
4. Weak on Women's health research.

Threats:

1. Decrease in funding base.
2. Lack of acceptance by clinician providers.
3. Lack of acceptance by Veterans.



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