Patient Perspective on Pain Research

CHRISTIN VEASLEY
CO-FOUNDER & DIRECTOR, CHRONIC PAIN RESEARCH ALLIANCE
Pain affects 100 million Americans at an annual cost of $635 billion. More than COMBINED cost of cancer + heart disease + diabetes.
What does pain research mean to patients?
PAIN RESEARCH EFFORT
PAIN RESEARCH EFFORT
“My chronic pain continues to worsen, despite my best efforts and those of my health care providers. Research is one of a few things that still gives me hope. I’m so grateful to pain researchers who devote their todays to making my tomorrow better.”
Where are we?

AN HONEST ASSESSMENT
Public Health Impact of Chronic Pain

Most Americans Know Someone Who Sought Pain Medicine

Do you know anyone who experienced pain so severe that they sought prescription medicines to treat it?

- Yes: 63%
- No: 10%
- Not sure: 27%

Source: A ResearchAmerica poll of U.S. adults conducted in partnership with Zogby Analytics in March 2013.

Majority: Chronic Pain Tends to be Dismissed by Doctors, Public

Which statement is closer to your view?

- Chronic pain is overstated as a health condition: 16%
- Chronic pain tends to be dismissed by doctors and the public: 24%
- Not sure: 60%

Source: A ResearchAmerica poll of U.S. adults conducted in partnership with Zogby Analytics in March 2013.
### Chronic Pain Ranks Below Many Other Conditions as Major Health Problem

Which of the following would you describe as a major health problem in the U.S.? (multiple responses allowed)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>59%</td>
</tr>
<tr>
<td>Heart disease</td>
<td>52%</td>
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<tr>
<td>Diabetes</td>
<td>52%</td>
</tr>
<tr>
<td>Drug addiction</td>
<td>47%</td>
</tr>
<tr>
<td>Depression</td>
<td>42%</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>37%</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>34%</td>
</tr>
<tr>
<td><strong>Chronic pain</strong></td>
<td><strong>18%</strong></td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>15%</td>
</tr>
<tr>
<td>Not sure</td>
<td>15%</td>
</tr>
</tbody>
</table>

Source: A Research America poll of U.S. adults conducted in partnership with Zogby Analytics in March 2013.
Current Federal Investment in Pain Research
Current Federal Investment in Pain Research

**Figure 6. FY2011 Total Pain Research Expenditures by Federal Agencies**

Source: Interagency Pain Research Coordinating Committee

- NIH ~$386M*
- DoD ~$21M
- VA ~$13.4M
- CDC ~$0.9M
- FDA ~$0.5M

Total $429,829,185

*NIH RePORTER data only

Note: NIH: National Institutes of Health; DoD: Department of Defense; VA: Veterans Affairs Administration; CDC: Centers for Disease Control and Prevention; AHRQ: Agency for Healthcare Research and Quality; FDA: Food and Drug Administration
The federal investment in chronic pain research equals less than 5 cents per affected American adult!
Translation – Research to Patient Care

Is the standard research model working? Are scientific discoveries surviving the valley(s) of death and translating to improved patient care?
Where are we going?

RECENT DEVELOPMENTS
Dr. Collins: “10 for 10”
10 Predictions for Scientific Breakthroughs Over Next 10 Years

Subcommittee Hearing
Hearing on FY2017 National Institutes of Health Budget Request

Labor, Health and Human Services, Education, and Related Agencies
Date: Thursday, April 7, 2016
Time: 10:00 AM
Location: Dirksen Senate Office Building 138

#8: “Genomics, neuroscience and structural biology will collaborate to unveil entirely new targets for the treatment of pain, allowing researchers in the public and private sectors to develop highly effective, non addictive medications for pain management...
We need new alternatives for pain management and NIH and our partners will develop them.”

http://www.appropriations.senate.gov/hearings/hearing-on-fy2017-national-institutes-of-health-budget-request
National Pain Strategy outlines actions for improving pain care in America

*Plan seeks to reduce the burden and prevalence of pain and to improve the treatment of pain*

**FOR IMMEDIATE RELEASE**
Friday, March 18, 2016

Contact: ASH Media Office
202-205-0143
ashmedia@hhs.gov

The Office of the Assistant Secretary for Health at the U.S. Department of Health and Human Services today released a National Pain Strategy, outlining the federal government’s first coordinated plan for reducing the burden of chronic pain that affects millions of Americans. Developed by a diverse team of experts from around the nation, the National Pain Strategy is a roadmap toward achieving a system of care in which all people receive appropriate, high quality and evidence-based care for pain.
Population Research Working Group

**Intent:** Provide methods and metrics to guide progress toward achieving improved prevention (primary, secondary, and tertiary) and management of pain in the United States.

3 Major Objectives

Short-, Medium- & Long-Term Deliverables

Key Federal & Non-Federal Stakeholders
Population Research Working Group

Short-Term Deliverable

HealthyPeople2020
To direct the NIH to intensify and coordinate fundamental, translational, and clinical research with respect to the understanding of pain, the discovery and development of therapies for chronic pain, and the development of alternatives to opioids for effective pain treatments.

IN THE SENATE OF THE UNITED STATES
March 15, 2016

Mr. Senate (for himself, Mr. Hatch, Mr. Tester, Mr. Cochran, Ms. Collins, and Ms. Baldwin) introduced the following bill, which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

A BILL

To direct the NIH to intensify and coordinate fundamental, translational, and clinical research with respect to the understanding of pain, the discovery and development of therapies for chronic pain, and the development of alternatives to opioids for effective pain treatments.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the “Safe Treatments and Opportunities to Prevent Pain Act” or the “STOP Pain Act”.

SEC. 2. ENHANCING BASIC AND APPLIED RESEARCH ON PAIN TO DISCOVER THERAPIES, INCLUDING ALTERNATIVES TO OPIOIDS, FOR EFFECTIVE PAIN MANAGEMENT.

(a) IN GENERAL.—The Director of the National Institutes of Health (referred to in this section as the “NIH”) may intensify and coordinate fundamental, translational, and clinical research of the NIH with respect to—

(1) the understanding of pain;

(2) the discovery and development of therapies for chronic pain; and

(3) the development of alternatives to opioids for effective pain treatments.

(b) PRIORITY AND DIRECTION.—The prioritization and direction of the federally funded portfolio of pain research studies shall consider recommendations made by the Interagency Pain Research Coordinating Committee in concert with the Pain Management Best Practices Inter-Agency Task Force, and in accordance with the National Pain Strategy, the Federal Pain Research Strategy, and the NIH-Wide Strategic Plan for Fiscal Years 2016–2020, the latter which calls for the relative burden of individual diseases and medical disorders to be regarded as crucial considerations in balancing the priorities of the Federal research portfolio.
STOP Pain Act Provisions Included in Senate HELP Committee Legislation

The Mental Health Reform Act of 2016 will help Americans suffering from mental health and substance use disorders

SEC. 804. NIH OPIOID RESEARCH.

(o) In General.—The Director of the National Institutes of Health (referred to in this section as the “NIH”) may intensify and coordinate fundamental, translational, and clinical research of the NIH with respect to—

(1) the understanding of pain;

(2) the discovery and development of therapies for chronic pain; and

(3) the development of alternatives to opioids for effective pain treatments.

(b) Project Area Direction.—The prioritization and direction of the Federally funded portfolio of pain research studies shall consider recommendations made by the Interagency Pain Research Coordinating Committee in concert with the Pain Management Best Practices Inter-Agency Task Force, and in accordance with the National Pain Strategy, the Federal Pain Research Strategy, and the NIH-Wide Strategic Plan for Fiscal Years 2016-2020, the latter which calls for the relative burden of individual diseases and medical disorders to be regarded as crucial considerations in balancing the priorities of the Federal research portfolio.
Federal Pain Research Strategy

First federal interagency strategic plan for research
Allan Basbaum, PhD (UCSF)
Ronald Dubner, PhD, DDS (Univ of MD)
Jon Levine, MD, PhD (UCSF)
Emeran Mayer, MD (UCLA)
William Maixner, DDS, PhD (Duke)
Sean Mackey, MD, PhD (Stanford)
Richard Lipton, MD (Albert Einstein)
Dan Clauw, MD (Univ of Michigan)
Alan Light, PhD (Univ of UT)
Philip Pizzo, MD (Stanford)
Allen Cowley, Jr, PhD (Medical College of WI)
Ursula Wesselmann, MD, PhD (Univ of Alabama-Birmingham)
Howard Jacob, PhD (HudsonAlpha Institute)
Suzanne Vernon, PhD (Bateman Horne Center of Excellence)
Martin Frank, PhD (American Physiological Society)
Ruby Nguyen, PhD, MHS (Univ of MN)
Denniz Zolnoun, MD, MPH (UNC-Chapel Hill)
Mounting scientific evidence demonstrates that a cluster of chronic pain conditions co-exist, predominantly in women—termed Chronic Overlapping Pain Conditions (COPCs).
Common Underlying Disease Mechanisms

Genetic and Environmental Factors
Abnormal Pain and Sensory Processing
Autonomic Nervous System Processing
Female Predominance & Role of Ovarian Hormones
Neuroendocrine & Neuroimmune Abnormalities
Role of Stress, Behavior & Psychological Behaviors
### COPCs - FY2013 & FY2014 NIH Funding Levels, Investment per Affected Individual and Primary Funding Institutes/Centers


<table>
<thead>
<tr>
<th>Condition</th>
<th>U.S. Prevalence</th>
<th>2013 NIH Funding Levels</th>
<th>2014 NIH Funding Levels</th>
<th>2013 Research Investment/Patient</th>
<th>2014 Research Investment/Patient</th>
<th>Primary NIH Funding IDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginodynia</td>
<td>6 million</td>
<td>$4 million</td>
<td>$3 million</td>
<td>$0.67</td>
<td>$0.56</td>
<td>1 - NICHD, 2 - NIDDK, 3 - NINDS</td>
</tr>
<tr>
<td>Temporomandibular Disorders</td>
<td>35 million</td>
<td>$19 million</td>
<td>$18 million</td>
<td>$0.54</td>
<td>$0.51</td>
<td>1 - NIDCR, 2 - NINDS, 3 - NEMHS</td>
</tr>
<tr>
<td>Myalgic Encephalomyelitis/Chronic Fatigue Syndrome</td>
<td>4 million</td>
<td>$5 million</td>
<td>$5 million</td>
<td>$1.25</td>
<td>$1.25</td>
<td>1 - NIAID, 2 - NINDS, 3 - NIMH &amp; NIDDK</td>
</tr>
<tr>
<td>Irritable Bowel Syndrome</td>
<td>44 million</td>
<td>$23 million</td>
<td>$14 million</td>
<td>$0.52</td>
<td>$0.32</td>
<td>1 - NIDDK, 2 - NINDS, 3 - NINDS</td>
</tr>
<tr>
<td>Interstitial Cystitis/Partial Bladder Syndrome</td>
<td>8 million</td>
<td>$10 million</td>
<td>$3 million</td>
<td>$1.25</td>
<td>$1.13</td>
<td>1 - NIDDK, 2 - NINDS, 3 - NICHID</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>6 million</td>
<td>$11 million</td>
<td>$10 million</td>
<td>$1.83</td>
<td>$1.67</td>
<td>1 - NIAMS, 2 - NINDS, 3 - NIAID, NCNIH, NINR, NIDDK</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>6.3 million</td>
<td>$7 million</td>
<td>$7 million</td>
<td>$1.11</td>
<td>$1.11</td>
<td>1 - NICHID, 2 - NCI, 3 - NIEHS</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Tension-Type Headache</td>
<td>7 million</td>
<td>$950,000</td>
<td>$265,000</td>
<td>$0.14</td>
<td>$0.04</td>
<td>1 - NIMH, 2 - NICHD</td>
</tr>
<tr>
<td>Chronic Migraine</td>
<td>7 million</td>
<td>$19 million</td>
<td>$20 million</td>
<td>$2.71</td>
<td>$2.86</td>
<td>1 - NIMH, 2 - NICHD, 3 - NIDDK</td>
</tr>
<tr>
<td>Chronic Low Back Pain</td>
<td>19.5 million</td>
<td>$26 million*</td>
<td>$24 million*</td>
<td>$1.44</td>
<td>$1.23</td>
<td>1 - NCI, 2 - NAMS, 3 - NDA</td>
</tr>
</tbody>
</table>

**Totals**

- **2013 NIH Funding Levels**: $127 Million
- **2014 NIH Funding Levels**: $110 Million
- **2013 Research Investment/Patient**: $1.15
- **2014 Research Investment/Patient**: $1.06

*Includes NIH investment in both "chronic low back pain" and "low back pain" studies
**Current Reality for Patients**

- Frequent misdiagnoses due to lack of education and training of health care providers
- Few FDA-approved treatment options
- Insufficient scientific evidence to guide clinicians and patients in making informed treatment decisions

*Vicious cycle ensues*

- Decreased treatment efficacy
- Poorer health outcomes
- Increased disability
- Diminished quality of life
- Worsening of localized and systemic symptoms
### Our Approach

#### Research

| Silo effort by Dx/body site – similar studies duplicated across conditions | Collective/collaborative effort - to parse out commonalities & uniqueness across phenotypic subgroups |

#### Clinical Care

| Fragmented medical care by specialists according to body area | Patient-centered medical home with team-based interdisciplinary treatment approach |
| Treatment is trial-and-error based & draws upon findings of better researched disorders | Treatment informed by scientific evidence, with proven efficacy in mechanism-based subtypes |
| Treatment of most painful symptom or body part | Individualized treatment of all affected domains and contributing factors (pain, sleep, mood, physical function, etc.) |

#### Translation of Evidence

| Evidence not widely disseminated or translated into improved care or tools | Heavy focus on translation of findings into improved care and tools |
**Mission**

CPRA works with invested stakeholders in a collaborative model to:

1. Promote a rigorous, standardized, collective and cost-effective **research** approach

2. **Translate** research findings into information for patients and educational and training programs for clinicians

3. Drive the development of safe and effective **treatments** for chronic overlapping pain conditions

**Vision**

A future where individuals with multiple pain diagnoses will receive a **timely and accurate diagnosis**, followed by **high-quality and comprehensive medical care** and **safe and effective treatment** that is **informed by the latest and most rigorous scientific evidence**.
National COPCs Studies: MAPP Research Network
Let's Talk OPPERA: A New Study on TMJ Disorders

The Inside Scoop

January 2008

The National Institute of Dental and Craniofacial Research (NIDCR), in conjunction with the University of North Carolina at Chapel Hill and the University of Washington, has initiated two studies to explore the relationship between oral health and chronic pain. The OPPERA (Oral Pain and Psychosocial Risk Factors in TMD: Health Services Research) project is aimed at understanding the factors that contribute to chronic pain in the mouth and how these factors may be linked to other chronic conditions. The OPPERA project is designed to identify key risk factors for chronic pain and to develop interventions to prevent or manage these conditions. The project is expected to have significant public health implications.

The OPPERA project is a large, multi-center study that involves investigators from several institutions. The primary aim of the project is to identify risk factors for chronic pain in the mouth and to develop interventions to prevent or manage these conditions. The project is expected to have significant public health implications.

One of the key risk factors identified in the OPPERA project is the presence of oral pain. Oral pain is defined as pain that is felt in the mouth or jaw, and it can be caused by various factors, including dental problems, TMJ disorders, and other medical conditions. The OPPERA project is exploring the relationship between oral pain and other chronic conditions, such as depression and anxiety.

The OPPERA project is also investigating the role of psychosocial factors in the development of chronic pain. Psychosocial factors include stress, anxiety, and depression, and they are known to play a significant role in the development of chronic pain.

In summary, the OPPERA project is a large, multi-center study that is designed to identify key risk factors for chronic pain in the mouth and to develop interventions to prevent or manage these conditions. The project is expected to have significant public health implications.
Complex Persistent Pain Conditions: Unique & Shared Pathways of Vulnerability

Maezer, William
University of North Carolina Chapel Hill, Chapel Hill, NC, United States

Abstract

Complex persistent pain conditions (CPPCs) such as headache conditions, fibromyalgia, temporomandibular disorders, irritable bowel syndrome, and vestibular disorders are highly prevalent and shared or contained chronic pain conditions. There are two features of CPPCs that are fundamental to the aims and goals of this proposal: 1) the etiology of CPPCs is multifactorial and 2) the clinical manifestations of CPPCs are diverse. In this Program Project, we seek to identify a mosaic of risk factors for each of five CPPCs: fibromyalgia (FM), episodic migraine (EM), vestibular disorder, irritable bowel syndrome (IBS), and temporomandibular joint disorders (TMD). Furthermore, we seek to characterize clusters of patients within each CPPC that vary significantly according to manifestations of their condition in addition to its painful characteristics (e.g., fatigue, dysfunction, sleep loss). Importantly, we expect some clusters of patients to be more alike across CPPCs than within any single CPPC, consistent with our view that there is some overlap in the manifestations of CPPCs. A unifying hypothesis integrating this Program is that multiple genetic factors, when coupled with environmental exposures (e.g., injury, infections, physical and psychological stress), increase the susceptibility to highly prevalent CPPCs by enhancing pain sensitivity and/or increasing psychological distress. To address the aims and goals of the subprojects and cores described in this application, a group of accomplished pain clinicians, pain researchers, psychophysicists, molecular and cellular geneticists, biostatisticians, and epidemiologists have been brought together to form this Program. Studies proposed in this Program Project application seek to identify the psychological and physical risk factors, clusters, and associated genetic polymorphisms, that influence pain amplification and psychological profiles in patients who have established CPPCs. Additionally, the proposed studies seek to characterize the biological pathways through which these genetic variations causally influence CPPCs.

Funding Agency

<table>
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<tr>
<th>Agency</th>
<th>National Institute of Health (NIH)</th>
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<tr>
<td>Institute</td>
<td>National Institute of Neurological Disorders and Stroke (NINDS)</td>
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<tr>
<td>Type</td>
<td>Research Program Projects (R01)</td>
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<tr>
<td>Project #</td>
<td>5R01NS045685-09</td>
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<tr>
<td>Application #</td>
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<tr>
<td>Study Section</td>
<td>National Institute of Neurological Disorders and Stroke Initial</td>
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<tr>
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<td>Project Start: 2009-03-01</td>
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<td>Project End: 2015-03-31</td>
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<td></td>
<td>Budget Start: 2013-04-01</td>
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<tr>
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<td>Budget End: 2014-04-01</td>
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<td></td>
<td>Support Year: 9</td>
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<td></td>
<td>Fiscal Year: 2013</td>
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<tr>
<td></td>
<td>Total Cost: $1,297,314</td>
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<td>Indirect Cost: $603,425</td>
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</table>
Our growing body of data contains structural and functional brain scans from patients with chronic pain conditions and healthy controls contributed by members and available for analysis. In addition, the PAIN Standardized Repository also offers clinical, psychosocial and behavioral data.

The Executive Committee evaluates all requests for data, and encourages collaborations among multiple researchers and institutions.

Current pain conditions include: chronic back pain (CBP), fibromyalgia (FM), migraine, irritable bowel syndrome (IBS), vulvodynia (VVD), inflammatory bowel disease (IBD).

**Standardized Repository**
- Standardized Structural Scans: 323
- Standardized Resting State Scans: 199
- Standardized DTI Scans: 146
- Total Standardized Scans: 664

[Go to List of Scans (Member login required)]

**Archived Repository**
- Structural Scans: 540
- Resting State Scans: 201
- DTI Scans: 130
- Total Archived Scans: 874

[Go to List of Scans (Member login required)]
Recent Publications from National Studies

Identification of clusters of individuals relevant to temporomandibular disorders and other chronic pain conditions.

MicroRNA expression profiles differentiate chronic pain condition subtypes.

Natural history of comorbid orofacial pain among women with vestibulodynia.

Toll-like receptor 4 and comorbid pain in Interstitial Cystitis/Bladder Pain Syndrome: a multidisciplinary approach.

Relationship between chronic nonurological associated somatic syndromes and symptom severity in urological chronic pelvic pain syndromes: baseline evaluation of the MAPP study.

Initiatives & Accomplishments Since Inception:

2010: Inclusion of first US Congressional appropriations language, directing the NIH to develop a research program on COPCs

2011: NIH Establishes first Trans-NIH Working Group (12 NIH Institutes/Centers)

2012: First US Senate hearing on chronic pain, including COPCs

2012: First federal workshop convened and research priorities developed for COPCs

2014: Release of first federal funding announcement on COPCs
Initiatives & Accomplishments – 2015/2016:

To maximize COPCs research investment & facilitate data pooling/analysis across studies, working with NIH to:

1) Develop a case definition
2) Common Data Elements program (including rigorous screening tool)
3) Data-Sharing Repository
Research Recommendations

Provides recommendations for advancing a coordinated, standardized and cost-effective research effort.

PDF Available on CPRA’s web site: www.ChronicPainResearch.org
Research Model – Shift Towards Mechanism-Based Individualized Treatment

CPRA 2015
White Paper

Reviews latest data on:
- Prevalence, Burden of Illness & Societal Impact
- Research Disparities
- Safety & Efficacy of FDA-Approved Therapies
- Emerging Research on Common Underlying Disease Mechanisms
- Promising National Studies

PDF Available on CPRA’s web site:
www.ChronicPainResearch.org
COPCs Research Advances

**Purpose:** Bimonthly electronic publication developed to keep the medical-scientific community abreast of recent scientific publications on COPCs.

**Provides:** Compiled list of recently published abstracts on the epidemiology, pathophysiology and clinical management of COPCs.

Sign-up & PDFs available at: www.ChronicPainResearch.org
PAIN RESEARCH EFFORT