

Portfolio title: Headache

40 Grants total

Excluded: 1 repetition, 1 Admin Core, 2 Scientific Cores, 1 thematically unrelated, 1 without abstract

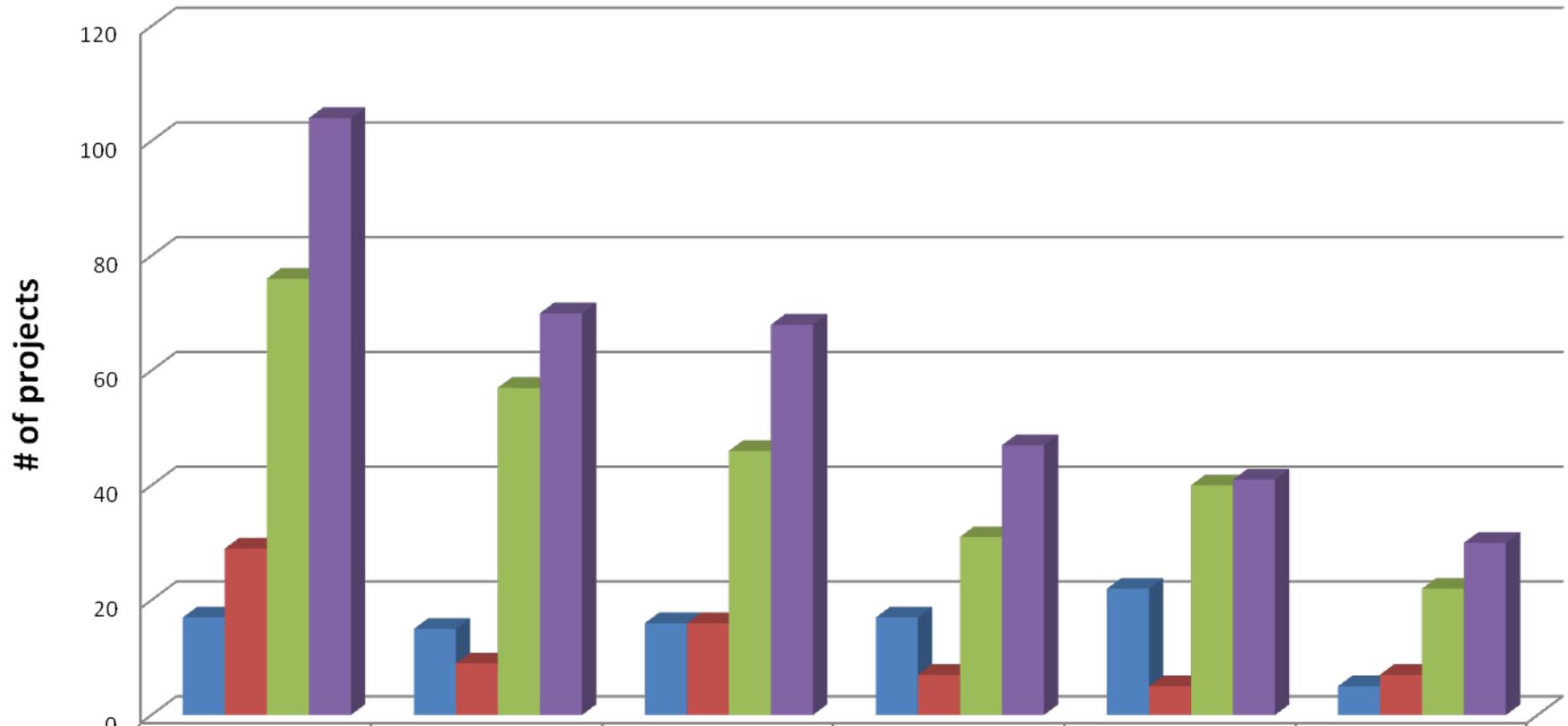
Final Number Analyzed: 35 grants

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Program Director: Linda Porter, Ph.D.

To compare number of projects in basic, translational or clinical research for each top condition

Basic Translational Clinical Total # grants



	Osteoarthritis	Cancer Pain	Low Back Pain	IBS	Headache	Sickle Cell Pain
Basic	17	15	16	17	22	5
Translational	29	9	16	7	5	7
Clinical	76	57	46	31	40	22
Total # grants	104	70	68	47	41	30

*Total # grants does not equal basic + translational + clinical because one grant can belong to more than one category

Headache Pain Research by Secondary Code (% of Projects)

Headache Pain	% of Projects
1. Neurobiological/glia mechanisms of nociception and pain	16%
28. Training in pain research	13%
5. Development and validation of animal and human pain models	11%
27. Pain and other non-pain comorbidities	9%
4. Mechanisms of and treatments for transitions in pain phases 19. Unique populations ¹	6% each
7. Pharmacological mechanisms and treatment 13. Pain outcomes assessments and measures, and novel health information technology as tools for decision making support of pain management	5% each
6. Diagnosis/case definitions 8. Non-pharmacological mechanisms and treatment 16. Epidemiology of pain and pain disorders 18. Pain and women's and minority's health research ²	4% each
Others	<3% each

¹Unique populations: elderly - 1, pediatric - 4

²Pain and women's and minority's health research: women - 3

Overview of the portfolio (n=)

Cortical Spreading Depression (9)

Ion Channels (2)

CGRP + CGRPr (4)

Central Mechanisms and Pain Processing (6)

Animal Models (5)

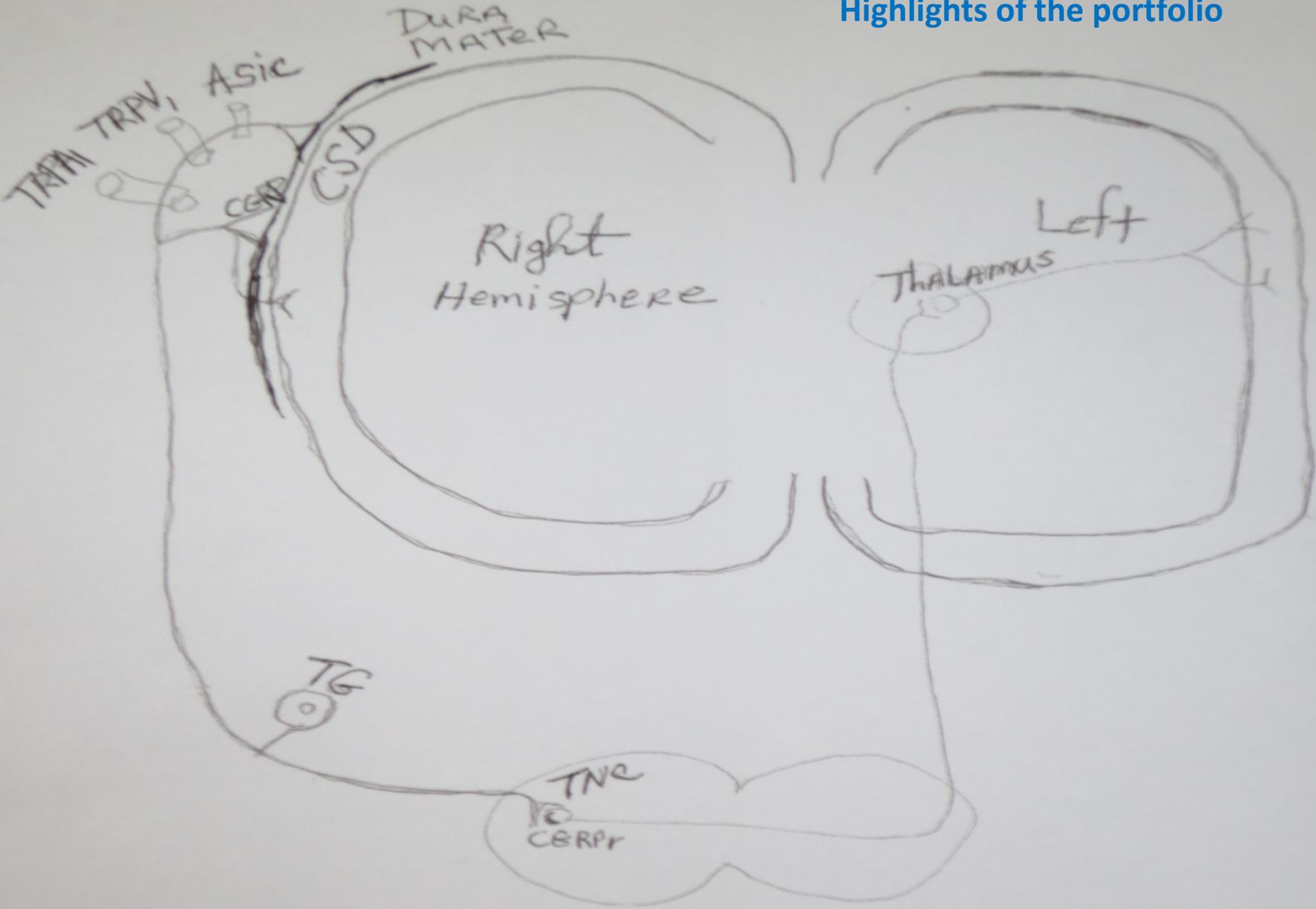
Imaging- biomarker (6)

Pediatric Migraine (5)

Co-morbidities (vascular, obesity, other pain states)(4)

*Training in Pain Research (10 of 35)

Highlights of the portfolio



Cortical Spreading Depression (9)

- Is it noxious?
- Are gene mutations as susceptibility factors?
- Are Sex hormones as modulators?
- Does CSD pose a stroke risk
- Is it a target for migraine Prevention
- Can it be modeled?

Ion Channels (2)

- ASICs- molecular properties, relation to NI and mast cells
- TRP Channels- TRPA1 and TRPV1 in environmental pollutant trigeminal activation

CGRP and CGRPr- central and peripheral roles

- How does stress trigger migraine?
- Does CGRPr in thalamus trigger photophobia?
- hRAMP-1 carrying VV will be injected focally to mimic behavior
- Is dizziness and vertigo a parallel CGRP system in vestibular ganglion cells?

Central Mechanisms & Processing (6)

- 5-HT null mice in central neurons
- The role of 5-HT_{1D} receptors in affective emotional processing regions
- Imaging: (a) comparing (fMRI, DTI, MRS) in infrequent and frequent episodic migraine patients
 - (b) Integrity and strength of functional networks and default mode networks
 - (c) u-opioid receptor binding in migraineurs
- Photophobia- thalamic convergence and cortical projections

Animal Model Development (5)

- No single model mimics the entire migraine spectrum and most require invasive approaches

Projects:

PTH: Mild head trauma causes persistent periosteal inflammation and is a key peripheral site for PTH?

CDH: Does repeated dural inflammation generate CDH?

MOH: Does MOH reflect enhanced TV response to migraine triggers?

CSD, mutant mice

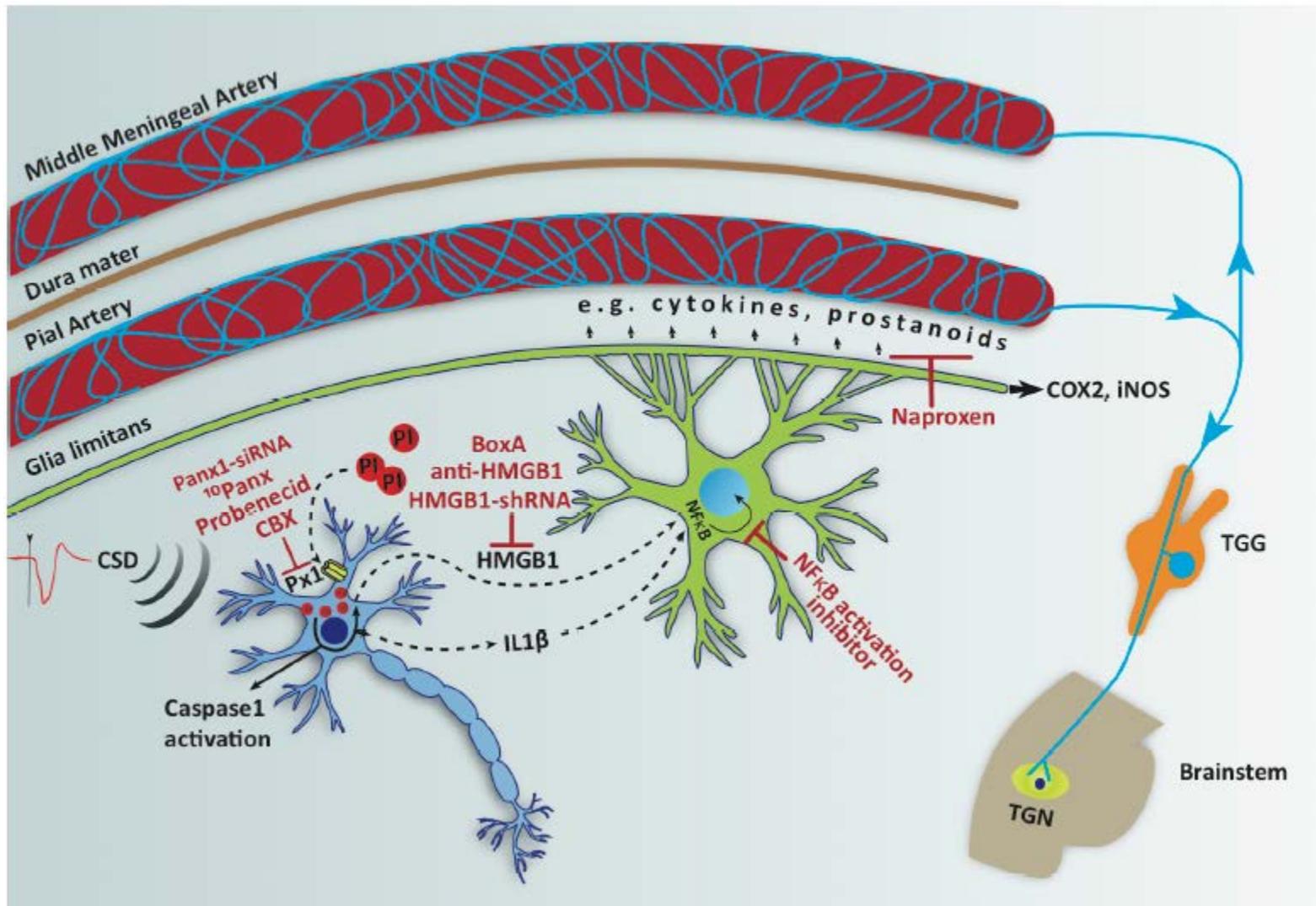
Pediatric Migraine (5)

- Controlled clinical trial for prevention
- MEG and migraine in children
- Physiologic responses to lab pain in migraine prediction
- Gender, puberty and family relationships as predictors

Recent Important Discoveries not part of the Portfolio

- Casein kinase 1 delta mutations,
(Brennan Science Translational Medicine
May 2013)
- CSD-induced inflammasome
response (Karatas et al, Science,
March 2013)

CSD initiates an inflammasome reaction in cortex



Gaps and Opportunities

Postrumatic HA

HA biomarkers- more imaging/blood, omics

Transitions states for other Pain Conditions- imaging

Rx, especially drugs for prevention (CSD, inflammasome response?) and CDH

The prodromal phase- imaging

Placebo response- Partner with other pain conditions

Tension Type Headache ?

Potential overlap or shared interests among agencies or NIH institutes

PTH-Military, Auto Industry,
Professional Sports

Integrative Self Management
Groups-OA, LBP

Comorbidities-Psychiatry and
Neurology: epilepsy, other pain
conditions, sleep, stroke, wml
(cardiology)

Strengths

Training Emphasis

Model Building/Validation

Solid preclinical research with
hypothesis testing

Conclusion

The number of recent advances in this field plus the great burden of illness suggest that headache is ripe for additional training and research opportunities. This is further justified by migraine being the most common neurological disorder, affecting 12% of the population (35 million), affecting young people in their prime, and causing significant economic burden (110 million days in bed and 13 billion dollar loss to the economy/year).

% of projects in a secondary code within top condition	Top Conditions					
	OA	Cancer	LBP	IBS	HA	SICKLE
Secondary Code						
1. Neurobiological/gliar mechanisms of nociception and pain:	8%	12%	6%	19%	16%	9%
2. Genetics and genomics of nociception and pain:	1%	3%	0%	4%	3%	7%
3-Other "omics" of pain:	5%	1%	1%	5%	0%	2%
4. Mechanisms of and treatments for transitions in pain phases:	3%	2%	4%	5%	6%	0%
5. Development and validation of animal and human pain models:	1%	4%	4%	10%	11%	9%
6. Diagnosis/case definitions:	14%	0%	2%	0%	4%	2%
7. Pharmacological mechanisms and treatment:	4%	12%	3%	2%	5%	7%
8. Non-pharmacological mechanisms and treatment:	28%	12%	26%	5%	4%	4%
9. Biobehavioral and psychosocial mechanisms and treatment of pain:	7%	8%	13%	10%	3%	4%
10. Medical management of pain	0%	4%	3%	1%	0%	7%
a. Self management approaches (subcategories are all set to zero)	0%	0%	0%	0%	0%	0%
b. Team based treatment approaches	0%	0%	0%	0%	0%	0%
11. Analgesic development:	0%	0%	0%	0%	0%	4%
12. Development of device and therapy delivery systems:	1%	2%	0%	0%	1%	4%
13. Pain outcomes assessments and measures, and novel health information technology as tools for decision making support of pain management:	6%	2%	9%	5%	5%	13%
14. Development of informatics, data bases, and information technologies as tools for pain research:	1%	0%	3%	1%	0%	0%
15. Pain education	5%	11%	0%	0%	0%	5%
a. Health care provider education (subcategories are all set to zero)	0%	0%	0%	0%	0%	0%
b. Caregiver education	0%	0%	0%	0%	0%	0%
c. Patient education	0%	0%	0%	0%	0%	0%
d. Public education	0%	0%	0%	0%	0%	0%
16. Epidemiology of pain and pain disorders:	1%	1%	1%	2%	4%	0%
17. Health disparities in pain, pain management, and access to care:	1%	5%	0%	0%	0%	11%
18. Pain and women's and minority's health research	0%	2%	1%	4%	4%	7%
a. women (subcategories are all set to zero)	0%	0%	0%	0%	0%	0%
b. minorities	0%	0%	0%	0%	0%	0%
19. Unique populations	8%	14%	4%	5%	6%	0%
a. Pediatric (subcategories are all set to zero)	0%	0%	0%	0%	0%	0%
b. Elderly	0%	0%	0%	0%	0%	0%
c. end of life	0%	0%	0%	0%	0%	0%
d. Disabled	0%	0%	0%	0%	0%	0%
e. military	0%	0%	0%	0%	0%	0%
20. Sex and gender differences in pain	1%	0%	2%	3%	3%	0%
a. Male (subcategories are all set to zero)	0%	0%	0%	0%	0%	0%
b. female	0%	0%	0%	0%	0%	0%
21. Comparative effectiveness research:	0%	1%	8%	1%	3%	0%
22. Pain and substance use and abuse/addiction	0%	0%	1%	0%	0%	0%
23. Analgesic drug safety	0%	0%	0%	1%	0%	0%
24. Pain and trauma	1%	0%	0%	0%	0%	0%
25. Pain prevention	5%	1%	3%	2%	1%	0%
26. Chronic overlapping pain conditions in an individual	0%	0%	0%	1%	1%	0%
27. Pain and other non-pain comorbidities	1%	1%	1%	1%	9%	2%
28. Training in pain research	2%	2%	3%	9%	13%	4%
29. Health care utilization	0%	0%	3%	0%	0%	2%
	100%	100%	100%	100%	100%	100%