Individual Differences Factors Associated with Risk for Chronic Pain

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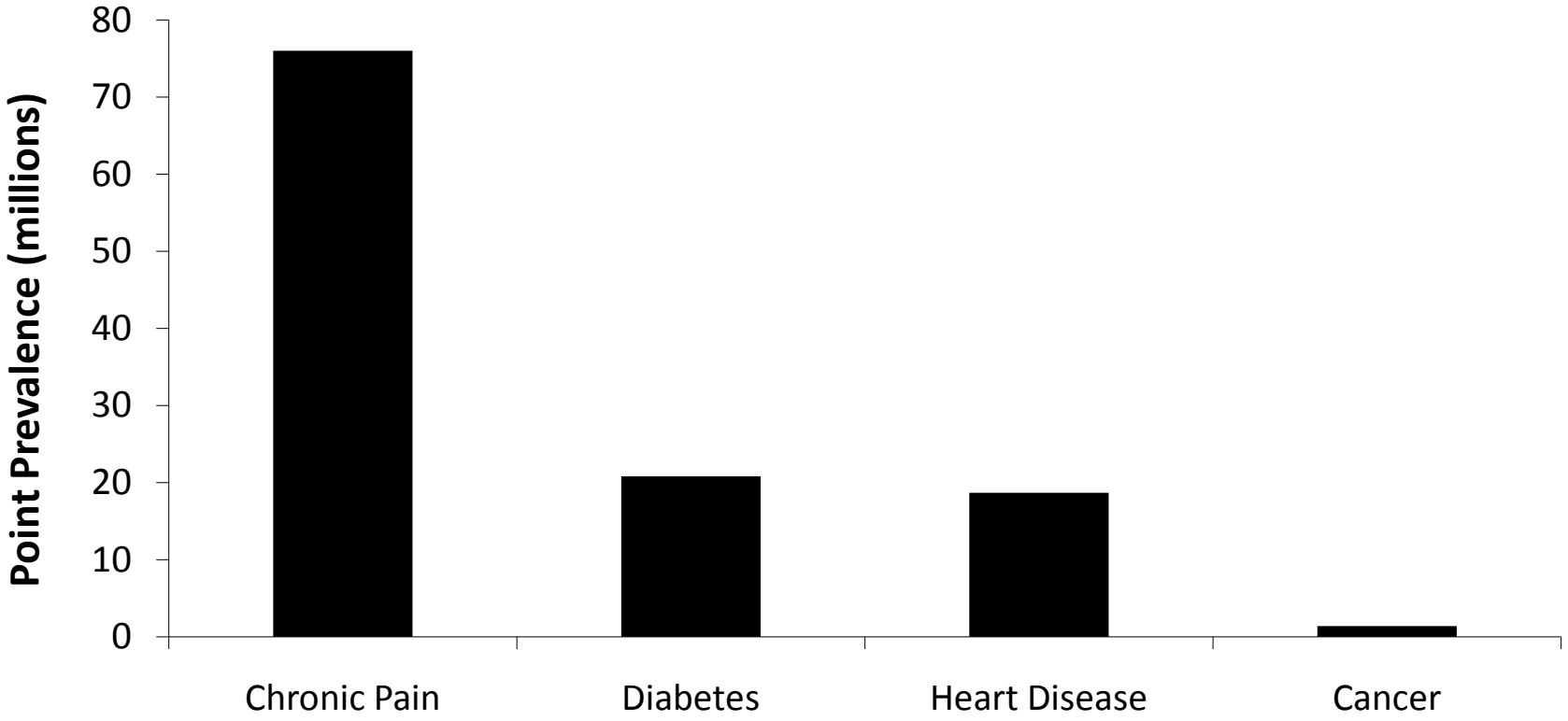
Topics to be Addressed

- **Overview of individual differences in pain**
- Factors contributing to individual differences
- Practical implications of individual differences

Pain as a Public Health Issue

- Pain is the number one reason for seeking health care, accounting for over 70 million total physician visits annually (Turk & Melzack, 2002)
- Between 20 and 50% of the population is experiencing chronic pain (Blyth, et al, 2001; Elliot, et al, 1999; Harstall, 2003)
- Pain costs $1 trillion annually in developed countries (Max & Stewart, 2008)
- The cost of treating pain may exceed the combined costs of treating AIDS, cancer and heart disease (Cousins, 1995)

Pain as a Public Health Issue



Pain in Veterans

- In a VA primary care setting, chronic pain was reported in 50% of patients (Clark, 2002)
- 42-46% of returning OEF and OIF military personnel registering for VA care identify pain issues when screened (Gironda, et al, 2006)
- 80-96% of soldiers treated in VA Polytrauma Rehabilitation Centers report ongoing pain problems (Gironda, et al, 2009)

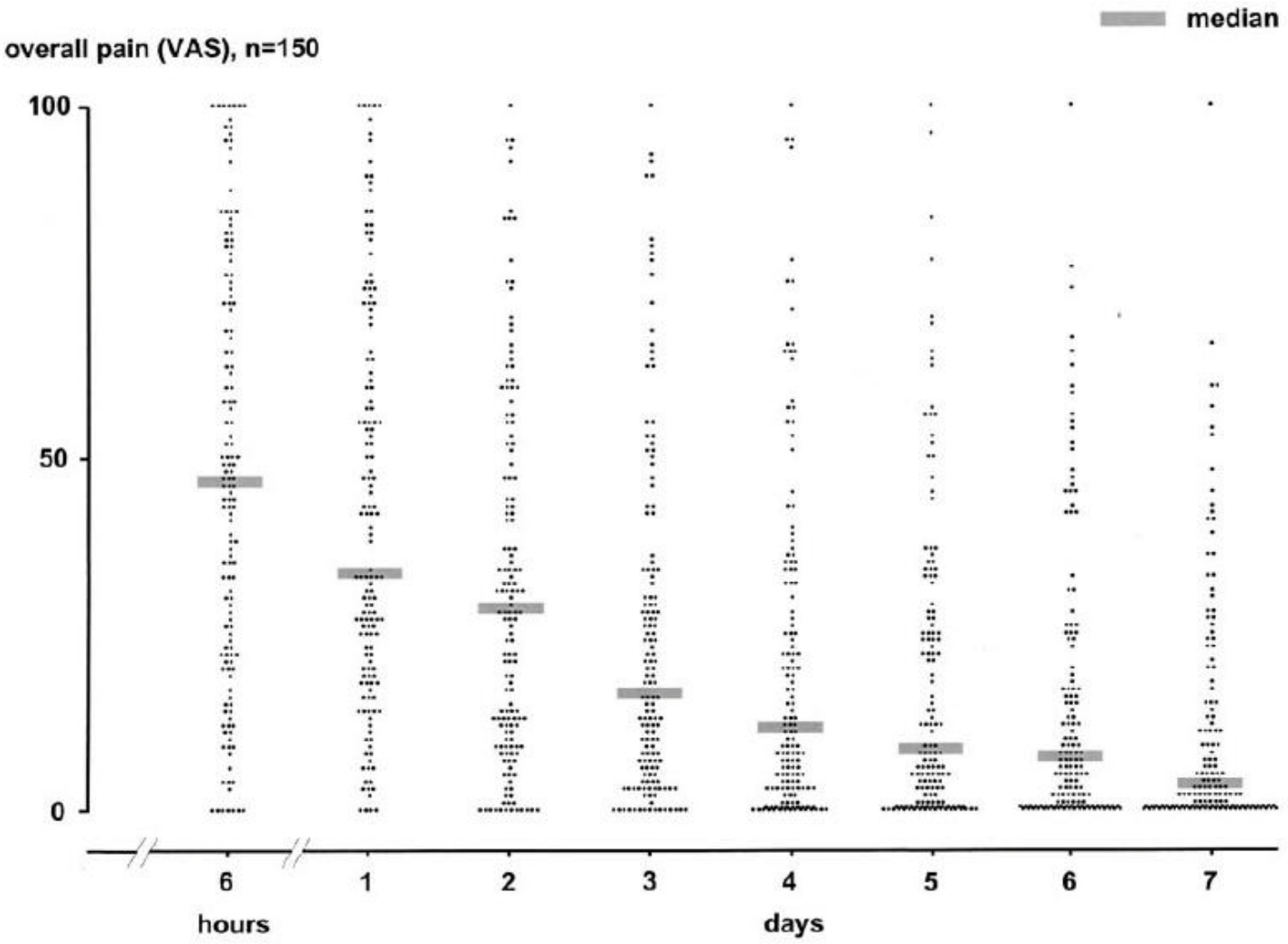
Individual Differences

- Definition: Deviations of individuals from the group average or from each other

It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has.

Sir William Osler (1849-1919)

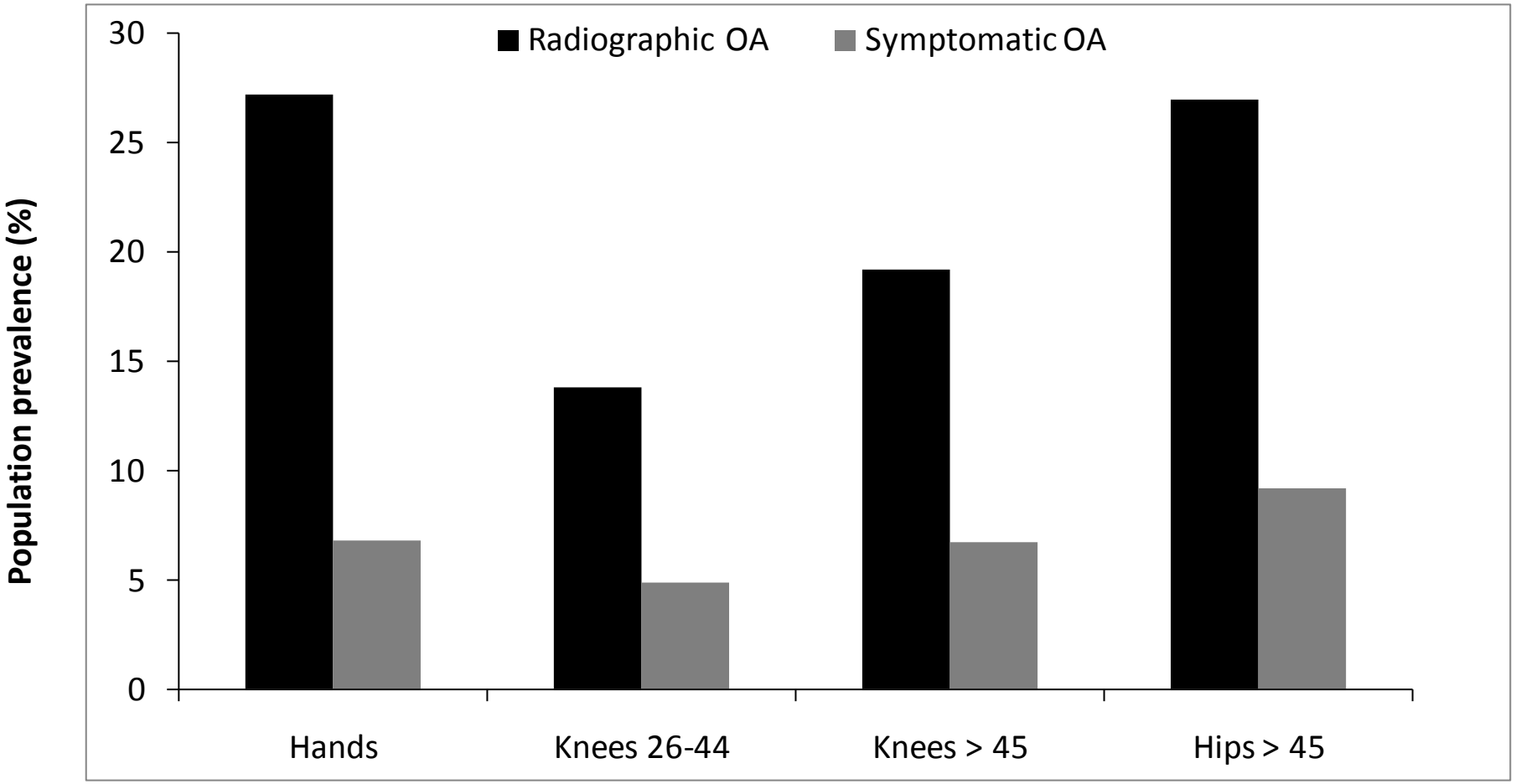
Pain After Laparascopic Cholecystectomy
(Bisgaard, et al, 2001)



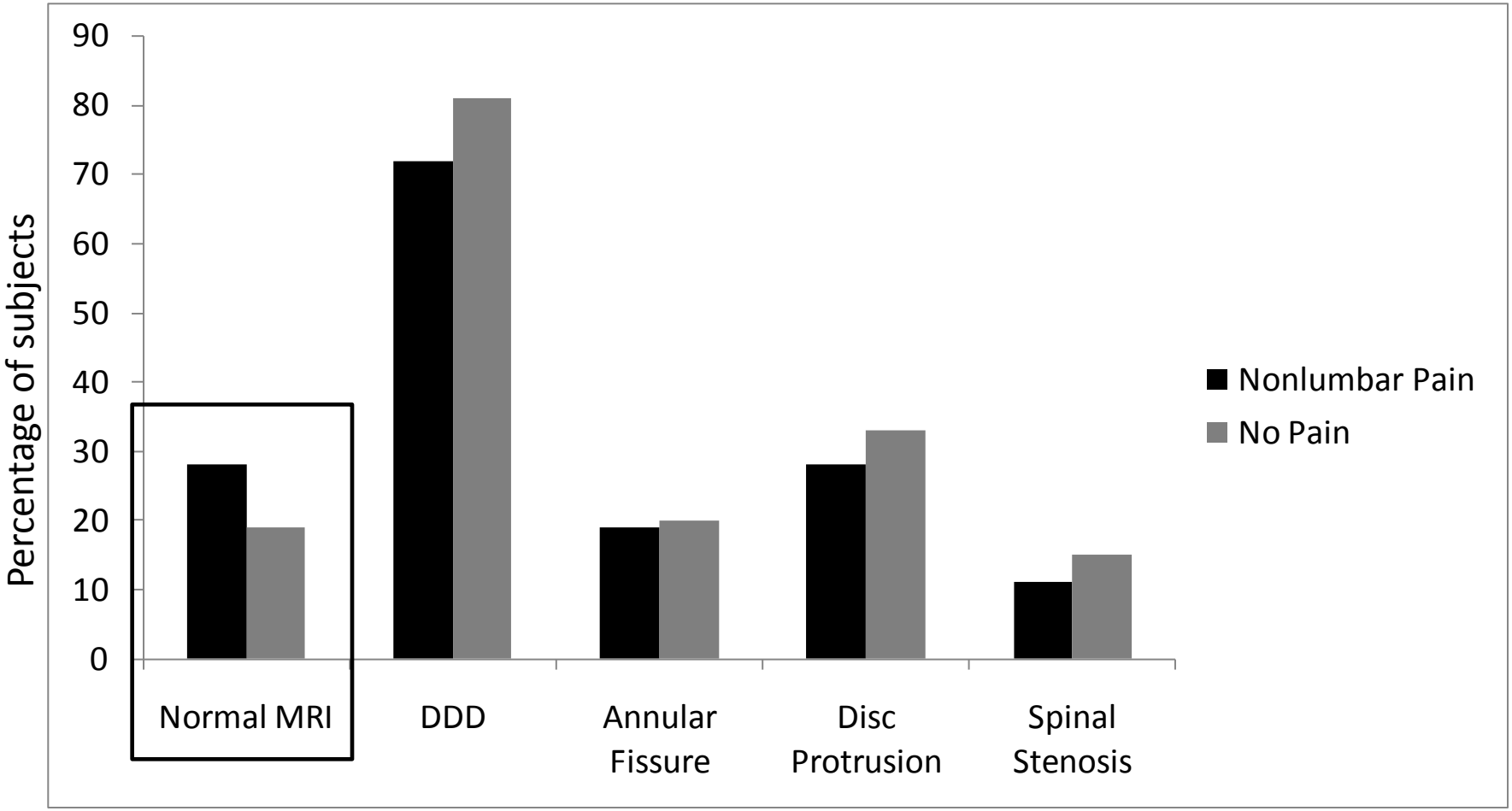
Individual Differences in Experimental Pain Responses

	Mean	Minimum	Maximum
Heat Pain Thr (°C)	**41.6**	**33.6**	**48.9**
Heat Pain Tol (°C)	**46.5**	**34.6**	**52***
PPT Trapezius (kg)	**6.0**	**1.8**	**10.2***
Ischemic Pain Tol (sec)	**468.2**	**46.0**	**900***
Cold Pain Tol (sec)	**81.7**	**6.0**	**300***
Rating 49 C (0-100)	**71.4**	**4.7**	**100***
Rating 52 C (0-100)	**81.2**	**6.2**	**100***

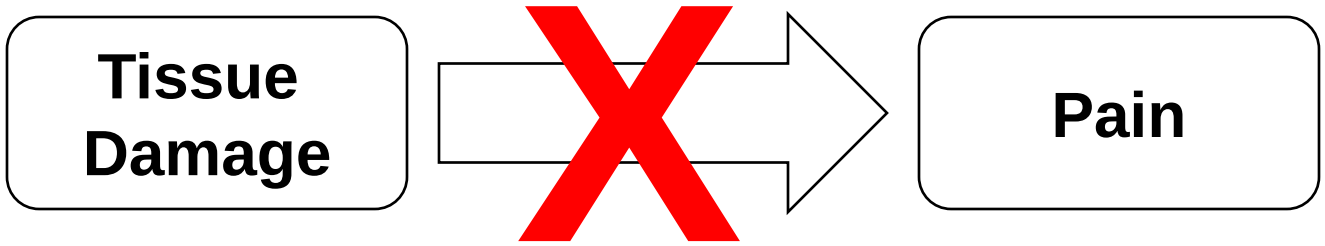
Radiographic vs. Symptomatic Osteoarthritis (Lawrence, et al, 2008)



Abnormal Lumbar MR Findings in Subjects with no Low Back Pain (Carragee, et al, 2006)



Biomedical Model



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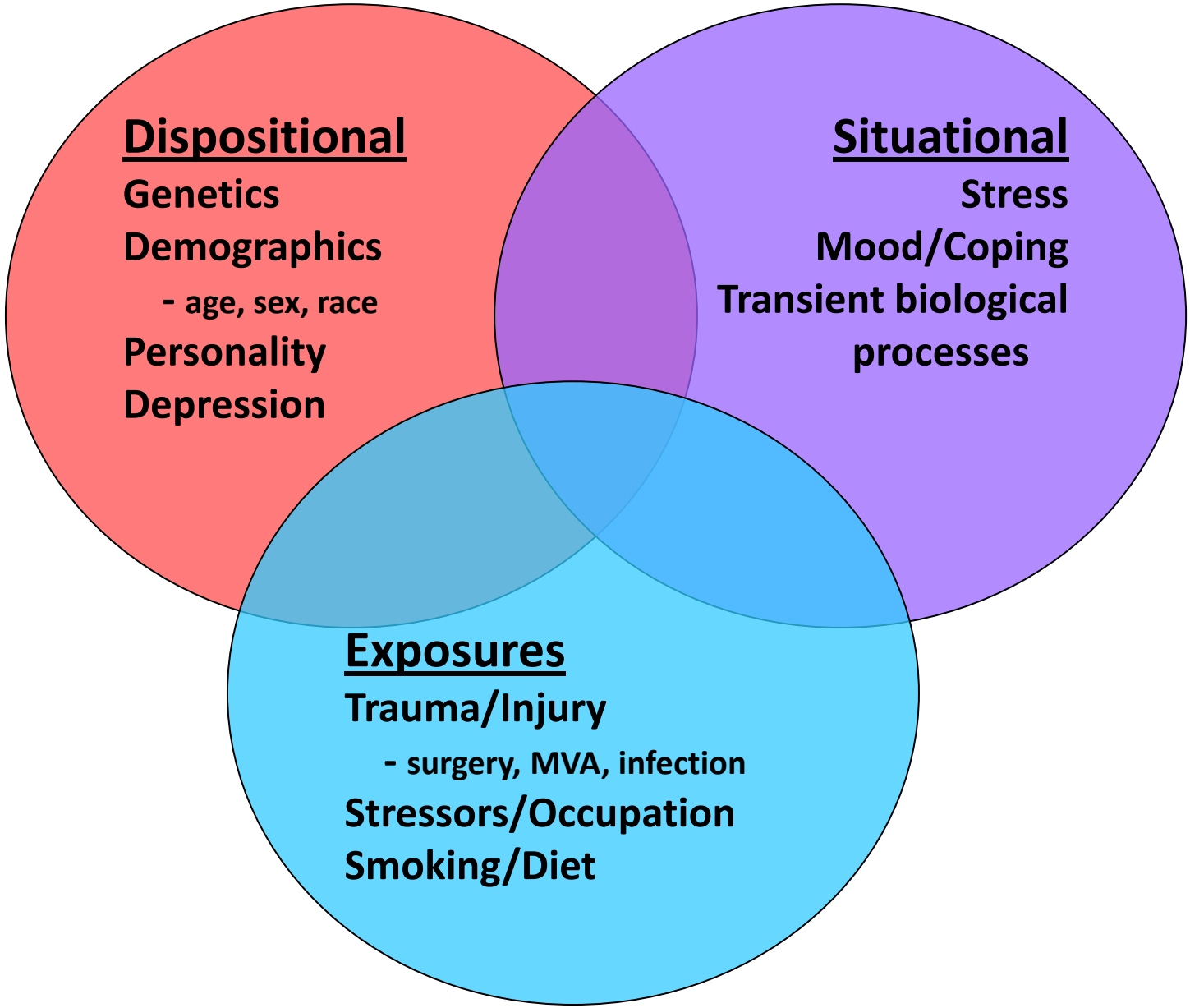
Types of Risk Factors



Dispositional Influences on Pain

- Age
- **Sex/Gender**
- Ethnicity
- **Pain Sensitivity**
- **Psychological Traits**
- **Genetics**

Sex Differences in Pain Responses

Table 1. Prevalence of Chronic Pain in Representative Samples

Study	Country	Prevalence	Female	Male
Bergman[30]	Sweden	12-month	**38%**	**31%**
Blythe[41,*]	Australia	6-month	20%	17%
Bouhassira[44]	France	Current	**35%**	**28%**
Breivik[47]	Europe	6-month	11%	10%
Gerdle[158]	Sweden	3-month	**59%**	**48%**
Rustoen[351]	Norway	Current	**28%**	**23%**
Smith[377]	United Kingdom	Current	**52%**	**49%**
Tsang[415]	17 countries	12-month	**45%**	**31%**
Von Korff[427]	United States	12-month	20%	18%
Wijnhoven[442]	Netherlands	12-month	**49%**	**41%**

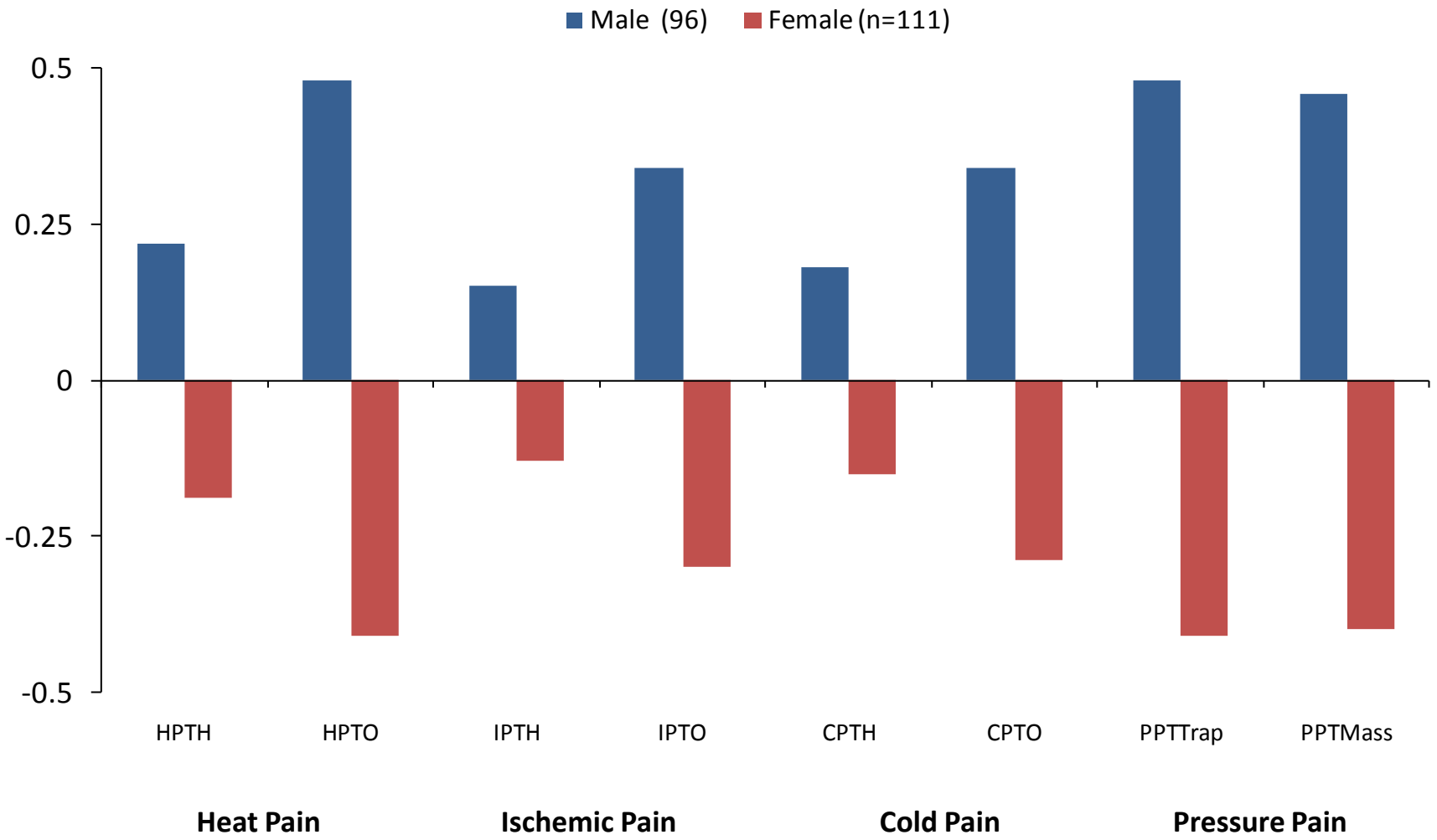
NOTE. **Bolded** numbers reflect significant sex differences in prevalence.
*Blyth et al did not indicate the significance of the difference.

Fillingim, et al, 2009, J Pain, 10: 447-485

Common Chronic Pain Disorders that are More Prevalent in Women

	Prevalence	F:M Ratio
Migraine	15-20%	2-3:1
Tension-Type Headache	4-5%	2:1
Temporomandibular Disorders	4-12%	1.5:1
Irritable Bowel Syndrome	15-20%	2:1
Rheumatoid Arthritis	1%	2.5:1
Osteoarthrits (age > 45)	> 80% (age 65)	1.5:1 – 4:1
Interstitial Cystitis	0.5%	9:1
Fibromyalgia	2-3%	6:1

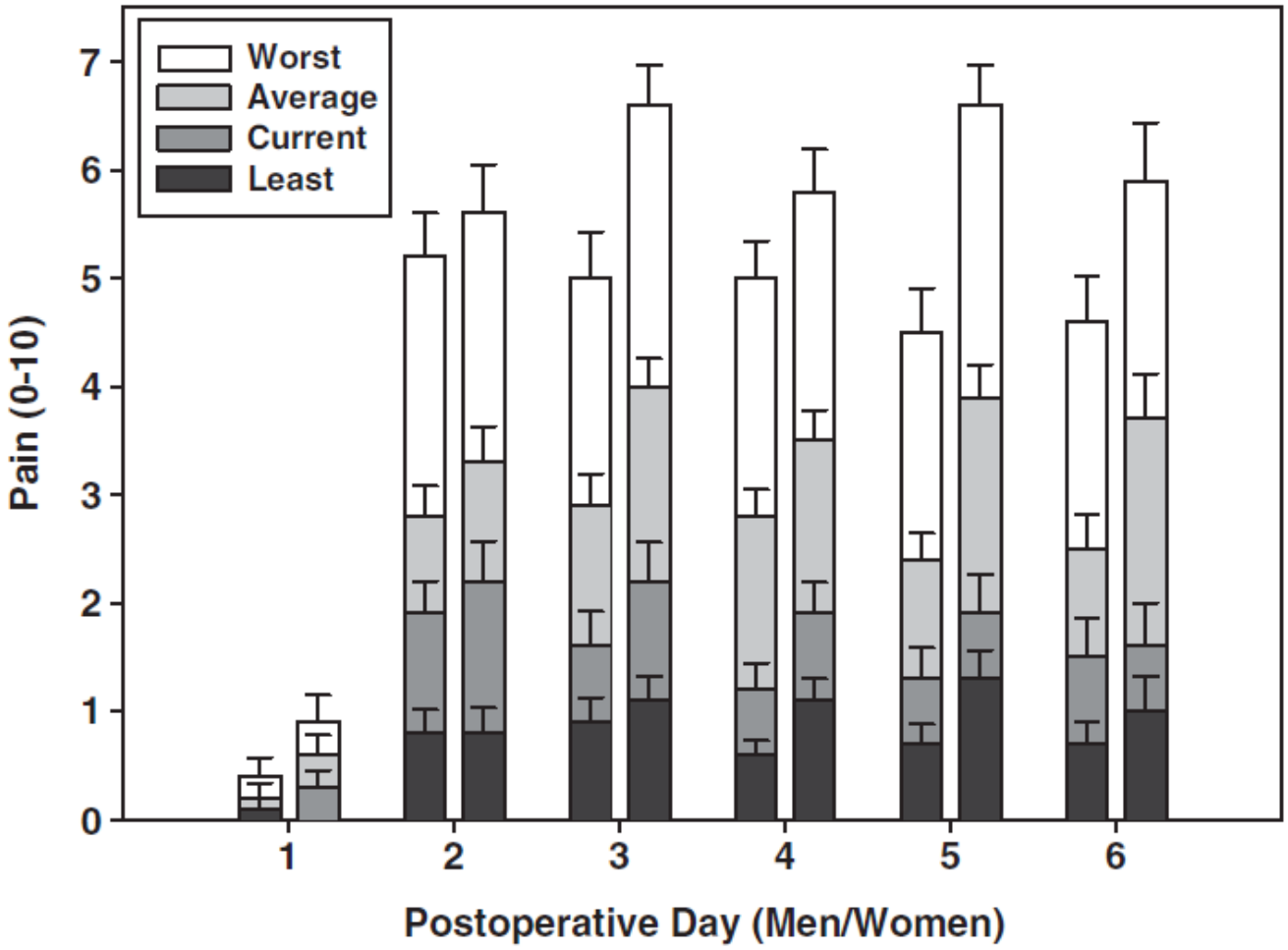
STANDARDIZED PAIN MEASURES ACROSS MULTIPLE PAIN TASKS FOR FEMALES AND MALES



Mean=0, higher numbers reflect higher pain threshold or tolerance

Gender and Post-Thoracotomy Pain

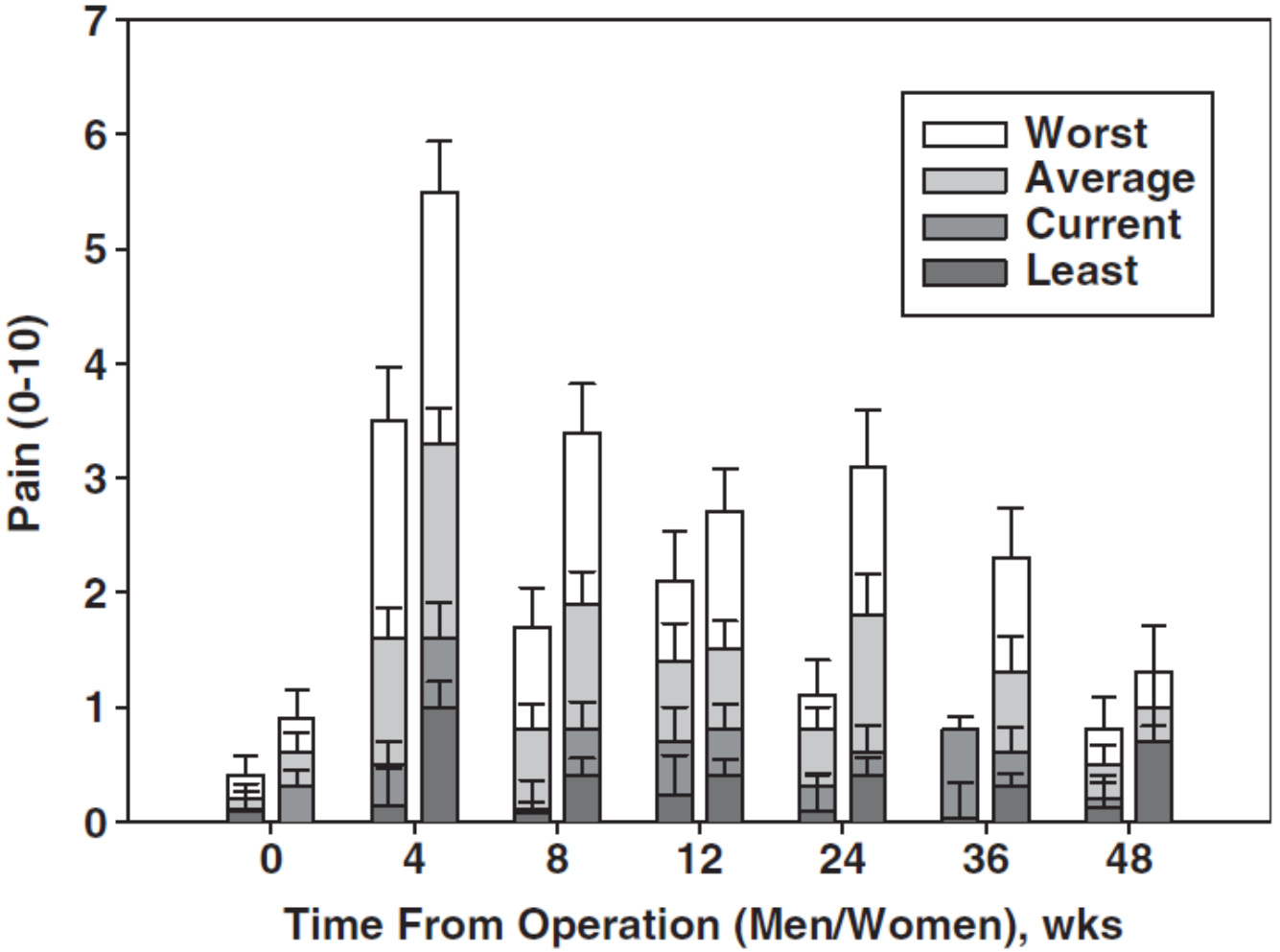
(Ochroch, et al, 2006)



Women (right bar) reported more acute pain than men (left bar)

Gender and Post-Thoracotomy Pain

(Ochroch, et al, 2006)



Women (right bar) reported more long-term pain than men (left bar)

Psychological Factors

Psychological Factors and Risk for Low Back Pain (Linton, 2000)

1. Psychosocial variables associated with reported onset of back and neck pain and transition from acute to chronic pain disability. (Level A evidence)
2. Psychosocial variables generally have more impact than biomedical or biomechanical factors on back pain disability. (Level A)
3. Cognitive factors (attitudes, cognitive style, fear avoidance beliefs) (Level A)
4. Self-perceived poor health (Level A)
5. Depression, anxiety, negative emotions (Level A)
6. Personality and traits (Level C)
7. Sexual and/or physical abuse (Level D)
8. Psychosocial factors as risk factors for long-term pain and disability. (Level A)

Level A: evidence from two or more good-quality prospective studies
Level C: inconclusive data
Level D: no studies available meeting criteria

Occupational Factors and Risk for Low Back Pain (Linton, et al, 2001)

Factor	Evidence
Job Satisfaction	Strong Evidence (13/14 studies)
Monotonous Work	Strong Evidence (4/6 studies)
Work Relations	Strong Evidence (5/6 studies)
Perceived Demands	Strong Evidence (3/3 studies)
Control	Moderate Evidence (2/2)
Work Pace	Moderate Evidence (2/3)
Occupational Stress	Strong Evidence (3/3 studies)
Perceived Ability to Work	Strong Evidence (3/3 studies)
Belief that Work is Dangerous	Moderate Evidence (2/2)

Spinal Mechanical Load and Risk for Low Back Pain (Bakker, et al, 2009)

Factor	Evidence
Heavy Physical Work	Conflicting Evidence
Standing/Walking at Work	Strong Evidence for no association
Sitting at Work	Strong Evidence for no association
Whole Body Vibration at Work	Conflicting Evidence
Bending/Twisting at Work	Conflicting Evidence
Nursing Tasks	Conflicting Evidence
Leisure Sport/Exercise	Strong Evidence for no association
Leisure Activities	Conflicting Evidence

Risk Factors for Chronic Widespread Pain

Category	Specific Risks	Reference
Demographics	Gender and older age (in kids) Gender (in adults) SES (mediated by psych factors)	Mikkelson, et al, 2008 Davies, et al, 2009 Davies, et al, 2009
Childhood Events	Financial difficulties Maternal death Institutional Care Multiple somatic symptoms	Jones, et al, 2007; 2009
HPA Axis Function	Low Morning Cortisol High Evening Cortisol High post-dex. cortisol	McBeth, et al, 2007
Psychological Distress	Depression	Mikkelson, et al, 2008; McBeth, et al, 2007
Pain Sensitivity	Tender Point Count (but not PPT)	Gupta, et al, 2007

Laboratory Pain Sensitivity

Reduced Endogenous Pain Modulation as a Risk Factor for Chronic Post-Thoracotomy Pain (Yarnitsky, et al, 2008)

DNIC predicted development of chronic pain (pain rating > 20) 7 months after thoracotomy

Table 3
Reduced model based on only DNIC and acute pain as predictors of chronic pain

Term	Chi-square	*p*	Odds ratio	OR lower 95% CI	OR upper 95% CI
Intercept	2.47	0.12			
DNIC	9.20	0.0024	0.52	0.33	0.77
Acute pain	9.20	0.0024	1.80	1.28	2.77

The odds ratios are based on changes of 10 U for both DNIC and acute pain, i.e., 10-point changes on scales ranging from −100 to 100 and 0 to 100, respectively.

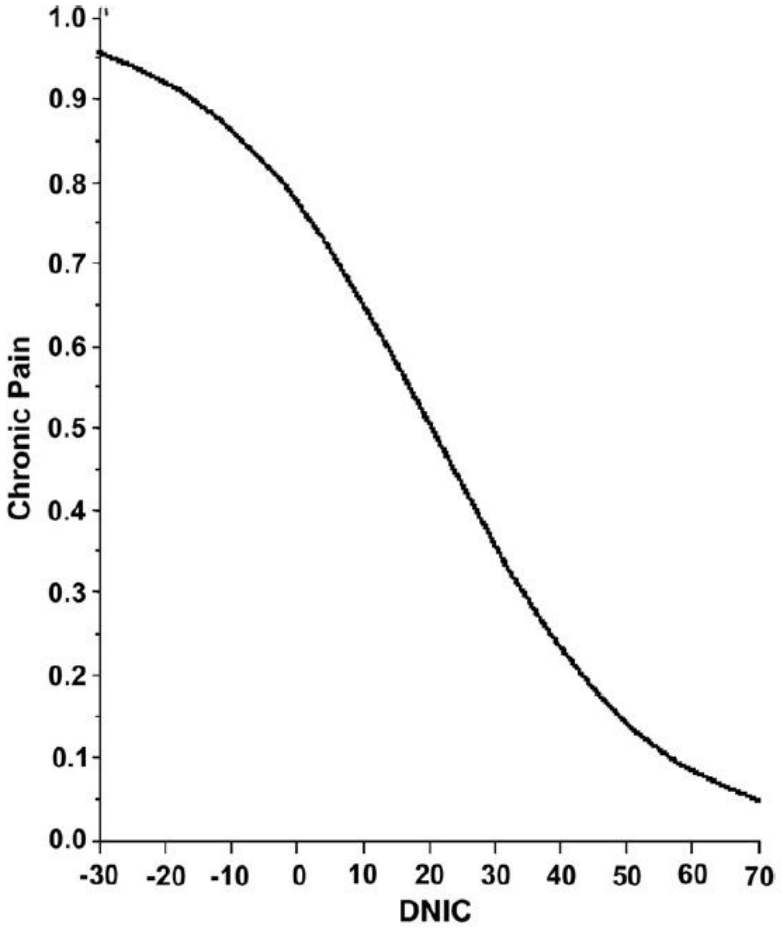


Fig. 2. Logistic regression probability plot relating DNIC to the probability of development of chronic pain.

Reduced cold pressor pain tolerance in non-recovered whiplash patients: a 1-year prospective study

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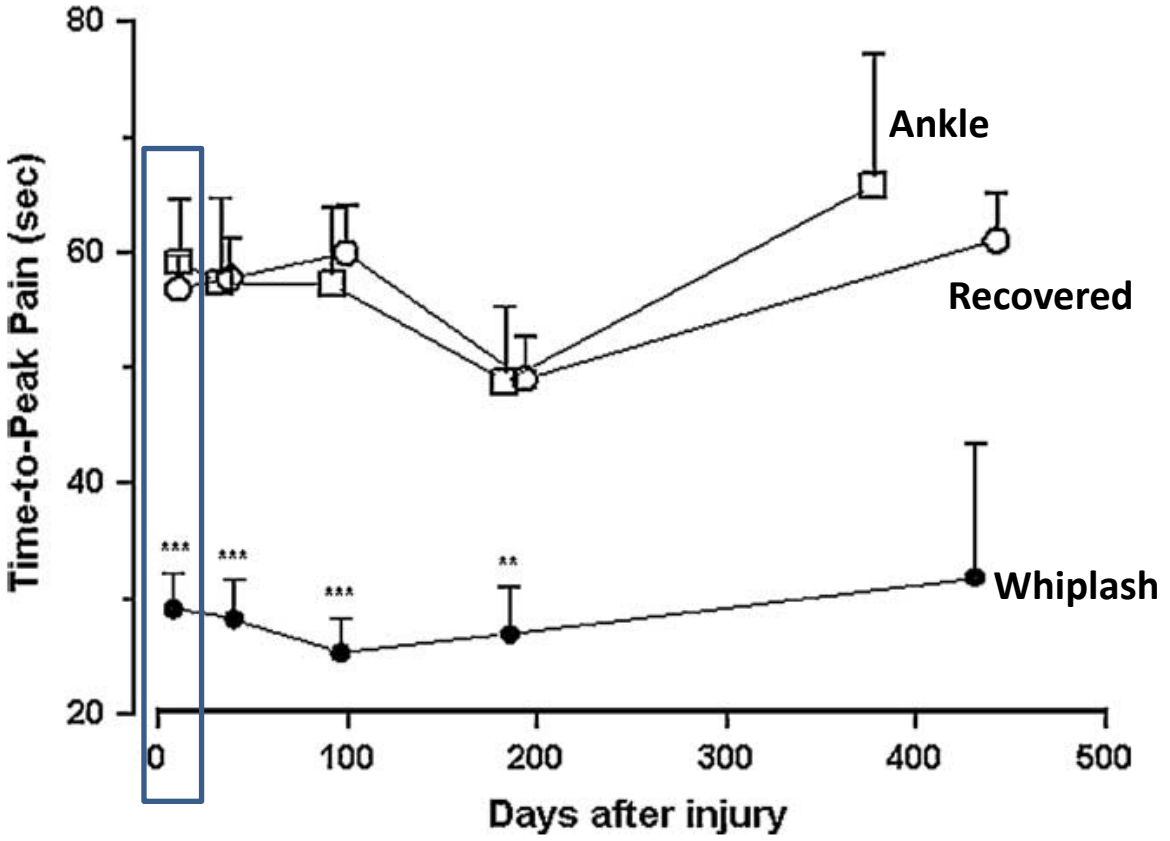
Patients with long-lasting whiplash symptoms after MVA had lower cold pressor pain tolerance at time 0 (1 week after injury), compared to recovered patients and a comparison group of patients with ankle injury



Genetic Factors

Advantages of Genetic Markers as Risk Factors

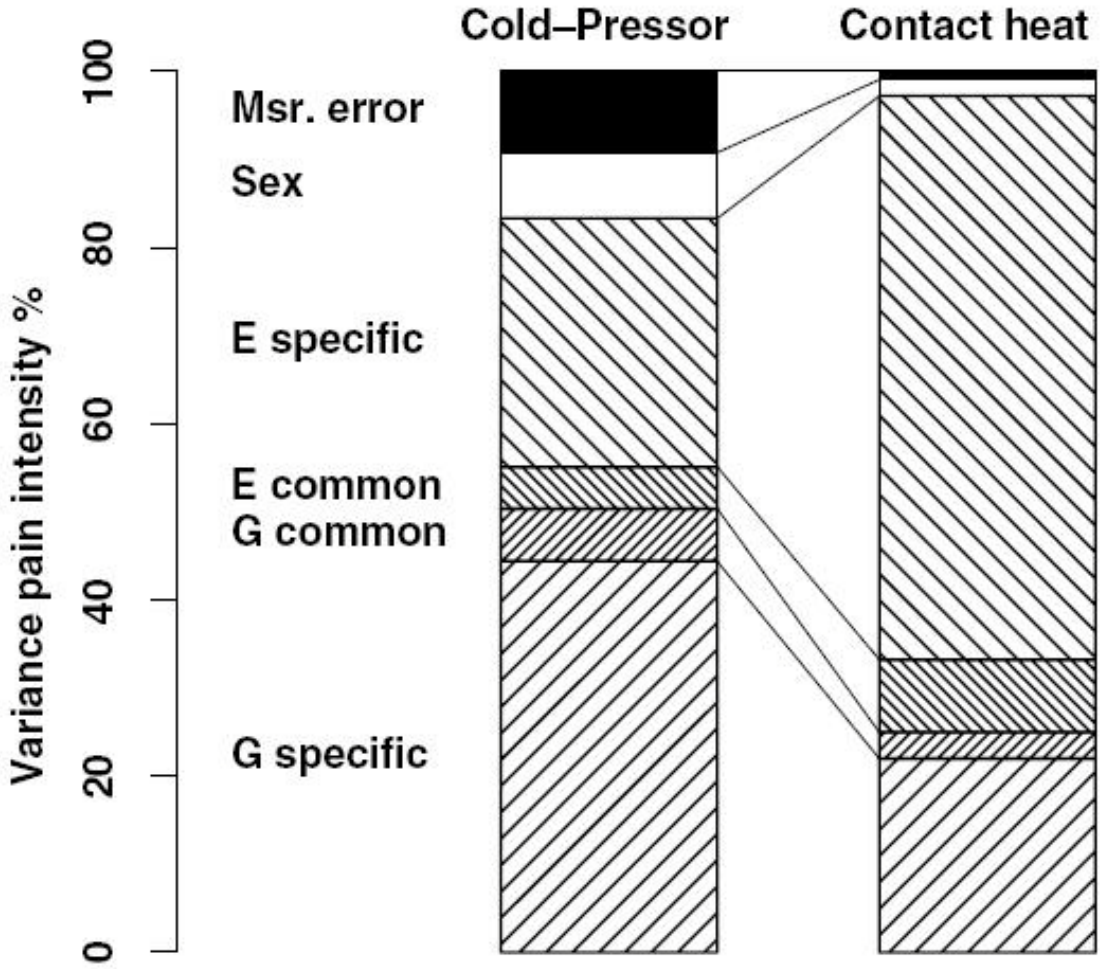
- No chicken and egg problem
- Highly reliable
- May reveal pathophysiology
- Can indicate new biological treatment targets

Heritability of Clinical Pain Conditions

Reference	Pain Condition	Study Design	Heritability Estimate
Mulder, et al 2003; Nyholt, et al 2004	Migraine	Twin Studies	.34 - .57
Fejer et al, 2006; MacGregor et al, 2004	Neck Pain	Twin Studies	.36 - .58
Hestbaek et al, 2004; MacGregor et al, 2004	Low Back Pain	Twin Studies	.40 - .68
Kato et al, 2006	Widespread Pain	Twin Studies	.48 - .54
Zondervan, et al 2005	Pelvic Pain	Twin Study	.41
Hakim, et al, 2002	Carpal Tunnel	Twin Study	.46

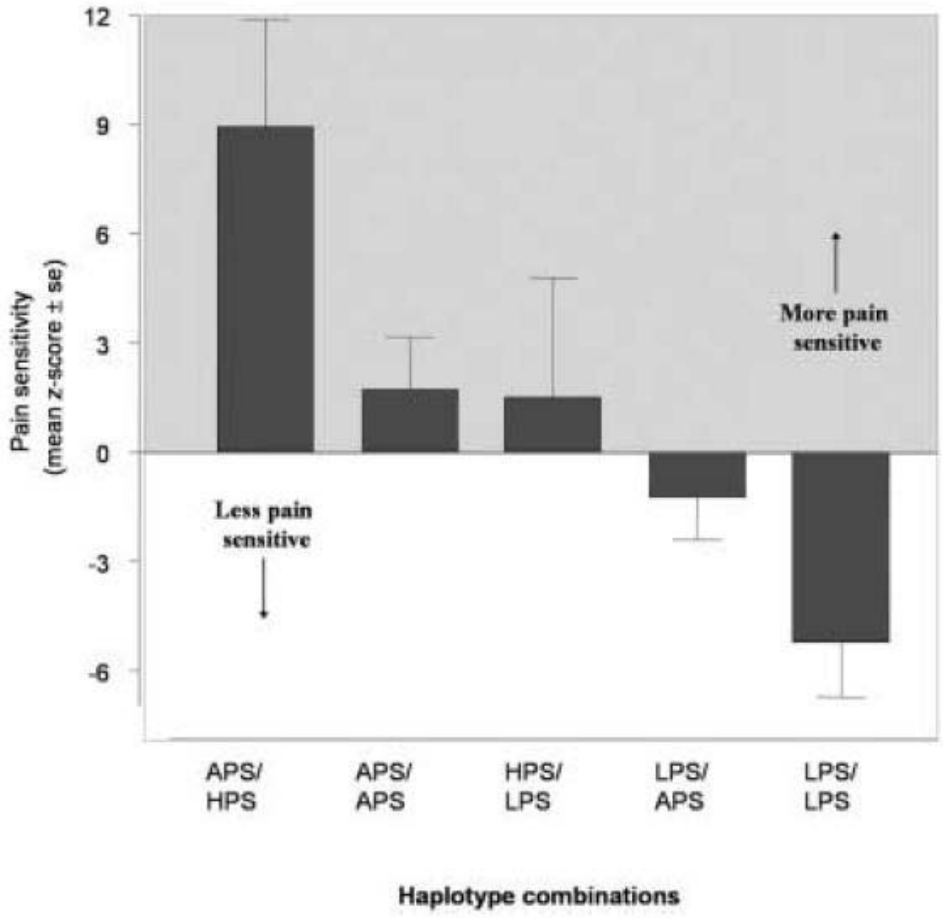
Sources of Variability in Heat and Cold Pain Ratings (Nielsen, et al, 2008)

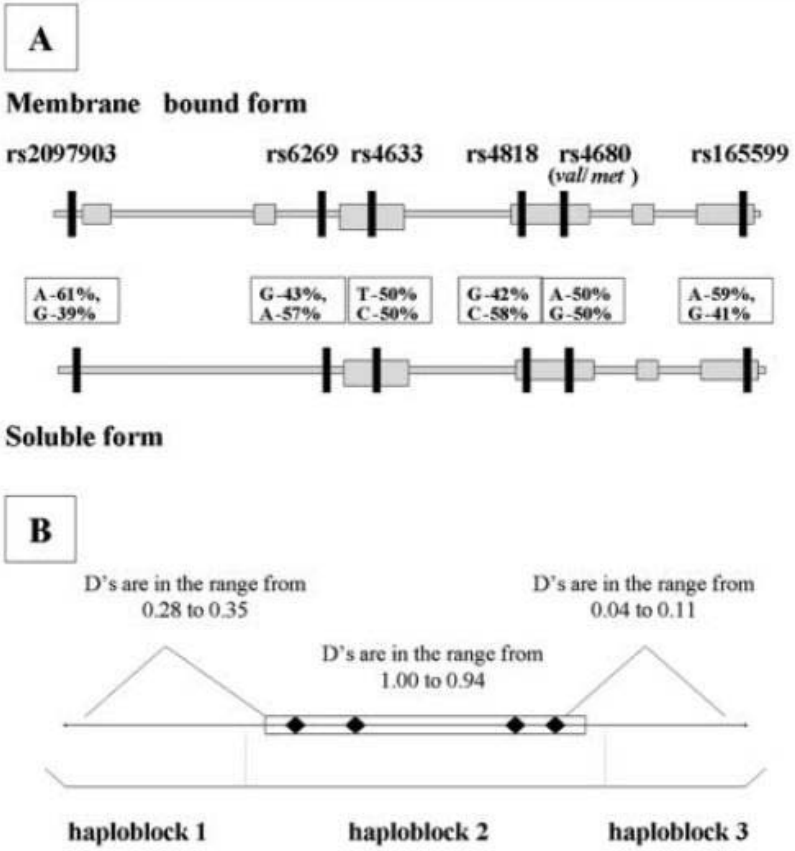
- Cold Pain ratings ranged from 0 to 100
- Heat pain ratings ranged from 0 to 95.2



COMT Haplotype and TMD Incidence

(Diatchenko, et al, 2005)

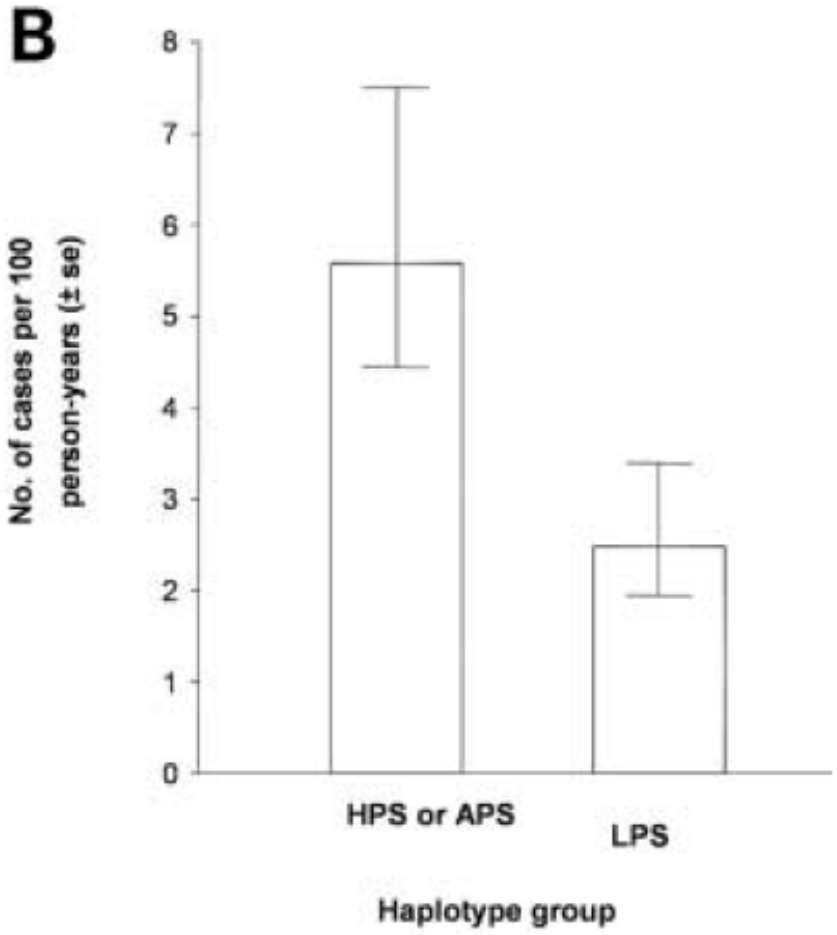




COMT Haplotype and TMD Incidence

(Diatchenko, et al, 2005)

Individuals with at least one low pain sensitive (LPS) haplotype were at lower risk for development of TMD compared to those with no LPS haplotypes.



COMT Haplotype and Symptoms after Motor Vehicle Accident

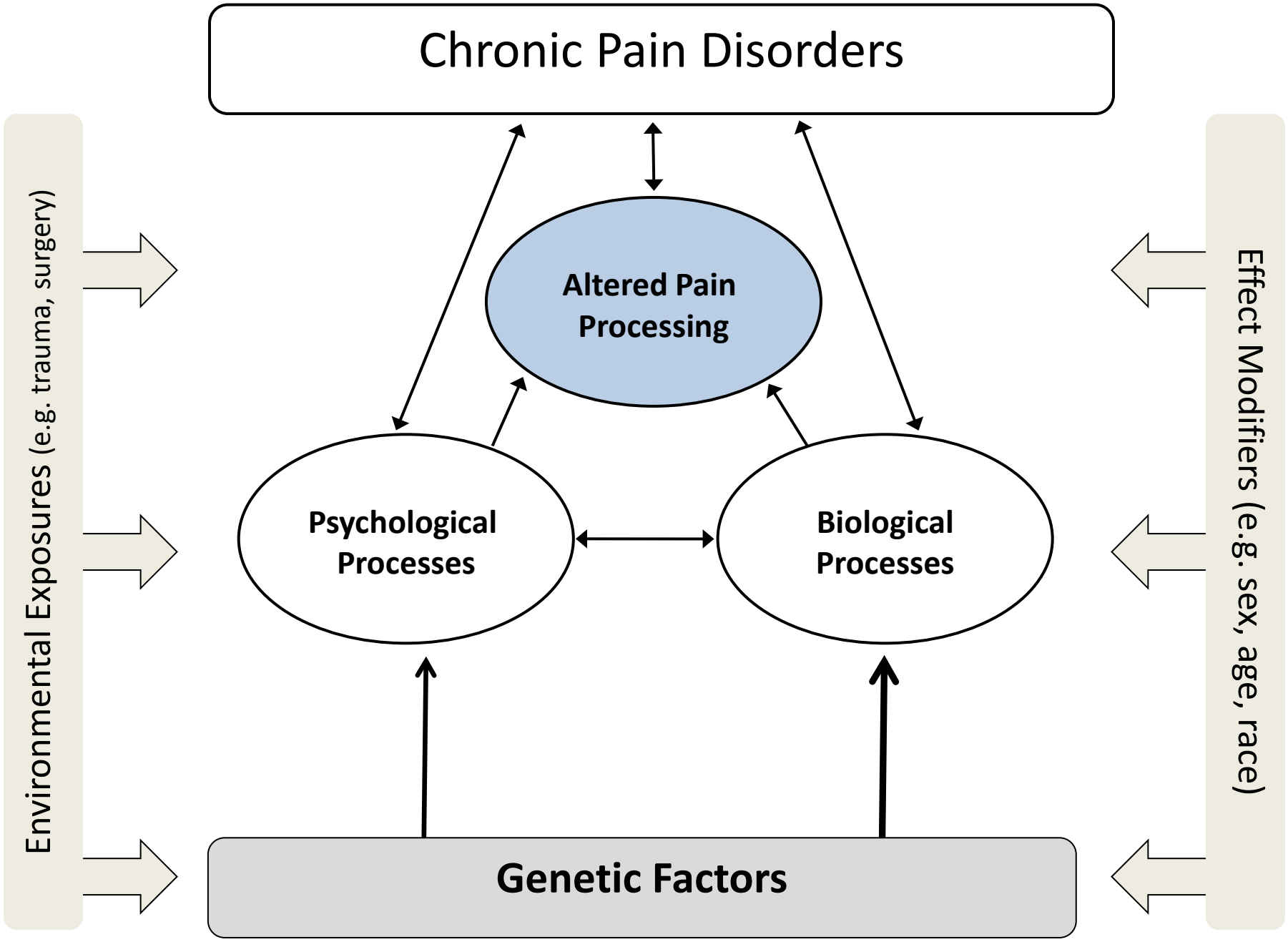
Individuals with a "COMT pain vulnerable genotype" reported greater neck pain, headache, and dizziness in the emergency room after MVA.

(McLean, et al, 2010, J Pain, in press)

Table 3. Final Stepwise Logistic Regression Models (*P* in = .1, *P* out = .15) Assessing Predictors of Emergency Department Somatic Symptoms After Motor Vehicle Collision

Dependent Variable*	Independent Variable	Exp (β)	Wald	P
Neck pain†	Constant	1.889	1.046	.306
	Income	.728	3.058	.080
	COMT pain vulnerable genotype	3.326	5.359	.021
Headache†	Constant	.577	2.878	.090
	COMT pain vulnerable genotype	2.667	4.146	.042
Dizziness†	Constant	.079	17.924	<.001
	COMT pain vulnerable genotype	4.222	3.942	.047

*Candidate predictors for each model: Demographic characteristics (age, gender, income, education), crash and injury characteristics (highest AIS score, car drivable at scene [yes/no], airbags deployed [yes/no]), and presence or absence of COMT pain vulnerable genotype.
†Dependent variable outcomes were moderate or severe [yes/no].


Chronic Pain Disorders
Environmental Exposures (e.g. trauma, surgery)
Effect Modifiers (e.g. sex, age, race)
Altered Pain Processing
Psychological Processes
Biological Processes
Genetic Factors

Summary of Findings

- Pain is characterized by robust individual differences, such that a given exposure can produce widely different pain outcomes
- Numerous factors contribute to individual differences and increase risk for chronic pain
  - Gender
  - Psychological Factors
  - Pain Sensitivity
  - Genetics
- A better understanding of individual differences may lead to improved chronic pain prevention and treatment efforts

Thank You