BURDEN OF ILLNESS

Overview

Consequences of Unrelieved Pain



Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.* The National Academies Press; Washington, DC: 2011.

Impact of Chronic Pain



1. Douglas C et al. J Neurosci Nurs 2008; 40(3):158-68; 2. Tang NKY et al. J Sleep Res 2007; 16(1):85-95;

3. Hawker GA et al. Osteoarth Cartil 2008; 16(4):415-22; 4. Munce SE et al. J Occup Environ Med 2007; 49(11):1206-1211;

5. Stewart WF et al. JAMA 2003; 290(18):2443-54; 6. Ritzwoller DP et al. BMC Musculoskelet Disord 2006; 7:72-81.

Physical Burden

Impact of Acute Pain on Daily Activities



*Patients who responded "Sometimes", "Often" or "Always" Adapted from: McCarberg BH *et al. Am J Ther*. 2008; 15(4):312-20.

Chronic Pain Has a Significant Impact on Daily Functioning



BPI = Brief Pain Inventory, which scores extent pain interferes with activities in last 24 hours from 0 (does not interfere) to 10 (completely interferes) Adapted from: Smith BH *et al. Clin J Pain* 2007; 23(2):143-9.

Pain and Disability*



*Extent of pain-related disability among adults with pain in the United States, 2009

Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research.* The National Academies Press; Washington, DC: 2011.

Pain and Quality of Life



Higher score represents better health state; *p* **<0.001 analysis of variance across 3 groups for each domain.** Smith BH *et al. Clin J Pain* 2007; 23(2):143-9.

Pain: A Significant Predictor of Premature Mortality



ALTD = acutely life-threatening disease; VAS = visual analog scale

Sokka T, Pincus T. Poster presentation at American College of Rheumatology 2005.

Economic Burden

Pain Reduces Productivity

| | Type of pain | | | | | | | |
|--|--------------|-------------|-------------|-------------|-------------|--|--|--|
| | Headache | Arthritis | Back | Other* | Any | | | |
| Total lost productive time | | | | | | | | |
| >0 h/week due to pain in past 2 weeks | 5.43 | 2.03 | 3.20 | 2.02 | 12.68 | | | |
| ≥2 h/week due to pain in past 2 weeks | 2.72 | 1.23 | 1.97 | 1.32 | 7.24 | | | |
| Hours per worker per week, mean (SE) | 3.51 (0.10) | 5.19 (0.25) | 5.28 (0.25) | 5.47 (0.22) | 4.56 (0.09) | | | |
| Missed workdays | | | | | | | | |
| ≥1 day/week due to pain in past 2 weeks | 0.39 | 0.11 | 0.39 | 0.23 | 1.12 | | | |
| ≥2 days/week due to pain in past 2 weeks | 0.02 | 0.01 | 0.06 | 0.03 | 0.12 | | | |
| Absent, hours per worker per week, mean (SE) | 0.64 (0.05) | 0.69 (0.12) | 1.35 (0.16) | 1.20 (0.13) | 0.92 (0.05) | | | |
| Reduced performance at work due to pain, hours per worker per week, mean (SE) | 2.87 (0.09) | 4.50 (0.26) | 3.93 (0.19) | 4.27 (0.22) | 3.54 (0.09) | | | |

Denominator includes 28,902 occupation-eligible participants *Includes unspecified musculoskeletal pain SE = standard error Stewart WF *et al. JAMA* 2003; 290(18):2443-54.

Comorbidities

Pain Comorbidities

| Pain | Comorbid pain conditions (%) | | | | | | | | | Maan | |
|---------------------------|------------------------------|-------|------|-------|------|------|----------|-----|-----|------|------|
| cohorts | Stroke | LR | CR | Fibro | OA | LBP | Migraine | RA | PBS | IC | Mean |
| Diabetic neuropathy | 11.7 | 3.3 | 1.3 | 2.3 | 16.0 | 13.3 | 1.0 | 0.8 | 1.8 | 0.1 | 1.6 |
| Postherpetic neuropathy | 7.7 | 4.7 | 1.7 | 2.8 | 14.3 | 14.5 | 1.7 | 1.4 | 1.6 | 0.2 | 1.57 |
| Trigeminal neuralgia | 9.3 | 3.2 | 2.3 | 3.4 | 12.4 | 11.7 | 4.7 | 0.7 | 2.1 | 0.3 | 1.6 |
| HIV-associated | 8.1 | 5.1 | 4.6 | 20.8 | 28.6 | 52.8 | 14.3 | 3.2 | 1.9 | 0.8 | 2.5 |
| MS-associated | 8.5 | 10.7 | 6.8 | 14.1 | 38.0 | 44.8 | 23.5 | 5.7 | 5.0 | 0.6 | 2.7 |
| Stroke-associated | 100.0 | 7.0 | 6.6 | 6.1 | 53.3 | 39.2 | 21.7 | 2.9 | 2.6 | 0.2 | 2.5 |
| Lumbar radiculopathy | 4.8 | 100.0 | 6.0 | 5.0 | 24.5 | 46.8 | 2.6 | 1.0 | 1.8 | 0.2 | 2.0 |
| Complex regional syndrome | 4.6 | 9.2 | 6.3 | 9.6 | 20.5 | 24.1 | 5.6 | 1.5 | 1.7 | 0.4 | 1.9 |
| Spinal cord injury | 5.4 | 7.9 | 10.9 | 8.2 | 43.8 | 68.9 | 2.1 | 0.9 | 2.1 | 0.0 | 2.6 |
| Surgically-induced | 4.3 | 2.1 | 1.2 | 1.6 | 15.6 | 9.1 | 2.0 | 0.3 | 1.6 | 0.3 | 1.4 |
| Phantom limb pain | 12.7 | 4.9 | 3.9 | 5.4 | 16.1 | 24.9 | 0.5 | 0.5 | 2.0 | - | 1.8 |

Note: infrequent comorbid conditions were omitted from the comorbid pain conditions in the table. CR = cervical radiculopathy; HIV = human immunodeficiency virus; IC = interstitial cystitis; Fibro = fibromyalgia; LR = lumbar radiculopathy; MS = multiple sclerosis; OA = osteoarthritis; PBS = painful bladder syndrome; RA = rheumatoid arthritis Davis JA et al. J Pain Res 2011; 4:331-45; Dworkin RH et al. J Pain 2010; 11(4):360-8; Riley GF. Med Care 2009; 47(7 Suppl 1):S51-5.

Pain Comorbidities (cont'd)

| Pain | Comorbid Pain Conditions (%) | | | | | | | | | Maara | |
|---------------------------|------------------------------|------|-------|-------|-------|-------|----------|-------|-------|-------|------|
| Cohorts | Stroke | LR | CR | Fibro | OA | LBP | Migraine | RA | PBS | IC | mean |
| Cervical radiculopathy | 3.5 | 7.4 | 100.0 | 5.6 | 23.7 | 18.0 | 3.4 | 0.9 | 1.7 | 0.2 | 1.7 |
| Fibromyalgia | 3.4 | 4.7 | 3.3 | 100.0 | 17.3 | 21.8 | 4.5 | 2.1 | 2.2 | 0.4 | 1.7 |
| Osteoarthritis | 6.4 | 4.8 | 2.6 | 3.3 | 100.0 | 19.3 | 1.7 | 2.1 | 2.1 | 0.2 | 1.5 |
| Low back | 4.2 | 9.8 | 2.1 | 4.0 | 17.0 | 100.0 | 2.7 | 0.8 | 2.1 | 0.2 | 1.5 |
| Migraine | 3.1 | 2.3 | 2.1 | 3.9 | 7.5 | 13.1 | 100.0 | 0.7 | 1.9 | 0.3 | 1.4 |
| Rheumatoid arthritis | 5.0 | 3.0 | 1.4 | 3.8 | 21.0 | 12.8 | 1.9 | 100.0 | 1.7 | 0.2 | 1.6 |
| Ankylosing spondylitis | 3.9 | 10.3 | 2.9 | 6.3 | 20.4 | 31.9 | 2.9 | 3.2 | 2.0 | 0.3 | 1.9 |
| Psoriatic arthropathy | 2.6 | 1.8 | 1.5 | 2.5 | 16.0 | 10.6 | 1.6 | 17.1 | 1.8 | 0.1 | 1.6 |
| Cancer | 3.6 | 3.6 | - | 3.6 | 3.6 | 10. | 10.7 | - | 3.6 | - | 1.4 |
| Irritable bowel syndrome | 3.0 | 2.4 | 1.5 | 3.6 | 9.0 | 12.2 | 3.6 | 0.6 | 2.5 | 0.5 | 1.4 |
| Painful bladder syndrome | 1.9 | 2.1 | 1.1 | 2.8 | 6.0 | 12.2 | 3.6 | 0.7 | 100.0 | 12.8 | 1.5 |
| Interstitial cystitis | 3.3 | 3.5 | 1.9 | 5.1 | 11.1 | 14.7 | 4.3 | 0.8 | 10.7 | 100.0 | 1.6 |

Note: infrequent comorbid conditions were omitted from the comorbid pain conditions in the table.

CR = cervical radiculopathy; IC = interstitial cystitis; Fibro = fibromyalgia; LR = lumbar radiculopathy; MS = multiple sclerosis; OA = osteoarthritis; PBS = painful bladder syndrome; RA = rheumatoid arthritis

Davis JA et al. J Pain Res 2011; 4:331-45; Dworkin RH et al. J Pain 2010; 11(4):360-8; Riley GF. Med Care 2009; 47(7 Suppl 1):S51-5.

Inter-relationship Between Pain, Sleep, and Anxiety/Depression



Nicholson B, Verma S. Pain Med 2004; 5(Suppl 1):S9-27.

Pain Conditions Have Sleep and Mental Health Comorbidities

| | | | | D | epression (% | | | |
|---------------------------|--------------------------------|---|---|------|---------------------------------|-------|---------------------------------|-------------|
| Pain cohorts | >1 sleep comorbidity (%) | >1 mental health comorbidity (%) | Mental health condition Mean (SD) | MDD | Other depressive symptoms | Total | Other psych disorders (%) | Anxiety (%) |
| Diabetic neuropathy | 11.4 | 6.7 | 1.4 (0.8) | 4.3 | 3.6 | 7.0 | 6.2 | 3.8 |
| Postherpetic neuropathy | 6.0 | 14.8 | 1.4 (0.7) | 3.0 | 3.2 | 5.4 | 5.7 | 3.9 |
| Trigeminal neuralgia | 6.5 | 6.4 | 1.4 (0.7) | 4.1 | 3.6 | 7.1 | 5.6 | 4.9 |
| HIV-associated | 5.9 | 42.6 | 1.8 (1.2) | 14.0 | 21.0 | 27.2 | 10.0 | 12.7 |
| MS-associated | 11.6 | 34.8 | 1.7 (1.1) | 8.8 | 11.0 | 17.0 | 14.4 | 12.8 |
| Stroke-associated | 8.5 | 33.7 | 1.5 (0.9) | 6.0 | 6.6 | 11.5 | 18.2 | 6.9 |
| Lumbar radiculopathy | 8.1 | 17.1 | 1.4 (0.7) | 4.5 | 3.7 | 7.5 | 4.4 | 5.6 |
| Complex regional syndrome | 9.0 | 30.9 | 1.5 (0.8) | 9.6 | 8.6 | 16.0 | 7.8 | 9.0 |
| Spinal cord injury | 8.5 | 29.6 | 1.8 (1.1) | 9.7 | 10.3 | 15.4 | 6.7 | 10.3 |
| Surgically-induced | 6.5 | 16.1 | 1.5 (0.9) | 3.3 | 4.9 | 6.9 | 4.1 | 5.7 |
| Phantom limb pain | 10.2 | 36.1 | 1.5 (0.8) | 8.8 | 9.8 | 15.6 | 11.7 | 9.3 |

HIV = human immunodeficiency virus; MDD = major depressive disorder; MS = multiple sclerosis; SD = standard deviation Davis JA *et al. J Pain Res* 2011; 4:331-45.

Pain Conditions Have Sleep and Mental Health Comorbidities (cont'd)

| Pain Cohorts | >1 sleep comorbidity (%) | >1 mental health comorbidity (%) | Mental health condition Mean (SD) | MDD | Other depressive symptoms | Total | Other psych disorders (%) | Anxiety (%) |
|-----------------------------|--------------------------------|---|---|------|---------------------------------|-------|---------------------------------|-------------|
| Cervical radiculopathy | 7.3 | 16.8 | 1.4 (0.7) | 4.2 | 3.8 | 7.3 | 3.8 | 5.8 |
| Fibromyalgia | 9.5 | 22.9 | 1.5 (0.8) | 6.4 | 5.9 | 10.9 | 5.8 | 8.2 |
| Osteoarthritis | 8.0 | 15.2 | 1.4 (0.7) | 3.5 | 3.4 | 6.2 | 4.8 | 4.5 |
| Low back | 7.3 | 18.4 | 1.4 (0.8) | 4.5 | 4.4 | 7.9 | 4.8 | 6.5 |
| Migraine | 8.0 | 21.9 | 1.5 (0.9) | 6.7 | 6.7 | 11.7 | 5.6 | 9.9 |
| Rheumatoid arthritis | 5.7 | 11.7 | 1.3 (0.7) | 3.2 | 2.8 | 5.5 | 3.5 | 3.6 |
| Ankylosing spondylitis | 7.4 | 17.3 | 1.4 (0.7) | 4.4 | 4.1 | 4.7 | 4.1 | 5.8 |
| Psoriatic arthropathy | 7.6 | 13.3 | 1.3 (0.6) | 3.5 | 3.2 | 6.1 | 2.8 | 3.9 |
| Cancer | 10.7 | 28.4 | 1.8 (0.9) | 10.7 | 14.3 | 14.3 | 17.9 | 3.6 |
| Irritable bowel syndrome | 6.6 | 21.5 | 1.4 (0.8) | 5.7 | 5.5 | 9.9 | 4.6 | 9.7 |
| Painful bladder syndrome | 5.5 | 22.6 | 1.4 (0.8) | 5.2 | 5.3 | 9.2 | 4.7 | 9.6 |
| Interstitial cystitis | 6.8 | 22.3 | 1.4 (0.8) | 6.0 | 4.8 | 9.6 | 5.2 | 8.9 |

MDD = major depressive disorder; SD = standard deviation Davis JA *et al. J Pain Res* 2011; 4:331-45.

Depression and Pain



- Depressive symptoms rather than major depressive disorder
- Mostly musculoskeletal pain

Prevalence of major depressive disorder in patients with chronic pain is 15–50%

 Mostly in patients with multiple pain symptoms

Trivedi MH. Prim Care Companion J Clin Psychiatry 2004; 6(Suppl 1):12-6.

Pain Stimuli Activate Brain Areas Related to Depression



BDI = Beck Depression Inventory; MPFC = medial prefrontal cortex Schweinhardt P *et al. Neuroimage* 2008; 40(2):759-66.

Fear-Anxiety-Avoidance Model



Anxiolytics or cognitive behavioral therapy are useful adjuvant treatments for patients with chronic pain

Asmundson GJG et al. In: Asmundson GJG et al (eds). Understanding and Treating Fear of Pain. Oxford University Press; Oxford, UK: 2004.

Sleep Deprivation and Pain



Call-Schmidt TA, Richardson SJ. Pain Manag Nurs 2003; 4(3):124-33.

Pain Disrupts Sleep

Noxious pain stimuli

Arousal

Delta waves decrease Alpha waves increase

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Pain Disrupts Sleep: Clinical Evidence

Sleep

deprivation

Pain

- Several longitudinal studies have suggested pain intensity prospectively predicts sleep disturbances
- However, prospective studies did not confirm sleep disturbances predict pain intensity
- May explain:
 - Lack of significant analgesic effects of hypnotics
 - Lack of association between cognitive behavioral therapy for insomnia and pain reduction

Drewes AM *et al. Scand J Rheumatol* 1991; 20(4):288-93; Drewes AM *et al. Rheumatology (Oxford)* 2000; 39(11):1287-9; Edinger JD *et al. Arch Intern Med* 2005; 165(21):2527-35; Jungquist CR *et al. Sleep Med* 2010; 11(3):302-9; Moldofsky H *et al. J Rheumatol* 1996; 23(3):529-33; Nicassio PM, Wallston KA. *J Abnorm Psychol* 1992; 101(3):514-20; Quartana PJ *et al. Pain* 2010; 149(2):325-31; Smith MT *et al. Pain* 2008; 138(3):497-506.

Pain Intensity, Sleep Disturbance and Neuropathic Pain



Mean MOS Sleep Scale 9-item index score

Worse sleep

603 patients with neuropathic pain of multiple etiologies MOS = Medical Outcomes Study

Rejas J et al. Eur J Pain 2007; 11(3):329-40.

How Sleep Disruption Contributes to Pain

- Sleep deprivation leads to hyperalgesia
- Relationship between pain and sleep appears to be reciprocal



- Deprivation or disruption of slow-wave sleep and sleep continuity disturbances may be associated with hyperalgesia
- Concurrent management of disturbed sleep and pain may break the vicious circle and alleviate both problems

Kundermann B *et al. Pain Res Manage* 2004; 9(1):25-32; Lautenbacher S *et al. Sleep Med Rev* 2006; 10(5):357-69; Smith MT *et al. Sleep* 2007; 30(4):494-505; Smith MT, Haythornthwaite JA. *Sleep Med Rev* 2004; 8(2):119-32.

Psychiatric Comorbidities Significantly Increase the Impact of Pain on Quality of Life

- Fear of pain has a higher impact on physical functioning than pain itself
- Psychiatric comorbidities significantly increase impact of pain on work and consumption of drugs
- Presence of severe depression and/or anxiety may significantly reduce the efficacy of analgesics

Boulanger L *et al. Curr Med Res Opin* 2009; 25(7):1763-73; Cherkin DC *et al. Spine (Phila Pa 1976)* 1996; 21(24):2900-7; Crombez G *et al. Pain* 1999; 80(1-2):329-39; Druss BG *et al. Am J Psychiatry* 2000; 157(8):1274-8; Edwards RR *et al. Pain*. 2007; 130(1-2):47-55; von Korff M *et al. Pain* 2005; 113(3):331-9.

Summary

Burden of Illness: Summary

- Pain affects every aspect of a patient's life
 - Activities of daily living
 - Ability to work
 - Sleep
 - Psychological well being
- All aspects of pain, sleep and mood in patients suffering from chronic pain must be evaluated
- Addressing pain and comorbidities may improve daily functioning and enhance quality of life