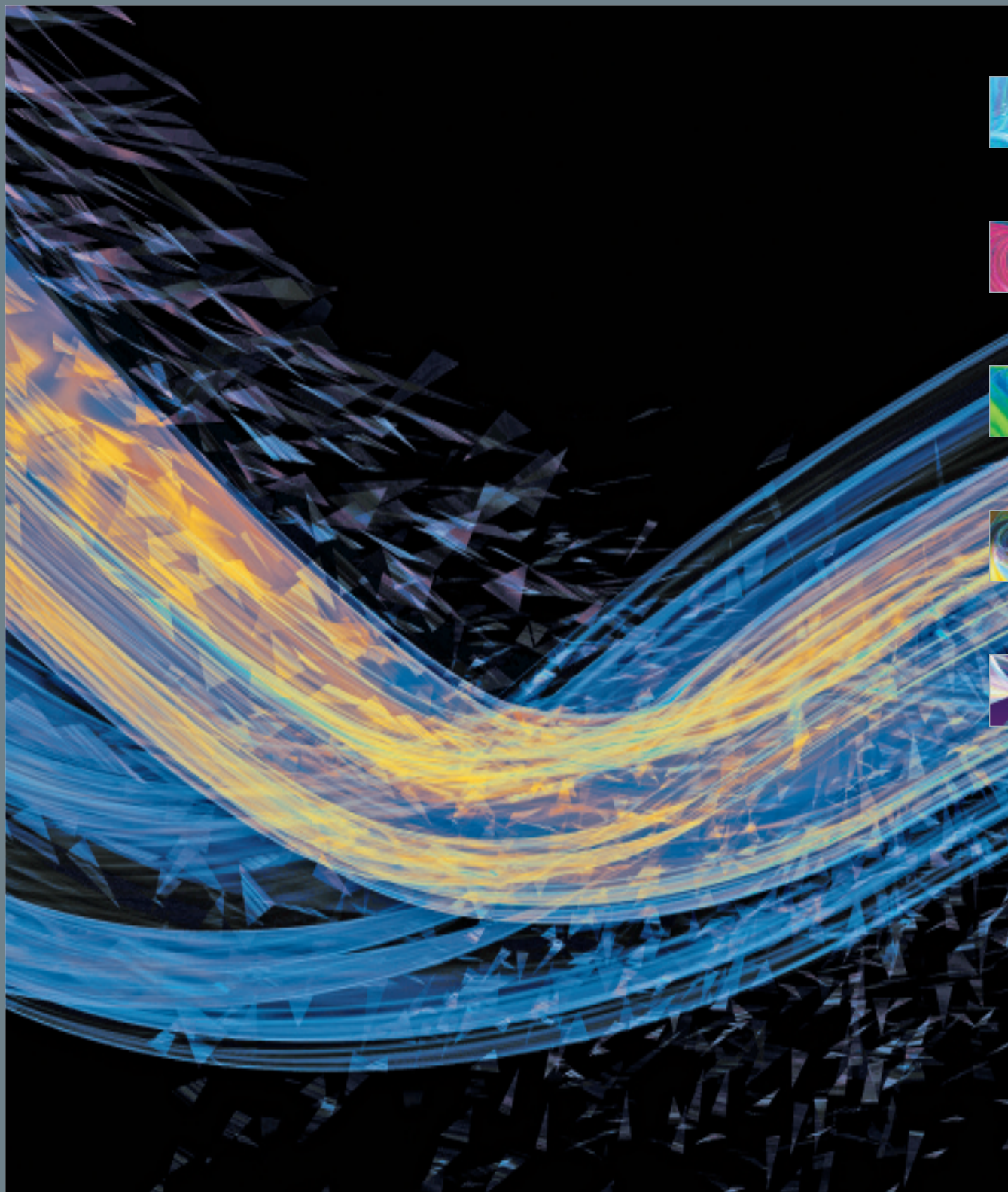
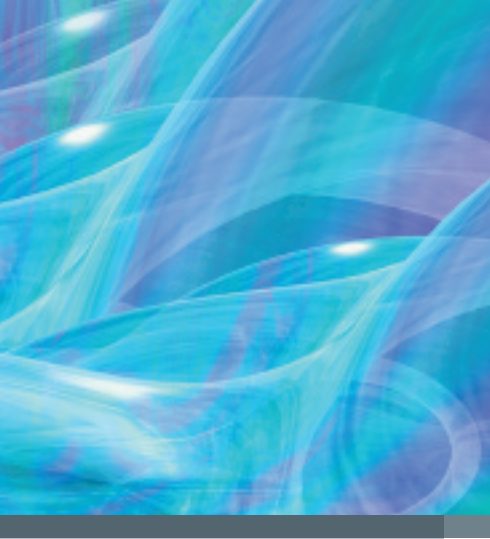


*Chronic Disease and Medical Innovation in an Aging Nation*

# The Silver Book<sup>®</sup>: Persistent Pain







# Introduction

**E**ven though Americans are living longer than ever before, their added years of life are not often enjoyed in good health. Chronic diseases and conditions impact 85% of Americans who often spend their later years at medical visits, in extensive hospital stays, and with disabilities and lost independence. Age-related diseases also impose a huge burden on our health care system and economy—costing our nation \$1.7 trillion a year.

With the leading edge of the Baby Boomers now entering Medicare rolls, a Silver Tsunami of disease and disability threatening to cripple our economy, and talks of extensive budget cuts to discretionary spending to control the national debt, policymakers are not surprisingly searching for ways to curb the growth of health spending. In order to promote national policies that turn to investments in research and innovation, rather than short-term cost cutting and health care rationing, the not-for-profit Alliance for aging Research publishes *The Silver Book®: Chronic Disease and Medical Innovation in an Aging Nation*.

Now in its 8th year, *The Silver Book®* has become a trusted resource for policymakers, thought leaders, and health advocates across the nation. An almanac of compelling statistics that spotlight the mounting burden of chronic diseases and the power of innovation to reduce that burden, *The Silver Book* extracts the key findings from dense reports and technical studies and provides the essential information in a single, easy-to-use, and well-referenced resource. Previous volumes have included data on cancer, cardiovascular disease (including stroke and thrombosis), diabetes, neurological disease (including Alzheimer's and Parkinson's disease), osteoporosis, and vision loss.

This newest volume brings together the leading data on persistent pain, an enormous problem for Americans—particularly older adults (note that information pertaining specifically to the older population is in silver type). All facts and statistics are cited for integration into presentations and work, and for easy access to the original source.

All data are also made available and regularly updated on-line at the newly designed [www.silverbook.org](http://www.silverbook.org). Now populated by 1,000s of facts and figures from more than 600 sources, the new Silver Book site benefits from advanced search features, better organization of data, and a

*continued >*

Cost of Persistent Pain



Innovative Medical Research



Conclusion



References





more streamlined design. **All of the data on chronic disease, all in one place.** Data from this volume is available at [www.silverbook.org/PersistentPain](http://www.silverbook.org/PersistentPain).

This new volume on persistent pain is a much-needed addition to *The Silver Book* series. Currently around 100 million Americans live with persistent pain—more Americans than are affected by diabetes, heart disease, and cancer combined. At least 1 in 3 Americans will experience severe persistent pain during their lifetime; which often means more visits to health care professionals, more hospital stays, disabilities, interference with even simple activities of daily living, lost workdays and reduced productivity, loss of sleep, increased use of both over-the-counter and prescription medications, depression and serious psychological distress, and even thoughts of and attempts at suicide.

Persistent pain is also expensive, with an annual cost that is greater than the annual cost of heart disease, cancer, or diabetes. Every year persistent pain costs the U.S. at least somewhere between \$560 and \$635 billion. These figures are conservative since they do not include the cost of pain for institutionalized individuals, military personnel, children, and personal caregivers. They also do not include emotional costs or lost productivity for a large segment of the population.

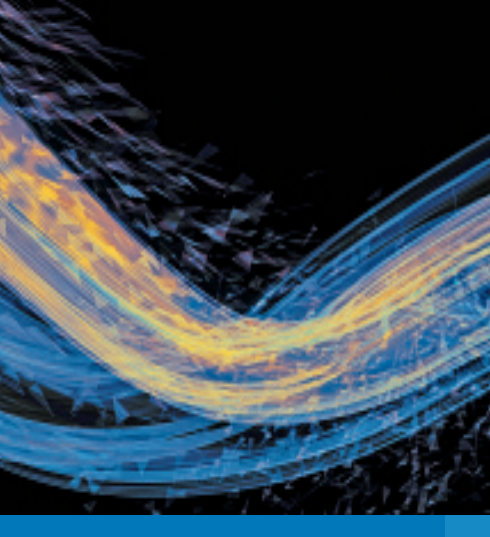
Thankfully, major research breakthroughs are being made in the understanding, prevention, and treatment of pain. Scientists are discovering ways to use growth hormone treatments, deep brain stimulation, new pharmacotherapies, stem cells, and more to manage pain. Researchers are also finding tremendous value in rehabilitation, complementary and alternative medicine, exercise, and psychological interventions. We at the Alliance for Aging Research believe that this volume of *The Silver Book* will showcase the value of these advances and enrich the national debate on health care and research funding.

Daniel Perry  
President & CEO  
Alliance for Aging Research



Advancing Science. Enhancing Lives.

[www.agingresearch.org/PersistentPain](http://www.agingresearch.org/PersistentPain)  
[SilverBook@agingresearch.org](mailto:SilverBook@agingresearch.org)



*Chronic Disease and Medical Innovation in an Aging Nation*

# The Silver Book<sup>®</sup>: Persistent Pain

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## The Human and Economic Burden

# Cost of Persistent Pain



■ Persistent (or chronic) pain has traditionally been defined, and differentiated from acute pain, according to how long it lasts—with durations set at 12 weeks from onset, 3 to 6 months, and even a year. Other definitions are not tied to a time period but instead classify it as “pain that extends beyond the expected period of healing.” (Turk and Okifuji 2000, *Pain Terms and Taxonomies*). Still others define it according to its impact as pain that disrupts sleep, normal living, and functional capabilities.

■ Persistent pain can be caused by an injury, disease, medical condition, medical treatment, inflammation, neuropathic pain, and even unknown causes. Common medical conditions which can cause persistent pain include migraine and other serious headaches, arthritis, fibromyalgia, musculoskeletal disorders, shingles, cancer, heart disease, stroke, diabetes, and more. In some cases, the pain becomes the disease itself.

■ Currently around 100 million Americans suffer with persistent pain. The aging of our population means that number will only rise as more and more Americans face the age-related diseases that are associated with persistent pain. On top of that, older Americans are more likely to need surgery, experience a fall or injury, or develop joint pain.

This means more Americans facing the tremendous toll of persistent pain. An individual suffering from persistent pain likely has multiple health care professionals that s/he sees with increased frequency, is admitted to the hospital more than the average individual, has difficulty getting around and performing a day’s activities, has trouble sleeping, misses more work than his/her coworkers, may lose income or a job, and faces increased medical expenses. All of this can lead to extreme depression, stress on relationships with friends and family, and even suicide.

The economic toll is also enormous—costing the United States at least \$560 to \$635 million each year. This is a cost to society equal to around \$2,000 for every person living in the U.S. And these figures don’t begin to incorporate the emotional costs or the lost productivity of workers affected by persistent pain. As a nation, we can’t afford a condition that over a lifetime can cost as much as \$1 million per person. We must begin to understand the true burden of persistent pain and properly fund and support research that will help reduce this burden.

## Prevalence and Incidence of Persistent Pain

- Approximately 100 million Americans live with persistent pain.

Institute of Medicine 2011, *Relieving Pain in America*

- Persistent pain affects more Americans than diabetes, heart disease, and cancer combined.

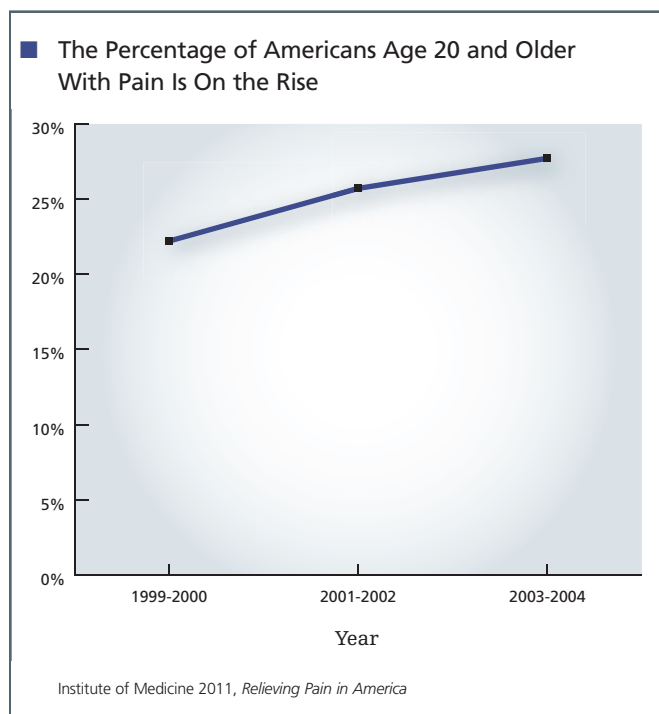
Tsang et al. 2008, *Common Chronic Pain Conditions in Developed and Developing Countries*

- Around 43% of the U.S. population lives with persistent pain.

Institute of Medicine 2011, *Relieving Pain in America*

- At least 1 in 3 Americans will experience severe persistent pain during their lifetime.

Johannes et al. 2010, *The Prevalence of Chronic Pain in United States Adults* AND Institute of Medicine 2011, *Relieving Pain in America*



## Duration and Severity

- More than half of persistent pain sufferers have been living with their pain for more than 5 years and experience their pain almost 6 days a week.

American Pain Society 1999, *Chronic Pain in America*

- Around 14% of adults who experience pain report that it lasts 3 months to a year and 42% report pain that lasts more than a year.

National Center for Health Statistics 2006, *Health, United States*

- An Internet study of patients with persistent pain found that the typical patient with persistent pain taking opioids to control their pain has had their condition for more than a decade. Those with chronic headaches or migraines have had their condition the longest—an average of almost 16 years.

American Pain Foundation 2006, *Voices of Chronic Pain*

- Around 10% of Americans have severe, disabling persistent pain.

Croft et al. 2010, *The Global Occurrence of Chronic Pain*

- Half of those with persistent pain report severe daily pain—rated as a 7 on a scale of 0 to 10.

Johannes et al. 2010, *The Prevalence of Chronic Pain in United States Adults*

## Types and Causes

- Most people with persistent pain have multiple sites of pain.

Croft et al. 2010, *The Global Occurrence of Chronic Pain* AND American Pain Foundation 2006, *Voices of Chronic Pain*

- An Internet study of patients with persistent pain found that on average, patients with persistent pain taking opioids for their pain experience more than 8 different types of pain on a monthly or more frequent basis—with 3 or more of these pains being severe.

American Pain Foundation 2006, *Voices of Chronic Pain*



- An estimated 80% of surgical patients report post-operative pain. Around 10% to 50% of those patients develop persistent pain, and for 2% to 10% of them the persistent pain is severe.

Apfelbaum et al. 2003, *Postoperative Pain Experience* AND Kehlet et al. 2006, *Persistent Postsurgical Pain*

- When asked about 4 common types of persistent pain, low back pain was ranked the most common at 27%, followed by severe headache/migraine pain (15%), neck pain (15%), and facial ache or pain (4%).

National Center for Health Statistics 2006, *Health, United States*

- More than 26 million Americans between the ages of 20 and 64 experience frequent back pain.

National Center for Health Statistics 2006, *Health, United States*

- Musculoskeletal pain, especially joint and back pain, is the most common single type of persistent pain.

Institute of Medicine 2011, *Relieving Pain in America* AND Elliott 1999, *The Epidemiology of Chronic Pain in the Community*

- Around 46 million Americans suffer from pain-causing arthritis or other rheumatic conditions.

NIAMS 2012, *Arthritis*

- Arthritis is the most common painful condition reported in U.S. nursing home residents.

Ferrell et al. 1995, *Pain in Cognitively Impaired Nursing Home Patients*

- Nearly 1 million Americans develop shingles each year and 10% to 15% of sufferers develop postherpetic neuralgia (PHN)—shingles associated pain that lasts for more than 3 months.

AHRQ 2008, *AHRQ News and Numbers* AND Dubinsky 2004, *Practice Parameter*

- Most people with advanced cancer report pain—60% to 85%.

Green et al. 2011, *Cancer-Related Chronic Pain*

- Fibromyalgia is a widespread pain disorder that affects 3.4% of women and 0.5% of men in the U.S.

Wolfe et al. 1995, *The Prevalence and Characteristics of Fibromyalgia in the General Population*

- A third of people in hospice report pain at their last hospice care visit before death.

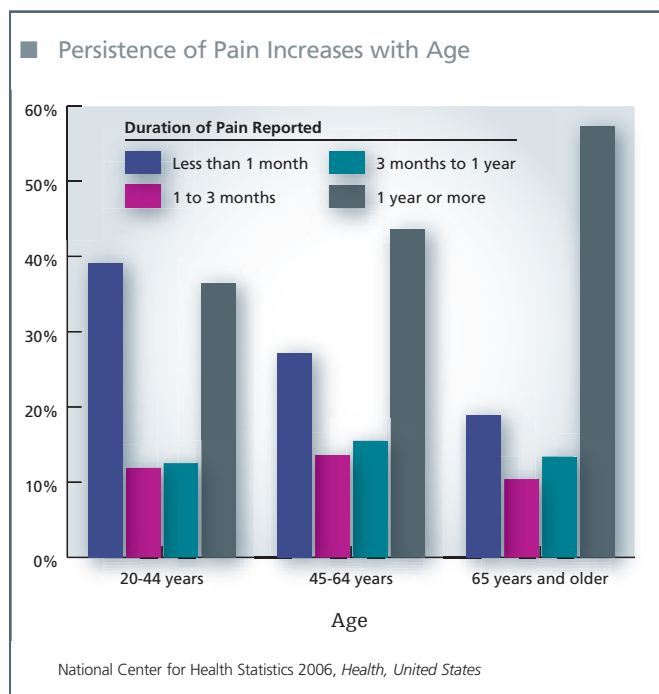
National Center for Health Statistics 2010, *Health, United States*

- More than 50% of all hospitalized patients experience pain in the last days of their lives and despite proven therapies for pain relief, family members report that the patient experienced moderate to severe pain at least half of the time.

Connors et al. 1995, *A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients*



## Age—A Major Risk Factor



- Around 50% of non-institutionalized older adults suffer from persistent pain.

Thomas 2010, *Pain in Older People*

- Between 62% and 83% of institutionalized elderly in the U.S. report a pain problem and 17% have substantial daily pain.

Ferrell et al. 1995, *Pain in Cognitively Impaired Nursing Home Patients* AND Gagliese 1997, *Chronic Pain in the Elderly* AND Sawyer et al. 2007, *Substantial Daily Pain Among Nursing Home Residents*

- A survey of U.S. nursing homes found that in most states, at least 39% to 46% of residents are in persistent pain.

Teno et al 2001, *Persistent Pain in Nursing Home Residents*

- Surgery is a common cause of persistent pain, and adults ages 65 and older are 2.6 times more likely to have surgery than those ages 45-64.

Hall et al. 2010, *National Hospital Discharge Survey*

- Shingles—a common cause of persistent pain—affects 1 in 3 Americans in their lifetime, with half of all cases occurring in people age 60 and older.

CDC 2012, *Shingles Overview*

- Around half of adults 65 and older have been diagnosed with arthritis, a common cause of persistent pain.

CDC 2010, *Prevalence of Doctor-Diagnosed Arthritis*

- The risk of developing invasive cancer, a common source of persistent pain, increases from 1 in 69 for men and 1 in 46 for women under the age of 39, to 1 in 3 for men and 1 in 4 for women ages 60 and older.

American Cancer Society 2013, *Cancer Facts and Figures 2013*

## The Burden of Persistent Pain

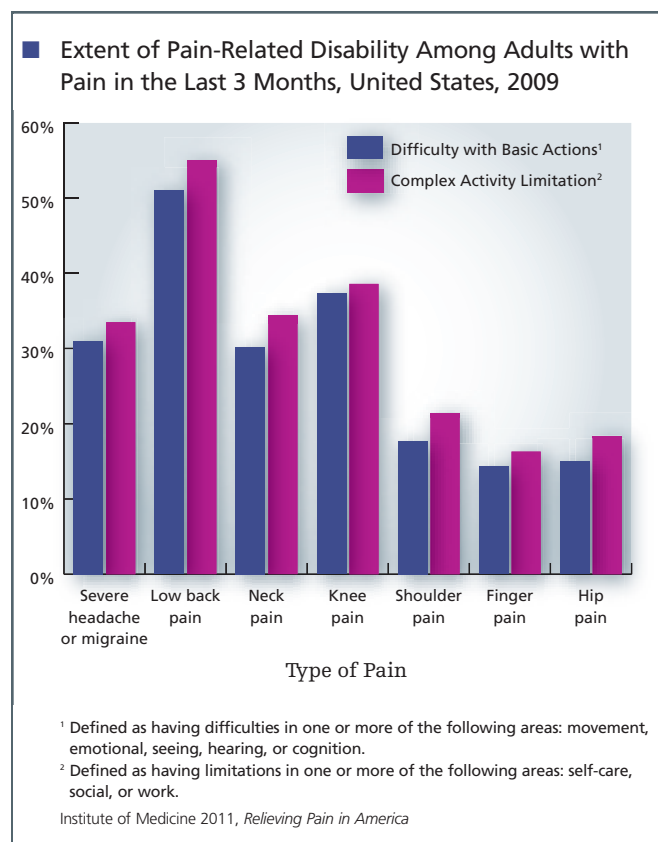
### The Human Burden

- 71% of patients with persistent pain taking opioids for their pain have seen a health care professional in the past month. 1 in 4 have seen a health care professional within the past three months.

American Pain Foundation 2006, *Voices of Chronic Pain*

- Patients with persistent pain are 5 times more likely than those without persistent pain to use health care services.

Becker et al. 1997, *Pain Epidemiology and Health Related Quality of Life*



- 47% of persistent pain sufferers report that they have changed doctors—22% have changed doctors three or more times. The most common reported reason is that they “still had too much pain” (42%).

American Pain Society 1999, *Chronic Pain in America*

- 83 million Americans have pain that impacts their participation in various activities.

Gallup 2000, *Pain in America*

- In an Internet survey of patients with persistent pain 97% currently using opioids for their pain reported either a physical or social hardship as a direct result of their pain. 93% reported multiple effects from their pain. The most common limitation is difficulty walking or moving—experienced by 89% of these patients.

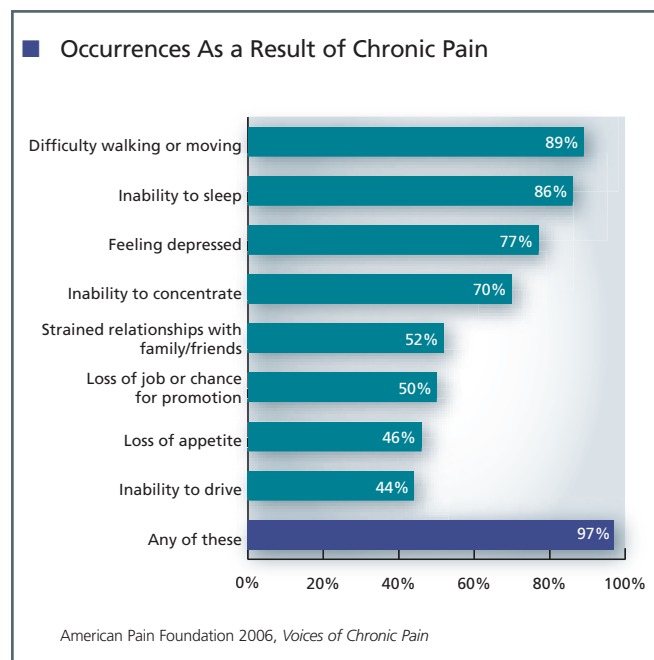
American Pain Foundation 2006, *Voices of Chronic Pain*

- As many as 45% to 80% of nursing home residents have pain that contributes to functional impairment and a decreased quality of life.

Ferrell 1995, *Pain Evaluation and Management in the Nursing Home*

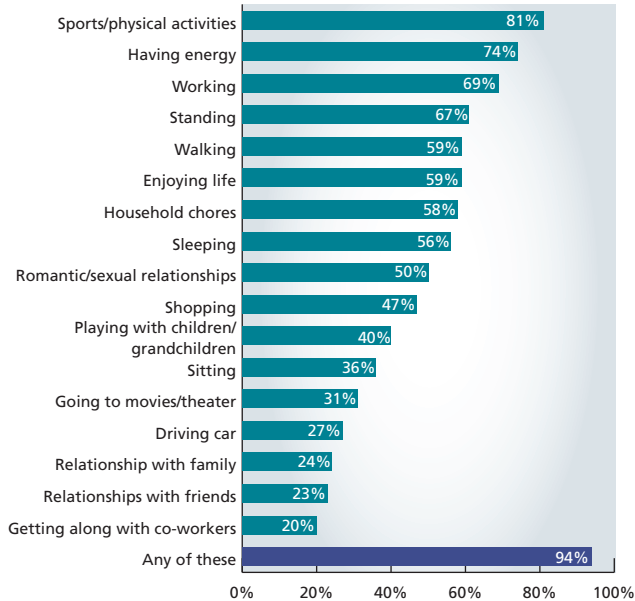
- Among adults age 65 and older who reported low back pain, more than ½ had a limitation in their daily activities—compared with 27% without recent low back pain.

National Center for Health Statistics 2006, *Health, United States*





### ■ Impact of Pain on Day-to-Day Activities Those Who Say "Great Deal of Impact"



American Pain Foundation 2006, *Voices of Chronic Pain*

- Back pain is the leading cause of job-related disability and a leading contributor to missed work.

NINDS, *Low Back Pain Fact Sheet*

- A survey about how persistent pain patients deal with pain found that 20% have taken disability leave from work, 17% have changed jobs, 13% have sought help with activities of daily living, and 13% have moved to a home that is easier to manage.

Research!America 2003, *Americans Talk About Pain*

- At least 36 million Americans miss work each year due to pain.

Gallup 2000, *Pain in America*

- Pain is a leading cause of medically-related work absenteeism—results in more than 50 million lost workdays each year.

Ortho-McNeil 1997, *Pain and Absenteeism in the Workplace*

- More than half of workforce adults surveyed reported experiencing headache, back pain, arthritis, or musculoskeletal related pain in the previous 2 weeks. 12.5% of the workforce reported that their pain caused a loss of productivity—and an average of 4.6 hours per week was lost. People with severe pain report missing an average of 5 to 5.9 more work days per year than people without pain.

Stewart et al. 2003, *Lost Productive Time and Cost Due to Common Pain Conditions in the U.S. Workforce* AND Institute of Medicine 2011, *Relieving Pain in America*

- Adults age 65 and older who report low back pain are twice as likely to be in fair or poor health compared to those without pain—40% rate their health as fair or poor—compared to 19% without recent low back pain.

National Center for Health Statistics 2006, *Health, United States*

- During the 4-year period between 2005 and 2008, 5.7% of the U.S. population reported using opioids for pain.

Institute of Medicine 2011, *Relieving Pain in America*

- An Internet survey found that the typical patients with persistent pain takes pain medication as many as 4 times a day—including a prescription 2.6 times a day. 43% of patients with persistent pain take medications 3 to 4 times a day.

American Pain Foundation 2006, *Voices of Chronic Pain*

- An Internet survey found that 31% of patients with persistent pain supplement their prescription medications with over-the-counter medications.

American Pain Foundation 2006, *Voices of Chronic Pain*

- In an Internet survey of patients with persistent pain who were currently using opioids to treat their pain, only 6% report having a "great deal of control" over their pain. More than half felt that they had little or no control over their pain and 60% experienced breakthrough pain about twice a day—severely impacting their quality of life and well-being.

American Pain Foundation 2006, *Voices of Chronic Pain*

- 1 in 5 American adults—42 million people—report that pain or physical discomfort disrupts their sleep three nights a week or more.

National Sleep Foundation 2000, *Sleep in America Poll*



- Adults with low back pain are more than four times as likely to experience serious psychological distress, compared to those without back pain.

National Center for Health Statistics 2006, *Health, United States*

- An Internet survey found that 94% of patients with persistent pain taking opioids report at least one major impact on their lives from the pain—3 in 4 (77%) report feeling depressed, 70% report an inability to concentrate, 52% report strained relationships, and 46% report a loss of appetite.

American Pain Foundation 2006, *Voices of Chronic Pain*

- An estimated 40% to 50% of people with persistent pain also have mood disorders.

Institute of Medicine 2011, *Relieving Pain in America*

- One study found that 70% of persistent pain respondents expressed anger—62% toward health care providers, 39% toward significant others, and 30% toward insurance companies. The most frequent target of their anger was themselves—74%.

Okifuji et al. 1999, *Anger in Chronic Pain*

- In one study, around half of the patients with persistent pain reported that they had considered suicide.

Hitchcock et al. 1994, *The Experience of Chronic Nonmalignant Pain*

- The risk of suicide among people with persistent pain is around double that of those without pain—with 5% to 14% lifetime prevalence rates of attempted suicide in persistent pain sufferers.

Tang and Crane 2006, *Suicidality in Chronic Pain*

- A study of people with persistent pain found that they were 2.5 times more likely to think about suicide than those without pain, 3.5 times more likely to plan suicide, and 6.2 times more likely to have attempted suicide in the previous 12 months.

Ilgen et al. 2008, *Pain and Suicidal Thoughts*

## The Economic Burden

- The annual economic cost of persistent pain in the U.S. is at least \$560 to \$635 billion (in 2010\$).

Gaskin and Richard 2012, *The Economic Costs of Pain in the U.S.*

- The estimated annual cost of persistent pain of \$560 to \$635 billion includes health care costs (\$261 to \$300 billion) and lost productivity (\$299 to \$335 billion). However, these estimates are conservative because they do not include the cost of pain for institutionalized individuals, military personnel, children, and personal caregivers. They also do not include the emotional costs of persistent pain or the lost productivity of workers younger than 24 or older than 65.

Gaskin and Richard 2012, *The Economic Costs of Pain in the U.S.*

- The annual cost of pain is greater (in 2010\$) than the annual costs of heart disease (\$309 billion), cancer (\$243 billion), and diabetes (\$188 billion)—and nearly 30% higher than the combined costs of cancer and diabetes.

Gaskin and Richard 2012, *The Economic Costs of Pain in the U.S.*

- The cost of lost productivity from persistent pain includes days of work missed (\$11.6 to \$12.7 billion), hours of work lost (\$95.2 to \$96.5 billion) and lost wages (\$190.6 to \$226.3 billion).

Gaskin and Richard 2012, *The Economic Costs of Pain in the U.S.*

- The economic burden of treating persistent pain that develops from acute pain in a 30-year-old over a lifetime is as much as \$1 million.

Cousins et al. 2000, *Pain*

- The annual cost to society of persistent pain is equal to around \$2,000 for every person living in the U.S.

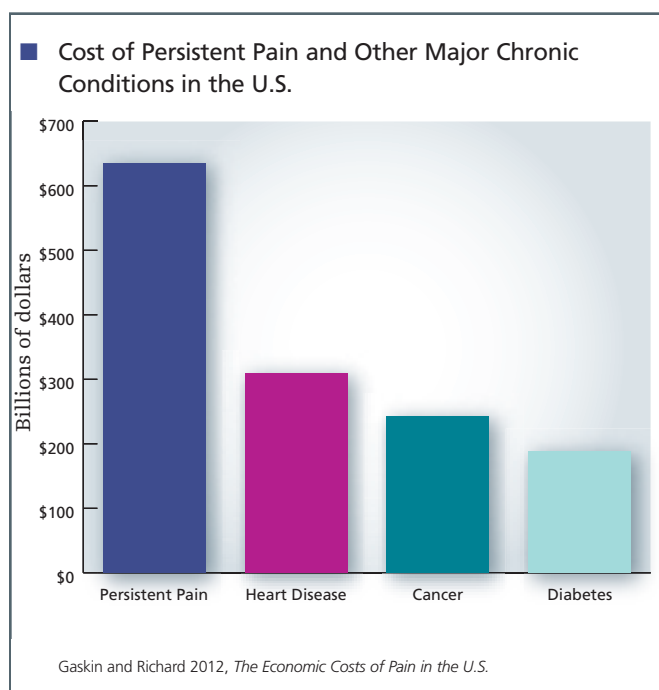
Institute of Medicine 2011, *Relieving Pain in America*

- Medicare bears one-fourth of all expenditures for pain-related treatment in the U.S.

Institute of Medicine 2011, *Relieving Pain in America*

- The cost of pain to Medicare was \$65.3 billion in 2008—14% of all Medicare costs.

Institute of Medicine 2011, *Relieving Pain in America*



- The cost of persistent pain to federal and state governments in 2008 was around \$99 billion.
- Low back pain alone was estimated to have contributed almost 3% to the total national increase in health care spending from 1987 to 2000.

Institute of Medicine 2011, *Relieving Pain in America*

Thorpe et al. 2004, *Which Medical Conditions Account for the Rise in Health Care Spending?*

- The annual direct and indirect costs of several pain-related conditions include:

- \$14 billion for migraines

Hu et al. 1999, *Burden of Migraine in the United States*

- \$189 billion for arthritis

Yelin et al. 2007, *Medical Care Expenditures and Earnings Losses Among Persons with Arthritis and Other Rheumatic Conditions*

- \$50 billion for low back pain

NINDS, *Low Back Pain Fact Sheet*

- \$61 billion for headache, arthritis, backache, and other musculoskeletal conditions

Stewart et al. 2003, *Lost Productive Time and Cost Due to Common Pain Conditions in the U.S. Workforce*

- A person with moderate pain has health care expenditures \$4,516 higher than those without pain. A person with severe pain has health care expenditures \$3,210 higher than those with moderate pain.

Gaskin and Richard 2012, *The Economic Costs of Pain in the U.S.*

- Persistent back problems reduce financial capacity by reducing wealth accumulation. Over 99% of individuals who are employed full-time have accumulated some wealth at 65 years, whereas only 74% of those who are out of the workforce due to back problems will have done so. Additionally, women who retire early due to back problems have a median value of total accumulated wealth at 65 of as little as \$3.708. The median value of accumulated wealth for women ages 55-64 who remained in the workforce full-time is \$214,432 at the age of 65.

Schofield 2012, *The Impact of Back Problems on Retirement Wealth*



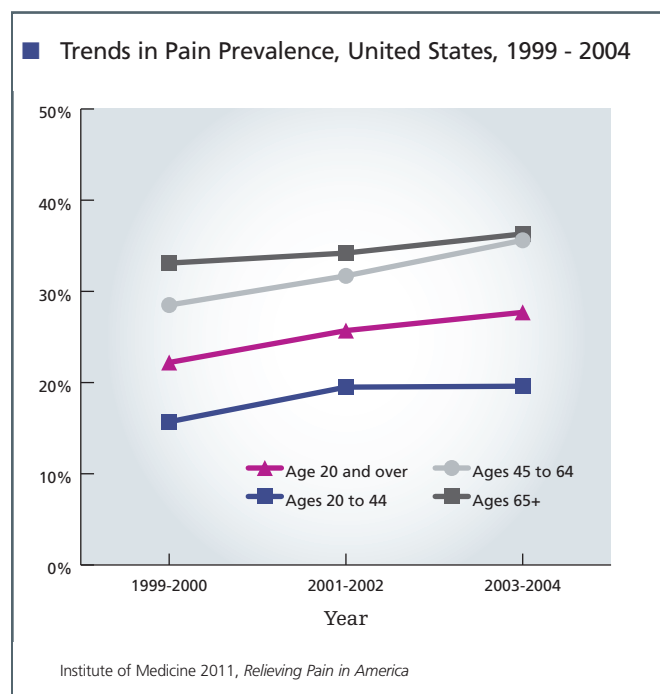


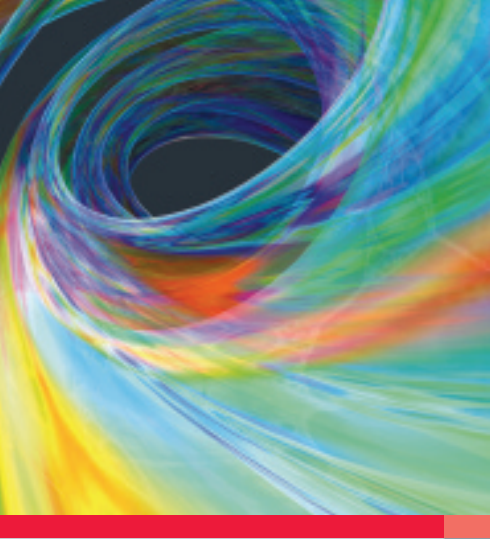
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## The Future Cost of Persistent Pain

- The prevalence of lower back pain amongst veterans is increasing by about 5% per year.

Sinnott 2009, *Low Back Pain in VA Users*





## Investing in Science

# Innovative Medical Research



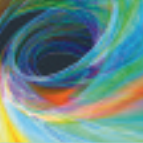
While 70% of adults with moderate persistent pain report sufficient pain control, that number decreases to 51% in patients with severe pain and 39% for patients with very severe pain. (American Pain Society 1999, *Chronic Pain in America*). Of those patients who report adequate pain control, it took almost half of them a year to reach it.

Older patients with persistent pain are too often undertreated or do not receive the appropriate therapy. Psychosocial factors, like the tendency of older adults to underreport their pain and the lower adherence rates to prescribed pain medications, complicate pain assessment and treatment. Additionally, prescribing treatment can be complicated since opioids in older adults increase fall risk and confusion and can produce other negative side effects. Treatment is often further complicated by the fact that opioid medications, while highly effective for many patients, do carry the risk of addiction and therefore must be managed in a manner best suited for the individual.

Then there are those individuals who are suffering from pain for which no adequate treatments yet exist. Fortunately, the field of persistent pain is experiencing tremendous breakthroughs in the use of current treatments and development of future therapies. Researchers are finding new ways to use rehabilitation, complementary and alternative medicine, exercise, and psychological interventions to prevent and reduce pain. For example, they are looking to neurorehabilitative approaches to reverse the maladaptive responses to pain in the brain.

There are also exciting developments in new therapies using opiate agonists, antiepileptics, antidepressants, anti-inflammatories, anti-nerve growth factor antibodies, and more to manage pain. Scientists are also turning to genetics to identify increased risk, using stem cells to replace damaged or lost neurons, and improving brain stimulation to help control pain.

Medical advances that prevent and effectively manage pain and thereby reduce its impact on both individuals and society will far outweigh the initial financial investments. As we experience a critical era in health-care for older Americans we must be sure to consider both the financial and human impact of innovation. Short-sighted efforts to reduce spending too often target the initial expenses of innovation, while ignoring the remarkable returns on investment.



## The Human and Economic Value

- An opiate agonist often used for persistent pain, tramadol was found in one meta-analysis to significantly reduce neuropathic pain when compared to placebo.

Duehmke et al. 2009, *Tramadol for Neuropathic Pain*

- Antiepileptic drugs relieve persistent neuropathic pain. One meta-analysis found gabapentin to be associated with moderate benefit (equivalent to 30% pain relief) in close to 1 in 2 patients, and a substantial benefit (equivalent to 50% pain relief) in close to 1 in 3 patients. Another meta-analysis found pregabalin effective in patients with postherpetic neuralgia, painful diabetic neuropathy, central neuropathic pain, and fibromyalgia.

Moore et al. 2011, *Gabapentin for Chronic Neuropathic Pain and Fibromyalgia in Adults*  
AND Moore et al. 2010, *Pregabalin for Acute and Chronic Pain in Adults*

- Pregabalin, an antiepileptic drug, produced around a 32% pain reduction (a significant reduction) at week 16 versus around 20% for placebo, in patients with neuropathic pain due to spinal cord injury.

Cardenas et al. 2013, *A Randomized Trial of Pregabalin in Patients with Neuropathic Pain Due to Spinal Cord Injury*

- Topical capsaicin was found in a meta-analysis to provide a degree of pain relief to some patients with painful neuropathic conditions.

Lloyd et al. 2009, *Topical Capsaicin for Chronic Neuropathic Pain in Adults*

- A meta-analysis of morphine taken by mouth found it to be an effective pain-killer for persistent cancer pain.

Wiffen and McQuay 2010, *Oral Morphine for Cancer Pain*

- A meta-analysis of antidepressants found that 1 in 3 patients with persistent neuropathic pain will get at least moderate pain relief. Another meta-analysis of duloxetine found it useful for treating persistent pain from fibromyalgia and diabetic neuropathy.

Saarto et al. 2007, *Antidepressants for Neuropathic Pain* AND Lunn et al. 2009, *Duloxetine for Treating Painful Neuropathy or Chronic Pain*

- Topical NSAIDs were found in a meta-analysis to be significantly more effective than placebo in reducing persistent pain from musculoskeletal conditions.

Derry et al. 2012, *Topic NSAIDs for Chronic Musculoskeletal Pain in Adults*

- In individuals with persistent low back pain, tanezumab, a humanized anti-nerve growth factor antibody, showed clinical and statistical analgesic efficacy that was superior to placebo and naproxen.

Katz et al. 2011, *Efficacy and Safety of Tanezumab in the Treatment of Chronic Low Back Pain*

- A meta-analysis of duloxetine, an anti-depressant, found a 50% reduction in pain at 12 weeks for diabetic peripheral neuropathy, and a 50% reduction in pain at 12 weeks for fibromyalgia.

Lunn et al. 2009, *Duloxetine for Treating Painful Neuropathy or Chronic Pain*

- A meta-analysis of psychological interventions for chronic low back pain found small but statistically significant effects for all interventions for as long as 5 years.

Hoffman et al. 2007, *Meta-Analysis of Psychological Interventions for Chronic Low Back Pain*

- A biopsychosocial approach (i.e., one that takes into account physical, emotional, and environmental factors in the assessment and treatment of pain) has been found to improve the pain care of patients with a range of conditions including neuropathic and musculoskeletal pain.

Kerns et al. 2002, *Pain in Multiple Sclerosis* AND Miro et al. 2009, *Impact of Biopsychosocial Factors on Chronic Pain in Persons with Myotonic and Facioscapulohumeral Muscular Dystrophy* AND Guzman et al. 2002, *Multidisciplinary Rehabilitation for Chronic Low Back Pain* AND Vranceanu et al. 2009, *Psychosocial Aspects of Disabling Musculoskeletal Pain*

- Exercise has been shown to be effective in reducing persistent pain from osteoarthritis of the knee.

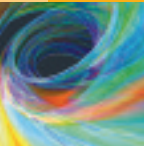
Fransen and McConnell 2009, *Land-Based Exercise for Osteoarthritis of the Knee*

- Exercise has a statistically significant effect in reducing work disability in patients with persistent back pain over the long-term.

Oesch et al. 2010, *Effectiveness of Exercise on Work Disability in Patients with Non-Acute Non-Specific Low Back Pain*

- 60% of people with persistent back pain who turned to complementary and alternative medicine perceived a "great deal" of benefit.

Kanodia et al. 2010, *Perceived Benefit of CAM for Back Pain*



- Acupuncture, in combination with routine care, was associated with marked clinical improvements in patients with persistent low back pain. It has also shown improvement in primary and secondary outcomes for patients with osteoarthritis of the knee.

Witt et al. 2006, *Pragmatic Randomized Trial Evaluating the Clinical and Economic Effectiveness of Acupuncture for Chronic Low Back Pain* AND Mavrommatis et al. 2012, *Acupuncture as an Adjunctive Therapy to Pharmacological Treatment in Patients with Chronic Pain Due to Osteoarthritis of the Knee*

- Opioids have been found to reduce pain intensity and improve physical functioning for patients with persistent noncancer pain. It's important to note that a decrease in mental health functioning was also seen.

Papleontiou et al. 2010, *Outcomes Associated with Opioid Use in the Treatment of Chronic Non-Cancer Pain Among Older Adults* AND Noble et al. 2010, *Long-Term Opioid Management for Chronic Noncancer Pain*

- Subthalamic nuclei deep brain stimulation (STN-DBS) raises pain thresholds in Parkinson's disease patients.

Dellapina et al. 2012, *Effect of Subthalamic Deep Brain Stimulation on Pain in Parkinson's Disease*

- An oral cannabinoid was found effective in relieving diabetic peripheral neuropathic pain symptoms and improving disturbed sleep, quality of life, and overall patient status.

Toth et al. 2012, *An Enriched-Enrollment, Randomized Withdrawal*

- Topical clonidine gel significantly reduces foot pain in patients with painful diabetic neuropathy.

Campbell et al. 2012, *Randomized Control Trial of Topical Clonidine for Treatment of Painful Diabetic Neuropathy*

- Growth hormone treatment in patients with fibromyalgia is effective in reducing pain with sustained action over time.

Cuatrecasas 2012, *Growth Hormone Treatment for Sustained Pain Reduction and Improvement in Quality of Life in Severe Fibromyalgia*

- The use of sodium oxybate (SXB) in fibromyalgia patients reduced pain by 30% or more in 54-58% of patients (versus 35.2% for placebo). SXB also reduced fatigue and sleep disturbance.

Russell 2011, *Sodium Oxybate Reduces Pain, Fatigue, and Sleep Disturbance and Improves Functionality in Fibromyalgia*

- Pain education programs and pain consultations have been found to improve pain (average pain was 31% versus 20%) and daily interference (20% versus 2.5%) in oncology outpatients. Patient adherence is also improved.

Oldenmenger et al. 2011, *A Combined Pain Consultation and Pain Education Program Decreases Average and Current Pain and Decreases Interference in Daily Life by Pain in Oncology Outpatients*

- The Mayo Clinic Pain Rehabilitation Center helps people with persistent pain return to an active lifestyle and has found that among patients who finish the program, nearly 84% report greater control over pain, 70% note a decrease in pain severity, 93% report an increase in aerobic activity levels, and 90% report a decrease in depressive symptoms.

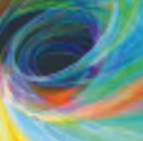
Mayo Clinic, *Pain Rehabilitation Center in Minnesota*

- 57% of American adults say they would pay an extra \$1 per week in taxes in order to support government research into the causes of and treatment for chronic pain.

Research!America 2003, *Americans Talk About Pain*

- People with persistent pain who used complementary and alternative medicine (CAM) had lower average health care expenditures than nonusers (\$3,797 versus \$4,153).

Lind et al. 2010, *Comparison of Health Care Expenditures Among Insured Users and Nonusers of Complementary and Alternative Medicine*



## The Future Value

- Resolvins, a family of lipid mediators, have shown potential in resolving persistent inflammatory pain.

Xu et al. 2010, *Resolvins RvE1 and RvD1 Attenuate Inflammatory Pain Via Central and Peripheral Actions*

- Nerve growth factor (NGF) has been found to be a major mediator of inflammatory and neuropathic pain and provides a new therapeutic target.

Watson et al. 2008, *Targeting Nerve Growth Factor in Pain: What is the Therapeutic Potential?*

- Use of stem cells to create neurons could enable the study of the response of human cells to new drugs in vitro, early in the drug development process.

Woolf 2010, *Overcoming Obstacles to Developing New Analgesics*

- The combination of information from neuroimaging and circulatory biomarkers could improve both the sensitivity and specificity of pain diagnosis and thereby improve treatment.

Woolf 2010, *Overcoming Obstacles to Developing New Analgesics*

- Understanding of the role of genetics in pain mechanisms is increasing and the potential now exists to conduct genome-wide screens in model organisms to look for pain-associated genes.

Institute of Medicine 2011, *Relieving Pain in America*

- Researchers have identified several sub-types of ion channels that allow inflammation and growth factors to trigger persistent pain.

Institute of Medicine 2011, *Relieving Pain in America*

- Researchers have discovered that some types of glial cells have a major impact on persistent neuropathic pain and that targeting these cells may result in a new class of disease modifying therapies.

Institute of Medicine 2011, *Relieving Pain in America*

- Advances in neuroimaging will continue to offer information on the brain's functioning and how it correlates to the pain experience.

Institute of Medicine 2011, *Relieving Pain in America*

- Targeting A-type K<sup>+</sup> channels in primary sensory neurons could provide a novel mechanism-based therapy for the treatment of bone cancer pain—one of the most severe types of chronic pain.

Duan et al. 2012, *Targeting A-type K<sup>+</sup> Channels in Primary Sensory Neurons for Bone Cancer Pain in a Rat Model*

- A proteasome inhibitor was found to reduce pain and joint destruction in an animal model of osteoarthritis, suggesting that nontoxic proteasome inhibitors could offer a novel pharmacotherapy option.

Ahmed 2012, *Suppression of Pain and Joint Destruction by Inhibition of the Proteasome System in Experimental Osteoarthritis*

- Statin use in mouse models show pain-alleviating effects for neuropathic pain.

Shi et al. 2011, *Statins Alleviate Experimental Nerve Injury-Induced Neuropathic Pain*

- Brain imaging is showing that pain changes the structure and function of brain regions that perceive pain, making it persistent. These brain networks and receptor targets are being identified as potential targets for future therapies.

Apkarian 2011, *The Brain in Chronic Pain*





## Conclusion

■ **A**t the same time that scientists are making exciting breakthroughs in pain prevention and management, the pain community is taking huge strides in raising awareness of the problem and creating crucial collaboration amongst key government agencies, advocates, and academics. The Institute of Medicine's 2011 report on persistent pain *Relieving Pain in America* offered a blueprint for action that would transform prevention, care, education, and research and provide relief for more Americans suffering with persistent pain.

■ Since the release of that report, the Department of Health and Human Services (HHS) has created The Interagency Pain Research Coordinating Committee in accordance with the Affordable Care Act. This committee was created to "enhance pain research efforts and promote collaboration across the government, with the ultimate goals of advancing fundamental understanding of pain and improving pain-related treatment strategies." The committee, once fully formed, will include seven Federal members from across HHS and twelve non-Federal members drawn from the scientific and medical communities and public and stakeholder groups.

■ These are critical efforts that are helping to promote understanding of persistent pain and combat the inevitable growth of an already large burden on patients, families, and societies. Without significant breakthroughs the number of Americans with persistent pain will continue to rise and add an intolerable burden to a society facing a Silver Tsunami of age-related disease.

■ Sound public policy should strive for cost containment strategies that assure high quality healthcare that is patient-centered, values-driven, knowledge-intense, innovation-rich, and prevention-oriented. We must ensure long-range plans for support of medical research and innovation that reduces the burdens imposed by persistent pain. Historically, investments that produce new medical innovations often pay for themselves through decreased medical expenses and increased human productivity. Medical innovation is essential if we want to attempt to contain the health care costs of an aging nation.

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