

Pharmacological Pain Management, the Evolving Role of Opioids, and Improving Education of Health Care Providers



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Conflict of Interest

Director, American Board of Anesthesiology

The ABA oversees preparation and administration of the physician subspecialty board certification examination in Pain Medicine

Objectives

- Explain the evolution of increased use of opioids for the treatment of chronic pain
- Outline recent trends in the pharmacological management of pain, including the evolving role for opioid analgesics
- Describe gaps in pain research and education

An Unmet Need

THE BURDEN OF PAIN

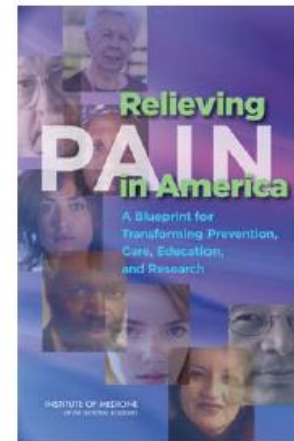
2011: Relieving Pain in America

For more information visit www.iom.edu/relievingpain

Relieving Pain in America

A Blueprint for Transforming Prevention, Care, Education, and Research

Pain represents a national challenge. A cultural transformation is necessary to better prevent, assess, treat, and understand pain of all types.



Chronic pain affects an estimated 116 million American adults—more than the total affected by heart disease, cancer, and diabetes combined. Pain also costs the nation up to \$635 billion each year in medical treatment and lost productivity.

The Universal Antidote

THE OPIATES & OPIOIDS

10,000 B.C. – 2016

Acute Pain and Opioids

- Opioid analgesics are used to effectively treat acute pain in the postoperative period and following trauma
- Opioid analgesics are an integral part of treating pain and minimizing suffering in those with advanced illness



Chronic Pain and Opioids

- Until recent years, use of opioids for treating chronic pain was limited
- The potential for adverse effects, including addiction and death due to overdose, has been known for as long as opium has been in use

Chronic Pain and Addiction

- The likelihood of patients progressing from taking legitimately prescribed opioids for pain to opioid addiction is low
- Pain in those with pre-existing opioid addiction is extremely high
- Individuals with severe pain and opioid addiction have over five times higher relapse rate compared with their counterparts with opioid addiction but no pain

Wachholtz A et al. Subst Abuse Rehabil 2011; 2:145–162.

A Newfound Panacea

OPIOIDS FOR CHRONIC PAIN

1988 - 2001

Opioids for Chronic Pain



“...these papers represent a phenomenon akin to ‘breaking the sound barrier.’ Our attitudes to narcotics are influenced by unfounded prejudice based on street addicts...”

Melzack R. *The tragedy of needless pain: a call for social action.* IASP President's Address, Vth World Congress on Pain, 1988.

Opioids for Chronic Pain

New Pharmacologic Preparations

1987: Extended-release morphine (MS-Contin®)

1990: Transdermal fentanyl (Duragesic®)

1996: Extended-release oxycodone (OxyContin®)

1998: Oral transmucosal fentanyl (Actiq ®)

2006: Oral buccal fentanyl (Fentora®)

2010: Extended-release hydromorphone (Exalgo ®)

2013: Extended-release hydrocodone (Zohydro ER ®)

Prescription Drug Abuse

AN EPIDEMIC EMERGES

2000 - 2010

An Epidemic Emerges

Red Sox crush Orioles, 10-1, Sports 6B

The Burlington Free Press

Wednesday, April 11, 2001 *** ☆ *A Local Custom • Serving Vermont for 174 years* 50 cents, three news sections

Read the labels on net food

Millions abuse prescription drugs, feds say

By Megan K. Doyle
N.Y. Times News Service

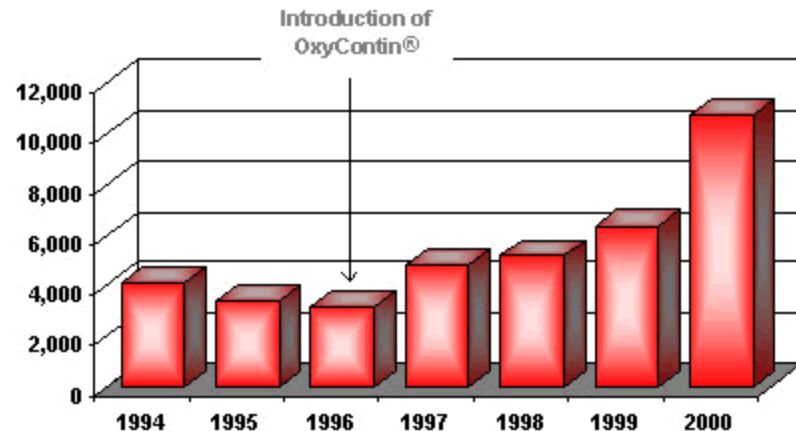
The most common drugs abused are pain-killers, de-

On the Web instructions. *Appropriately used pain

Examples of abuse

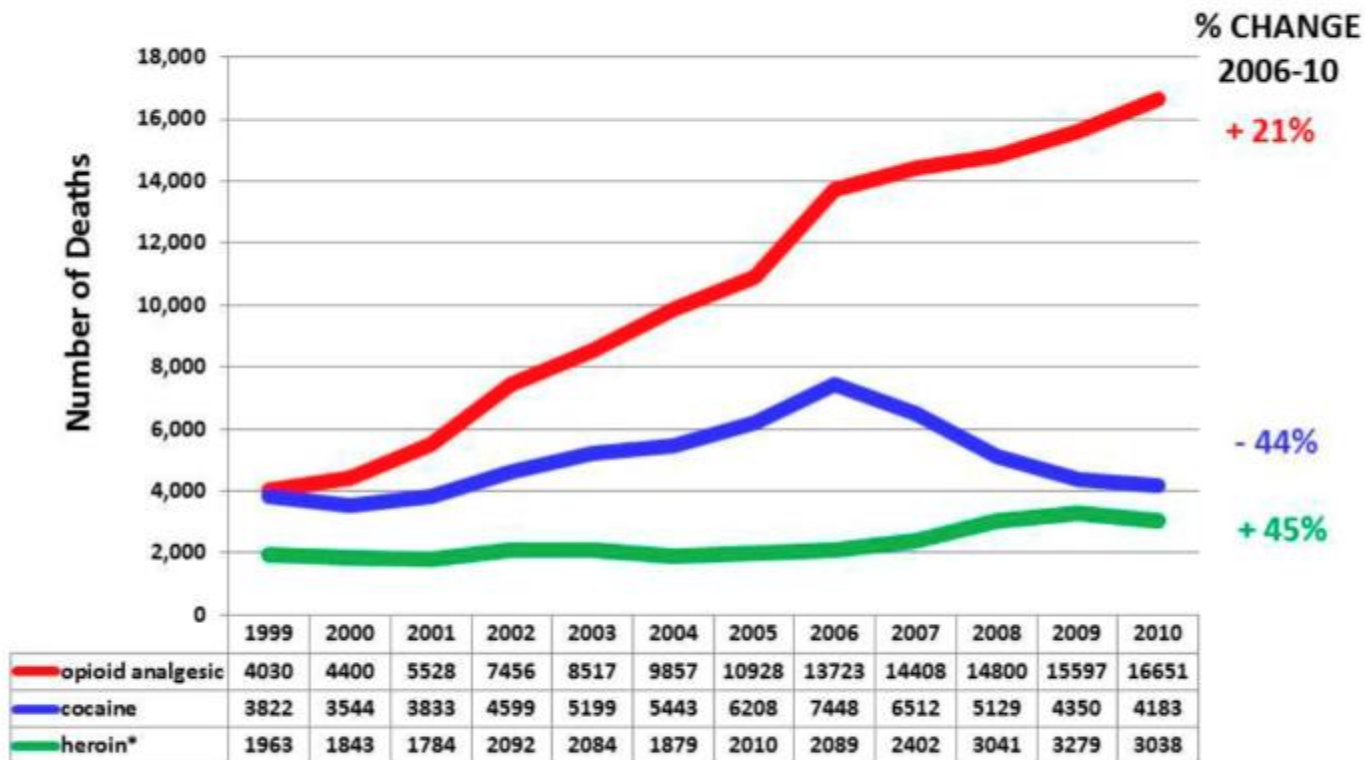


Table 1: Oxycodone DAWN ED Episodes



An Epidemic Emerges

Overdose Deaths Involving Opioid Analgesics, Cocaine and Heroin: United States, 1999–2010



Note: Not all overdose deaths specify the drug(s) involved, and a death may involve more than one specific substance. The rise in 2005-2006 in opioid deaths is related to non-pharmaceutical fentanyl (see <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5729a1.htm>). *Heroin includes opium.

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. *Multiple Cause of Death 1999-2010* on CDC WONDER Online Database, released 2012. Extracted on February 11, 2013..

Recent Trends

PHARMACOLOGICAL PAIN MANAGEMENT

2011-2016: The Evolving Role for Opioids

New Analgesics

- No novel analgesics
 - “Abuse-deterrent” formulations of opioids
 - New extended-release formulations
 - New routes of delivery for some agents (topical, transmucosal)
 - Label extension to new indications
- Little impact on managing those with chronic pain

Xtanza (oxycodone) extended release

Onzetra Xsail (sumatriptan nasal powder)

Troxyca ER (oxycodone + naltrexone)

Belbuca (buprenorphine)

Vivlodex (meloxicam)

Dyloject (diclofenac sodium) Injection

Targiniq ER (oxycodone hydrochloride + naloxone hydrochloride) extended-release tablets

Tivorbex (indomethacin)

Xartemis XR (oxycodone hydrochloride and acetaminophen) extended release

Zohydro ER (hydrocodone bitartrate) Extended-Release Capsules

Zubsolv (buprenorphine and naloxone)

Lyrica (pregabalin)

Subsys (fentanyl sublingual spray)

Naloxone

- Narcan (naloxone hydrochloride); For emergency treatment of known or suspected opioid overdose; Approved November 2015
- The effectiveness of naloxone in preventing opioid-related overdose deaths and who should receive this drug, particularly among those on chronic opioid therapy for pain, are unknown

The screenshot shows the CDC Newsroom website. At the top left is the CDC logo with the text "Centers for Disease Control and Prevention" and "CDC 24/7: Saving Lives. Protecting People™". To the right is a search bar and a "CDC A-Z INDEX" dropdown menu. Below the header is a green bar with "CDC Newsroom". A left sidebar contains a menu with items like "Newsroom Home", "Press Materials", "CDC Newsroom Releases", "CDC Newsroom Archives", "Journal Summaries", "Newsroom Image Library", "Audio/Video", "CDC Spokesperson", "Facts About CDC", and "Contact Media Relations". The main content area shows a breadcrumb trail: "CDC > Newsroom Home > Press Materials > CDC Newsroom Releases". The headline is "Expanding Naloxone use could reduce drug overdose deaths and save lives". Below the headline are social media icons for Facebook, Twitter, and a plus sign. A red notice states: "This website is archived for historical purposes and is no longer being maintained or updated." The "Press Release" section includes the date "For Immediate Release: Friday, April 24, 2015" and contact information: "Contact: [Media Relations](#) (404) 639-3286". The bottom of the page contains a snippet of the press release text: "Allowing more basic emergency medical service (EMS) staff to administer naloxone could reduce drug overdose deaths that involve opioids, according to a Centers for Disease Control and Prevention (CDC) study, 'Disparity in Naloxone Administration by Emergency Medical Service Providers and the Burden of Drug Overdose in Rural Communities,' published in the *American Journal of Public Health*."

Emphasis on Mimimizing use of Opioid Analgesics

Trends in the Pharmacological Management of Acute Pain

- Enhanced Recovery After Surgery (ERAS) protocols that combine multiple analgesics as part of comprehensive protocols have become commonplace
- Education for providers with emphasis on use of the smallest effective doses and shortest duration of analgesics after surgery have become common

Evaluating the Scientific Evidence

ARE OPIOIDS EFFECTIVE?

Twenty Years of Scientific Inquiry

Are Opioids Effective?

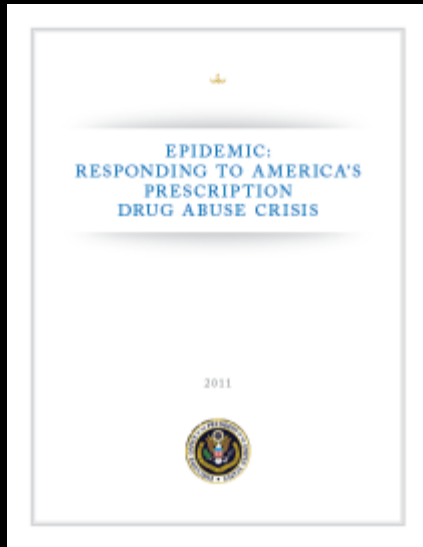
- A 2015 NIH workshop centered on the prescription drug abuse epidemic
- There is not one study long-term (>1 year) outcomes related to pain, function, quality of life, opioid abuse, or addiction
- Observational studies suggest that opioid therapy for chronic pain is associated with increased risk for overdose, opioid abuse, fractures, myocardial infarction, and markers of sexual dysfunction
- For some of these harms, higher dose was associated with increased risk

Addressing the Epidemic

CHRONIC OPIOIDS TODAY

2016 and Beyond

Chronic Opioids Today



The 2011 White House plan calls for:

- Expanded education of patients and health care practitioners
- An urgent call for new research
- Expansion of existing Prescription Drug Monitoring Programs (PDMPs)
- Better means for disposing of unneeded prescription drugs
- Tougher enforcement of existing laws focused on identifying and prosecuting practitioners

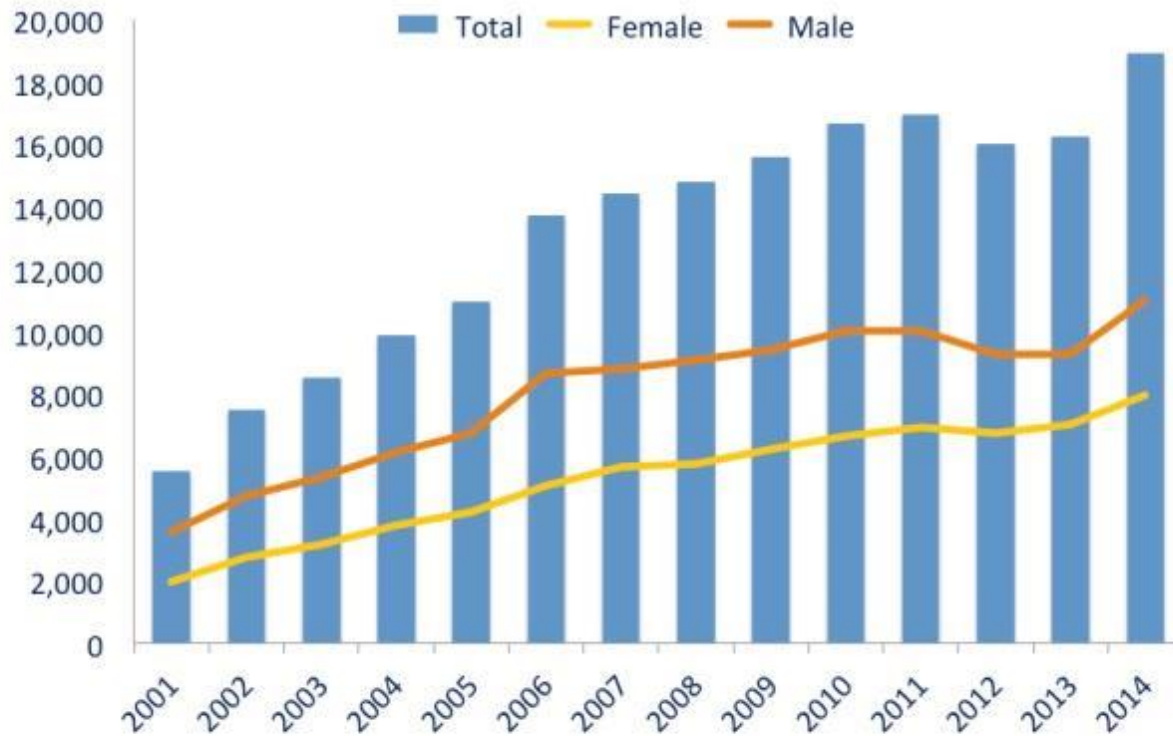
Chronic Opioids Today

NIH National Institute on Drug Abuse



National Overdose Deaths

Number of Deaths from Prescription Opioid Pain Relievers



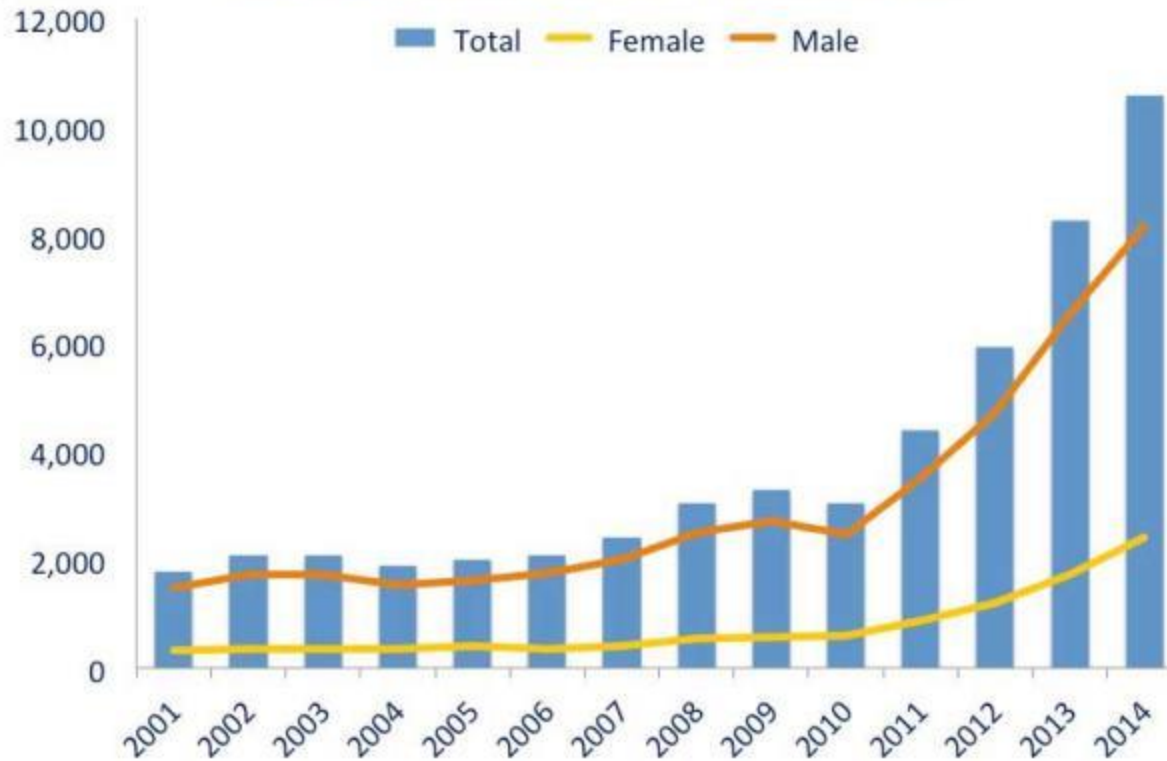
Source: National Center for Health Statistics, CDC Wonder

Chronic Opioids Today

NIH National Institute on Drug Abuse



National Overdose Deaths Number of Deaths from Heroin



Source: National Center for Health Statistics, CDC Wonder

Chronic Opioids Today

How do we appropriately select and manage patients with chronic non-cancer pain for chronic opioid therapy to treat only those with the greatest chance to benefit while minimizing the risk to the individual who is treated and our society?

Chronic Opioids Today

- Identify at-risk patients using validated screening tools
- Incorporate frequent monitoring, periodic urine screens, opioid therapy agreements, opioid checklists, and motivational counseling

Jamison RN, Mao J. Opioid analgesics. *Mayo Clin Proc* 2015; 90:957-968.

Chronic Opioids Today

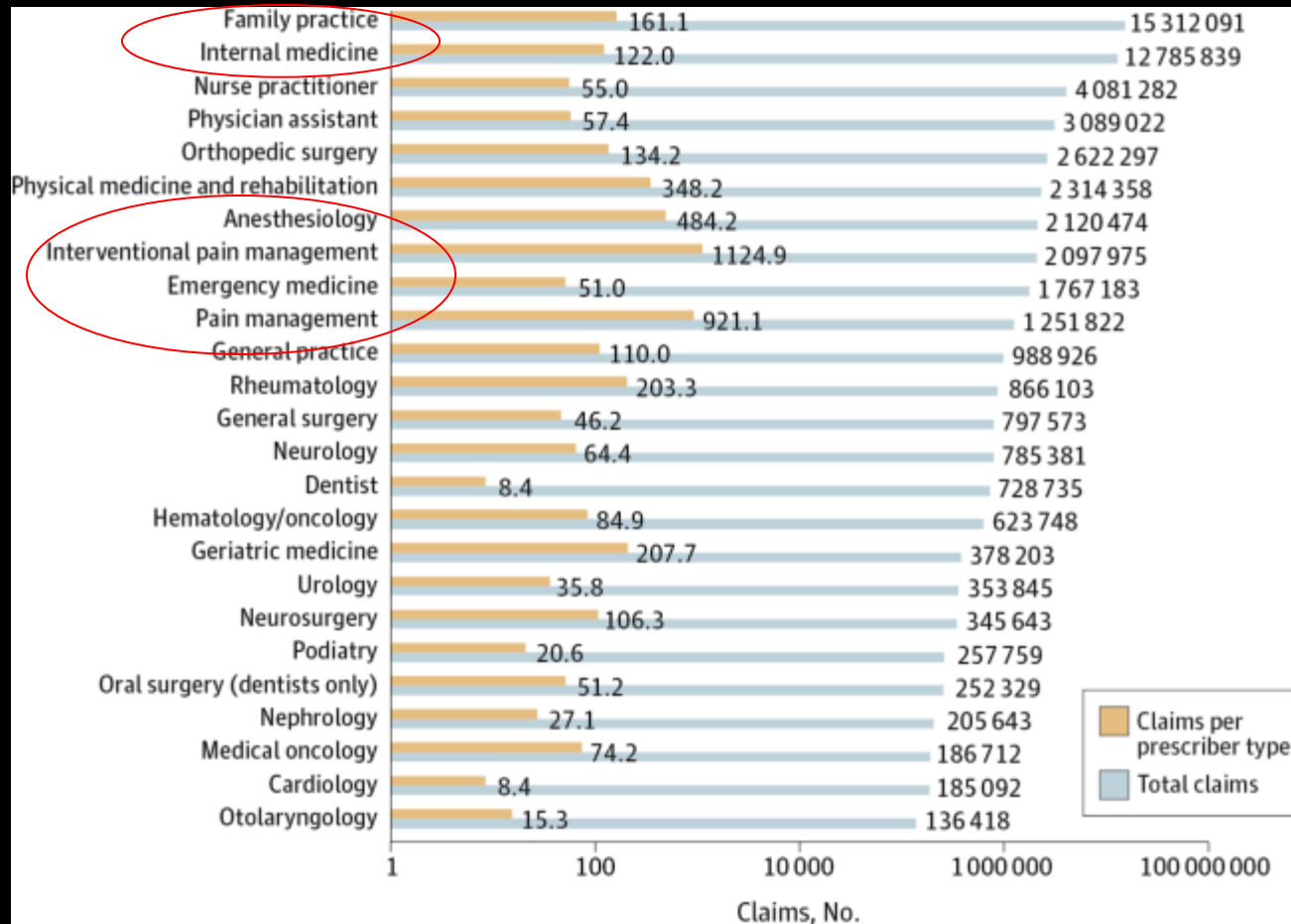
How do we identify and best manage those patients receiving chronic opioid therapy who are not benefiting from this course of treatment?

Chronic Opioids Today

Discontinuation and/or maintenance of chronic opioid therapy

- Guides for tapering opioids are non-existent
- Most studies are in those under treatment for substance use disorder
- Psychiatric co-morbidities and fears of medico-legal risk hinder treatment

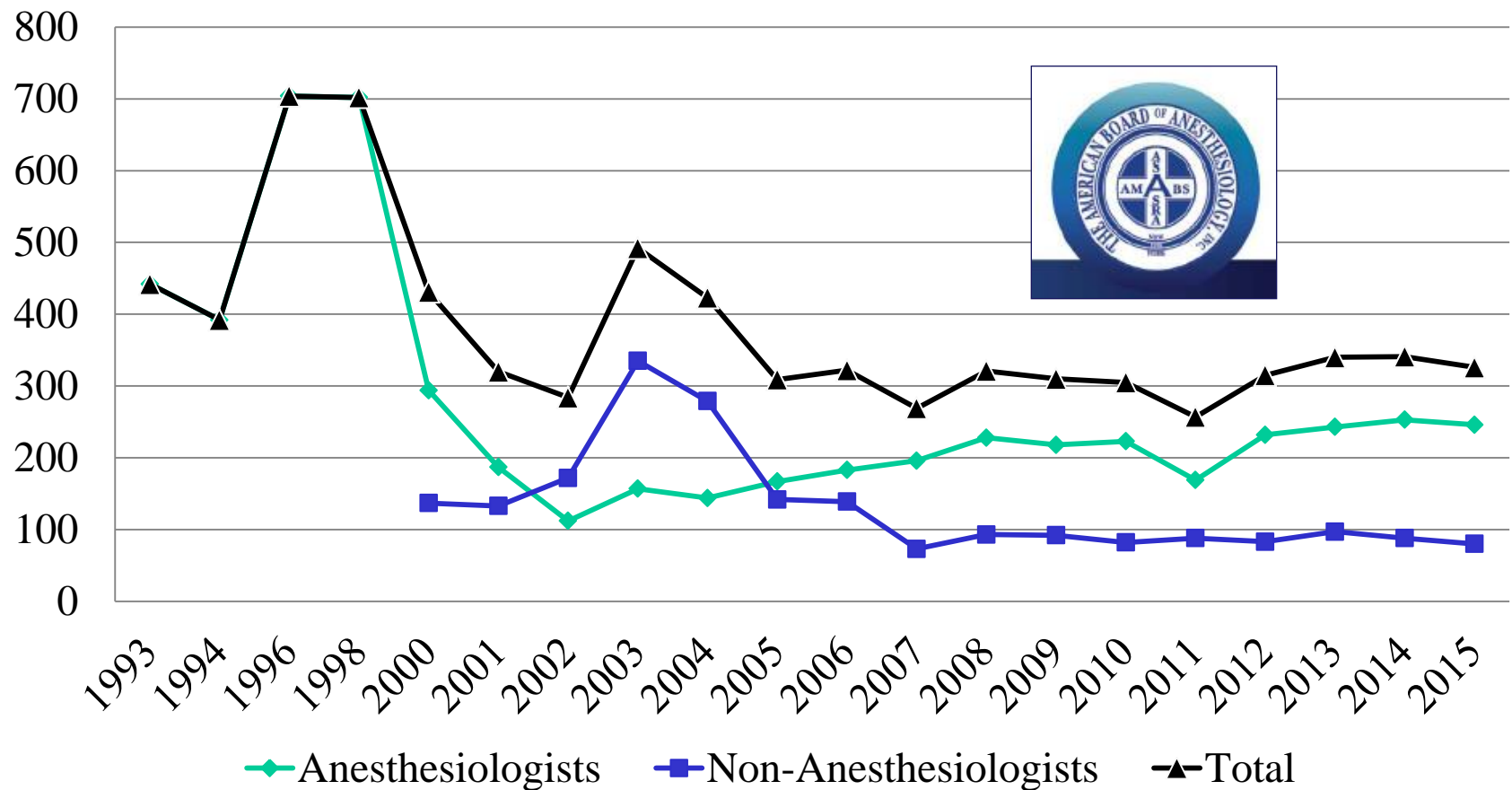
Chronic Opioids Today



JAMA Intern Med. 2016;176(2):259-261.

Physician Training in Pain Medicine

Number of ABMS Pain Medicine Diplomates





National Pain Strategy

A Comprehensive Population Health-Level Strategy for Pain

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Conclusions

- RESEARCH: Aimed at developing new analgesics that are more effective and less subject to abuse
- RESEARCH: Aimed at determining who will benefit most from chronic opioid therapy with an emphasis on measurable improvements in function
- RESEARCH: Aimed at identifying patients who are not benefiting from chronic opioid therapy and determining how best to discontinue opioids

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Conclusions

- **EDUCATION:** Improving the education of all health care providers in the compassionate and evidence-based management of chronic pain is needed
- **INNOVATION:** The magnitude of this problem calls for the adoption of new models for collaborative care among primary care and specialty providers for managing patients with chronic pain with an emphasis on measurable improvement in function



Boston Public Library

Boston, Massachusetts, 2012