

History of Malignant Pain: Treatment with Opioids

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**Pain, Opioids, and Addiction: An Urgent Problem for
Doctors and Patients**

March 5-6, 2007

Some of the Questions that Must be Answered

- 1) Who is involved in Rx drug abuse? (e.g. age, presence or absence of pain- real numerators and denominators)
- 2) What are the sources of the Rx drugs that are abused?
- 3) What is the relationship between the increase in opioid prescribing for pain and Rx drug abuse?

2004 National Survey on Drug Use and Health

Ball et. al, APS Talk

- 18% of US population admits to non medical use of pain relievers in the past year.
- Only 3% of the population over 26 admits to this abuse

2005 National Survey on Drug Use and Health

www.oas.samhsa.gov

- 4 million young adults aged 18 to 25 years (12.4%) used prescription pain relievers non-medically
- 17% met criteria for dependence or abuse
 - Source: 37.5% obtained them free from a friend or a relative
 - 19.9% bought them from a friend or relative
 - 13% obtained them from a doctor

Theft and Loss of Opioid Analgesics (DEA)

Total: 28 Million Dosages (2000-2003)

<u>6 Study Opioids</u>	<u>Dosage Units</u>
Fentanyl	81,371
Meperidine	132,950
Hydromorphone	325,921
Methadone	454,503
Morphine	1,026,184
Oxycodone	4,434,731
TOTAL (6 opioids)	6,455,660

Plus 3.9 Million DUs of Hydrocodone in 2003 alone

Some of the Questions that Must be Answered

- 4) What are the factors contributing to an increase in deaths from methadone?
- 5) What are the consequences of a lack of, or misinformation about, Rx drug abuse on physician prescribing and on the appropriate use of opioids by pain patients?

Some of the Questions that Must be Answered

- 6) What are the ethical responsibilities of physicians who prescribe opioids in a complex regulatory environment? How do we keep doctors from being cops?
- 7) Why is Rx drug abuse an "American" Problem?

Opioids in Cancer Pain Management

- The American experience
- 1940's-1960's - strong negative statements against the use of opioids
 - 1947 Lee: JAMA
 - 1956 Cole: The Management of Pain
Scriffen: The Management of Pain in Cancer

Opioids in Cancer Pain Management

1967-1976 – Clinical experience at St. Christopher's
Hospice and the Analgesic Studies
Group MSKCC

1981 - Introduction of slow release
morphine

1982 - Creation of Medicare Hospice
Benefit

Opioids in Cancer Pain Management

1986 - Publication of WHO Cancer Pain
Relief Monograph

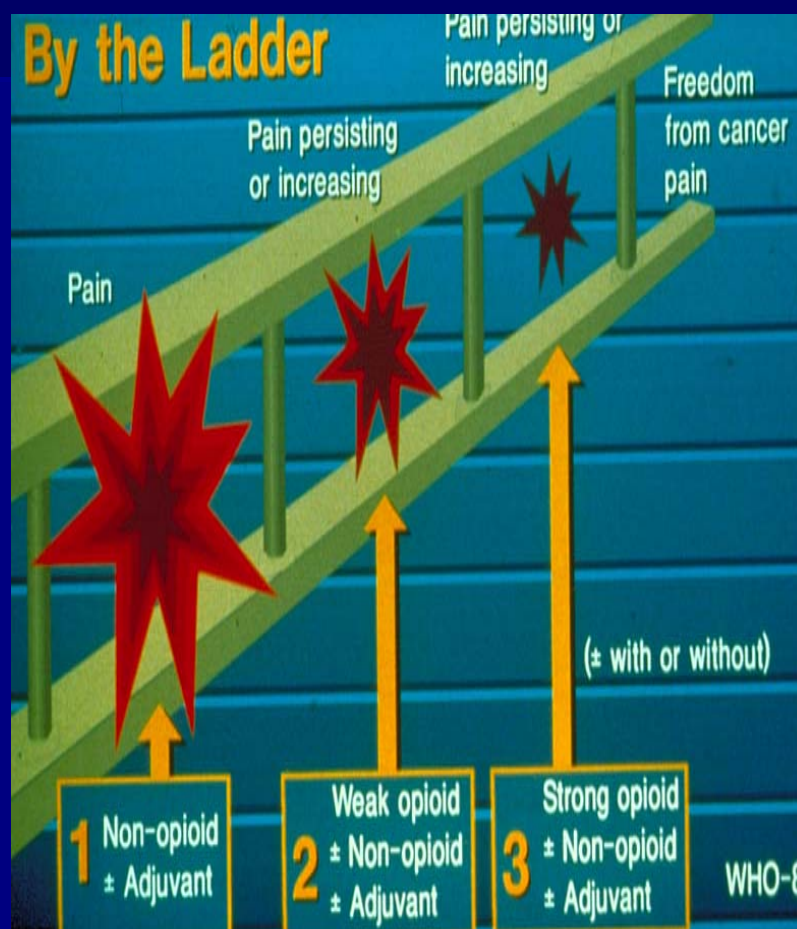
1990 - Publication of WHO Palliative
Care Monograph

Freedom from Cancer Pain



WHO-

By the Ladder



WHO-8

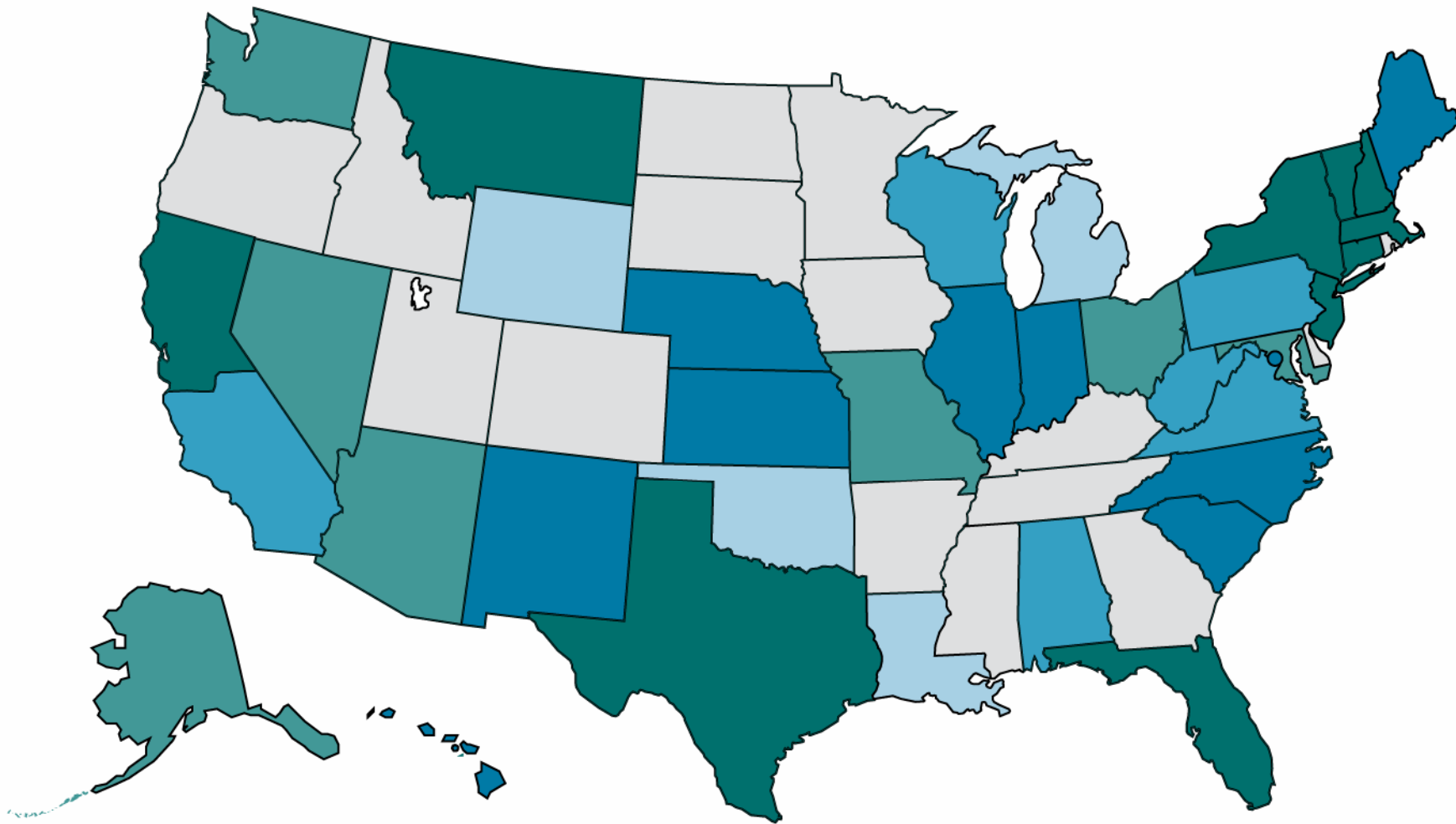
Opioids in Cancer Pain Management

- Controversy over the legalization of heroin for pain relief-1970's
- Advocacy for the decriminalization of cancer pain - 1980's

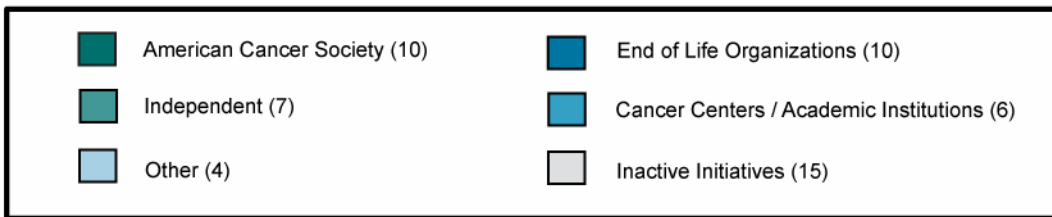
Opioids in Cancer Pain Management

- 1996-Development of American Alliance of Cancer Pain Initiative
- 2001-JCAHO pain standards
<http://www.jointcommission.org/>
- 1996-Creation of the University of Wisconsin Pain and Policy Center

Alliance of State Pain Initiatives SPI Partnerships



November 2006



Opioids in Pain Management

- Three Institute of Medicine Reports
 - Approaching Death
 - Improving Palliative Care for Cancer
 - When Children Die

<http://www.iom.edu/iom/iomhome.nsf>

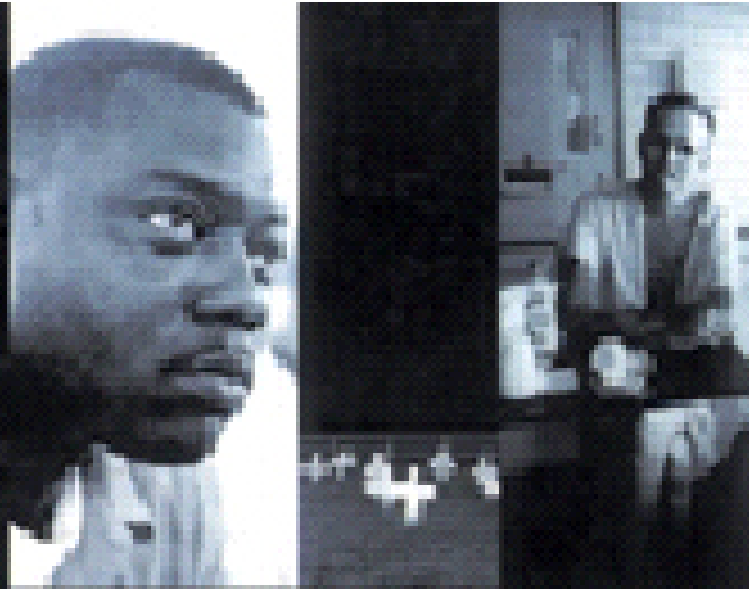
Improving Palliative Care for Cancer

S U M M A R Y A N D R E C O M M E N D A T I O N S



I N S T I T U T E O F M E D I C I N E
N A T I O N A L R E S E A R C H C O U N C I L

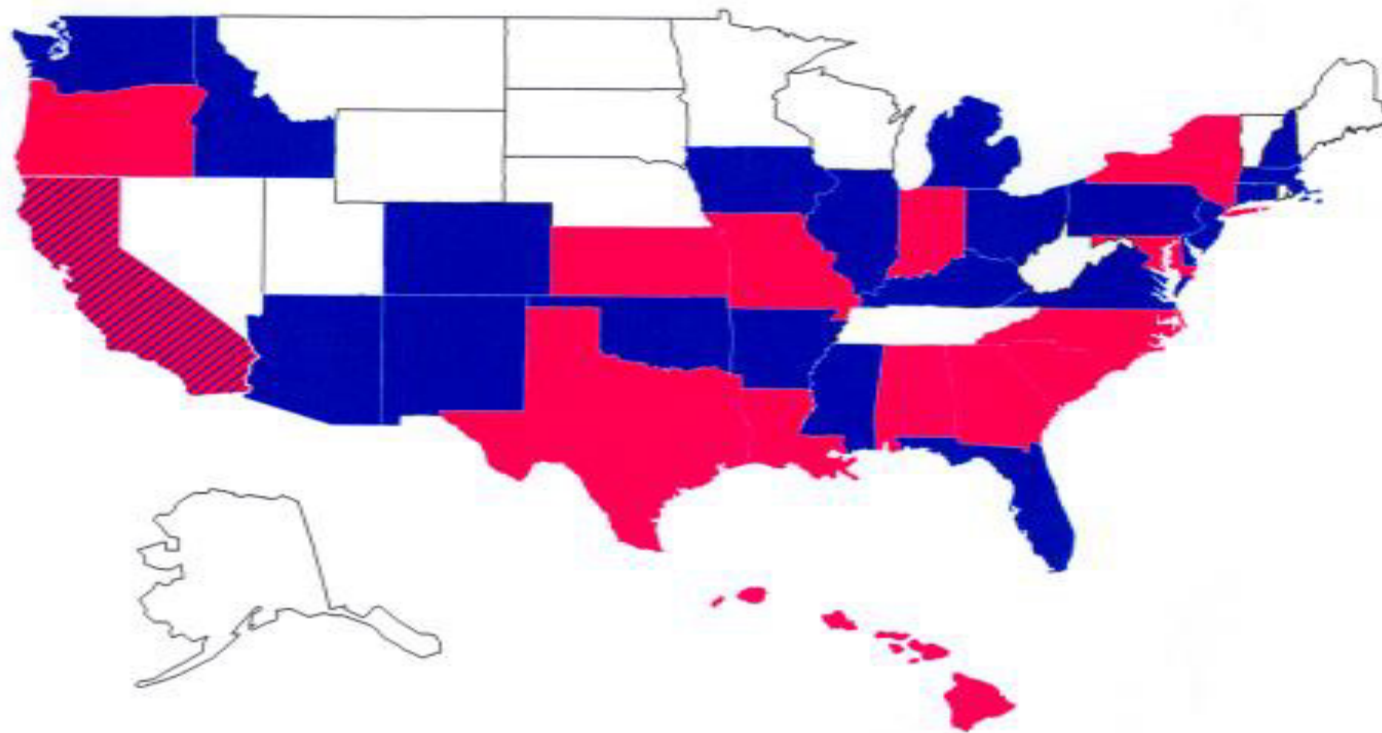
ANGOLA PRISON HOSPICE
Opening the Door






ANGOLA PRISON HOSPICE
Opening the Door



End of Life Care in Corrections Nationwide



-  Operating Programs
-  Requested Technical Assistance
-  No Information



Opioids in Cancer Pain Management

- Surveys of the under-treatment of cancer pain.

Documentation of Undertreatment

1994 Cleeland et al.

Less than half of persons with metastatic cancer were receiving adequate treatment of their pain

1996 The SUPPORT Study

40% had moderate to severe pain in the last three days of life

Documentation of Undertreatment

1998

Bernabei et al.

Daily pain is common among nursing home residents with cancer and is often untreated

2000

Wolfe et al. Children who die of cancer have substantial suffering in the last month of life

Documentation of Undertreatment

2001-Teno et al.

In US nursing homes persistent pain varies from 39 to 49% and is significantly undertreated

Advances in Cancer Pain 2007

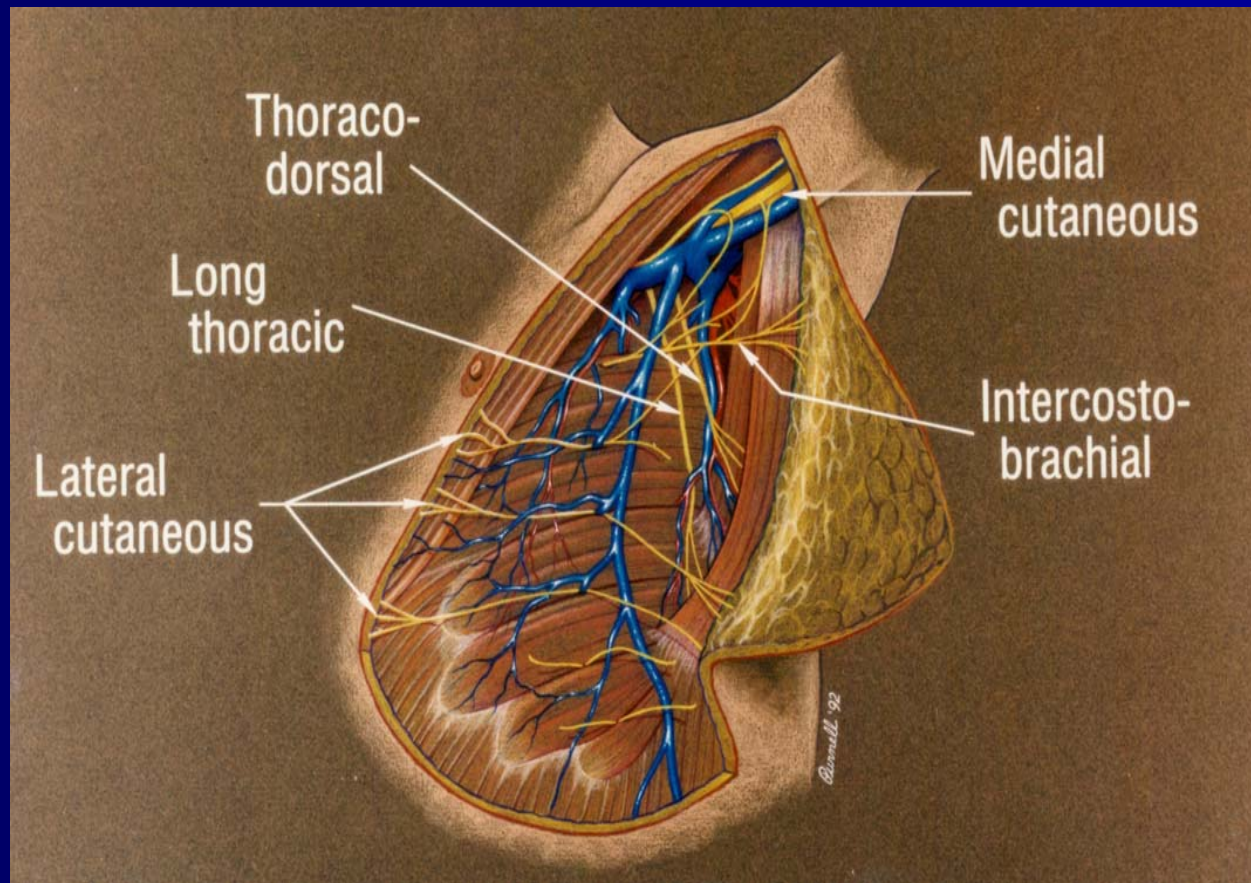
- defined the epidemiology of cancer pain in adults and children
- defined the physician, patient and institutional barriers to effective management

Advances in Cancer Pain 2007

- defined the tumor, treatment, and related pain syndromes
- defined evidence-based algorithms for assessment

Post Surgical Pain Syndrome

Postmastectomy Pain



Advances in Cancer Pain 2007

- validated pain and symptom assessment scales in adults and children
 - MPAC
 - MSAS
 - ESAS
 - BPI
 - MPQ

Advances in Cancer Pain 2007

- developed new methods and systems of drug delivery
 - slow release, transdermal, transmucosal opioids
 - PCA pumps and epidural and intrathecal infusion devices

Advances in Cancer Pain 2007

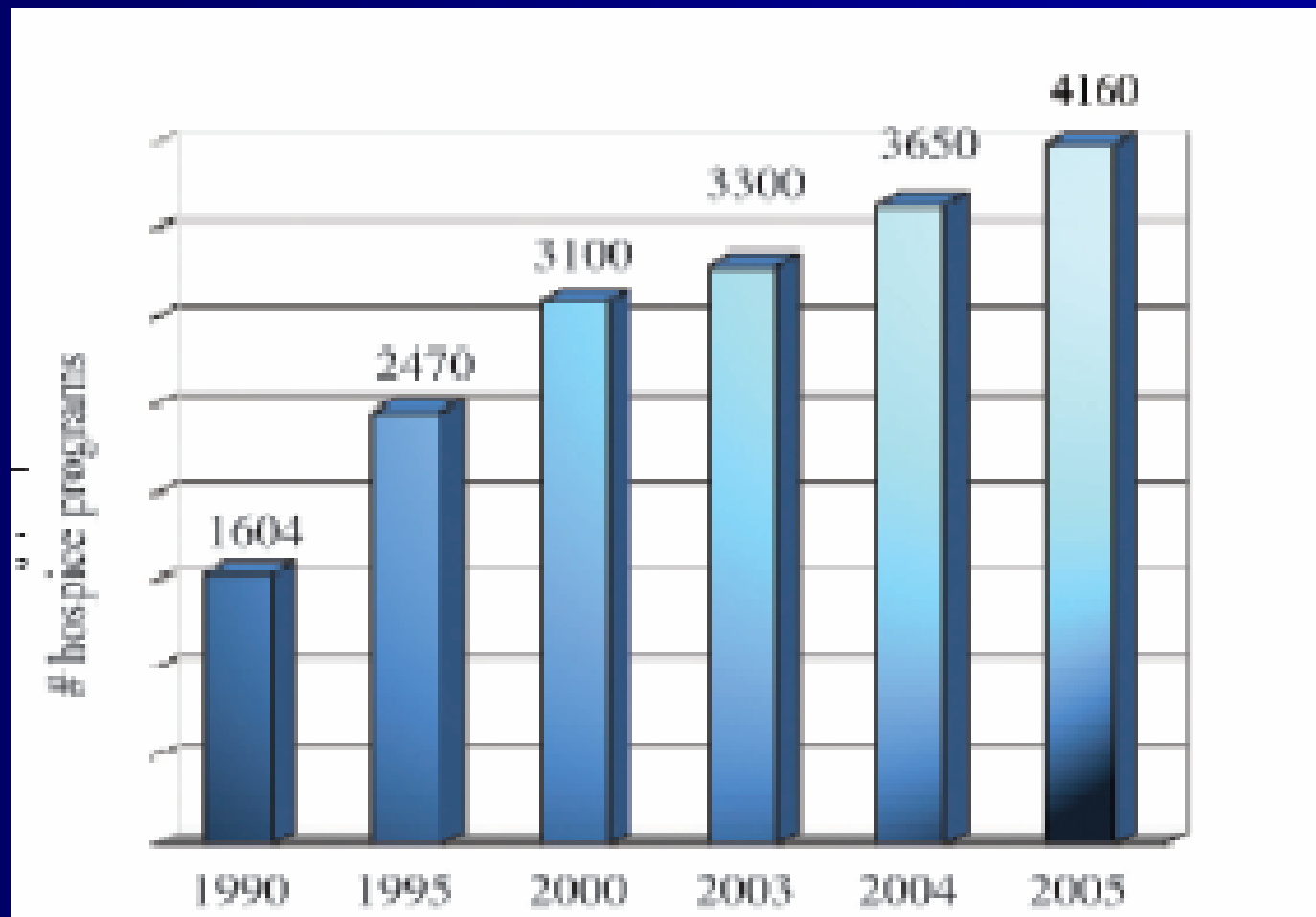
- developed evidence based guidelines for adjuvant analgesics

Advances in Cancer Pain 2007

- expansion of interdisciplinary pain management and palliative care programs

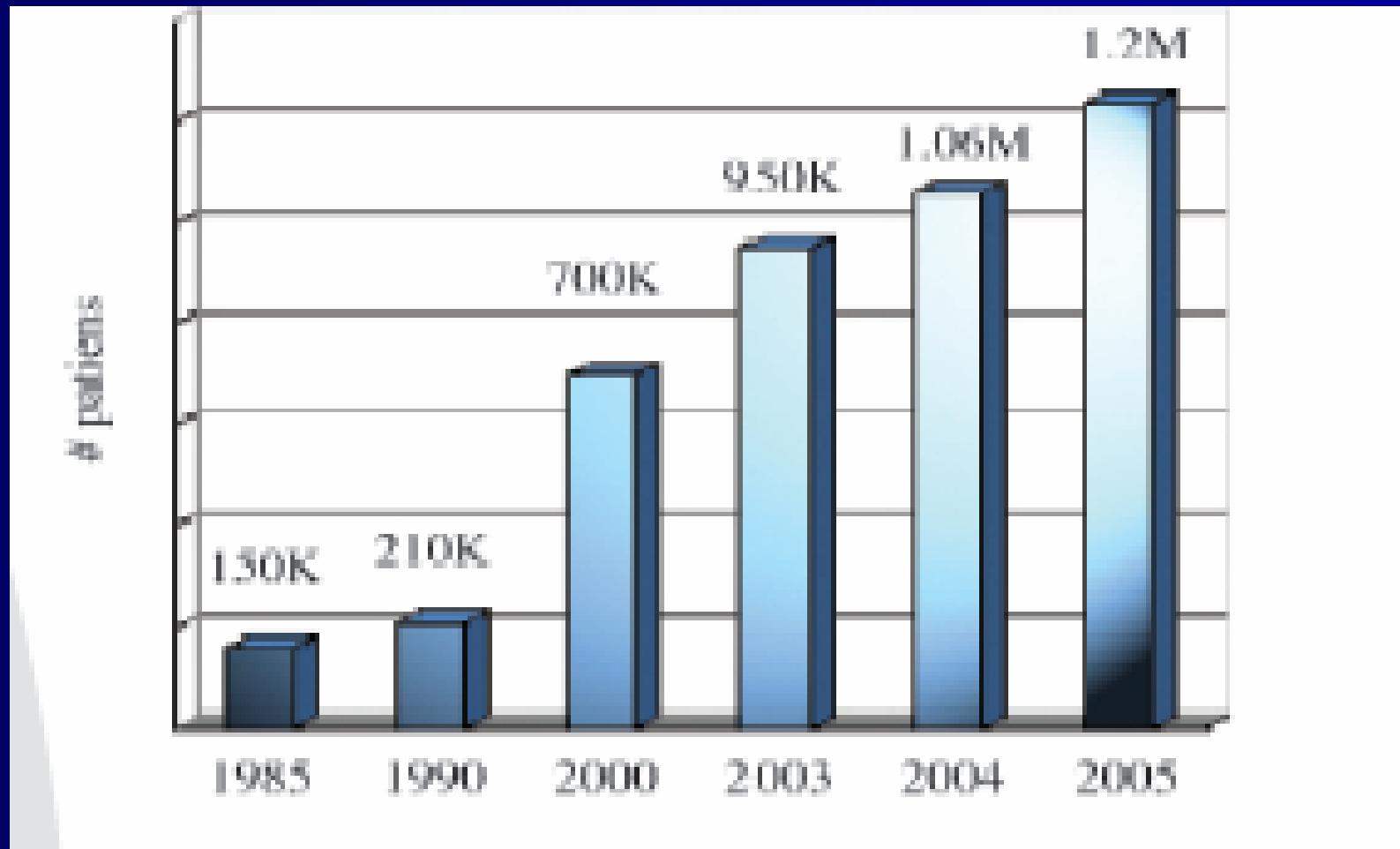
An Upward Trend in Program Growth

NHPCO



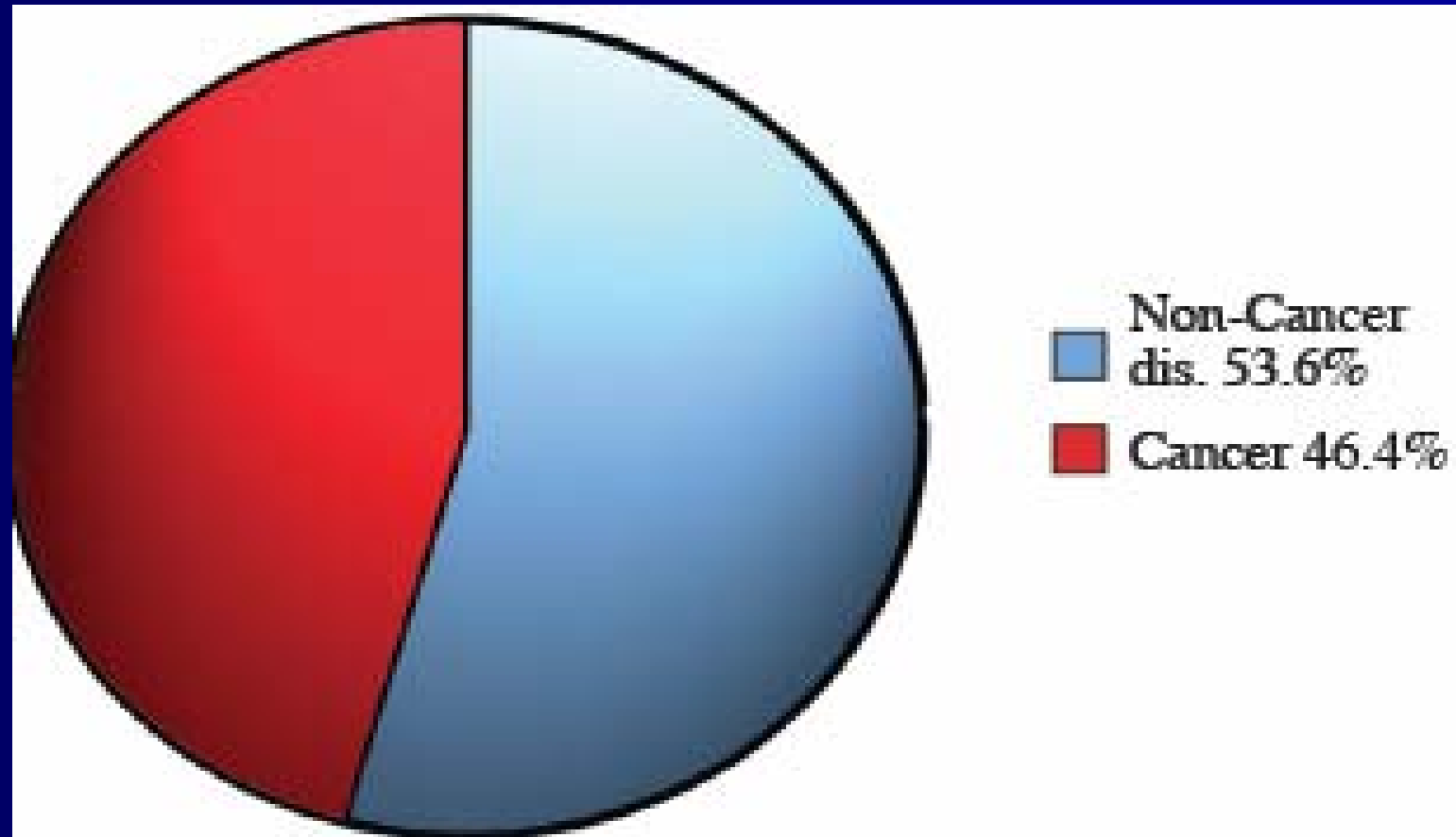
Patient Demographics

NHPCO



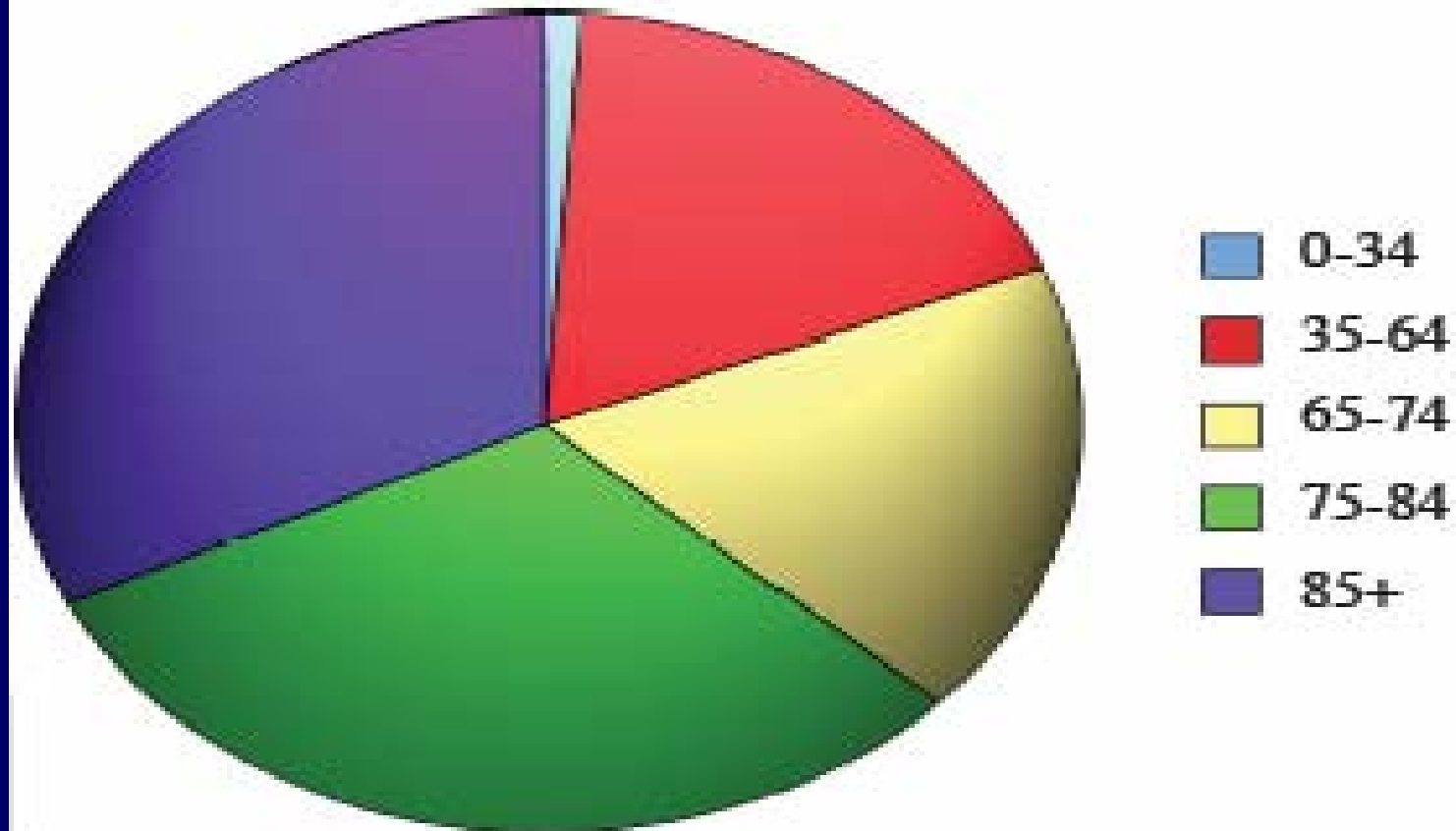
More Non-Cancer Admissions in 2005

NHPCO



More Hospice Patients Over 65

NHPCO

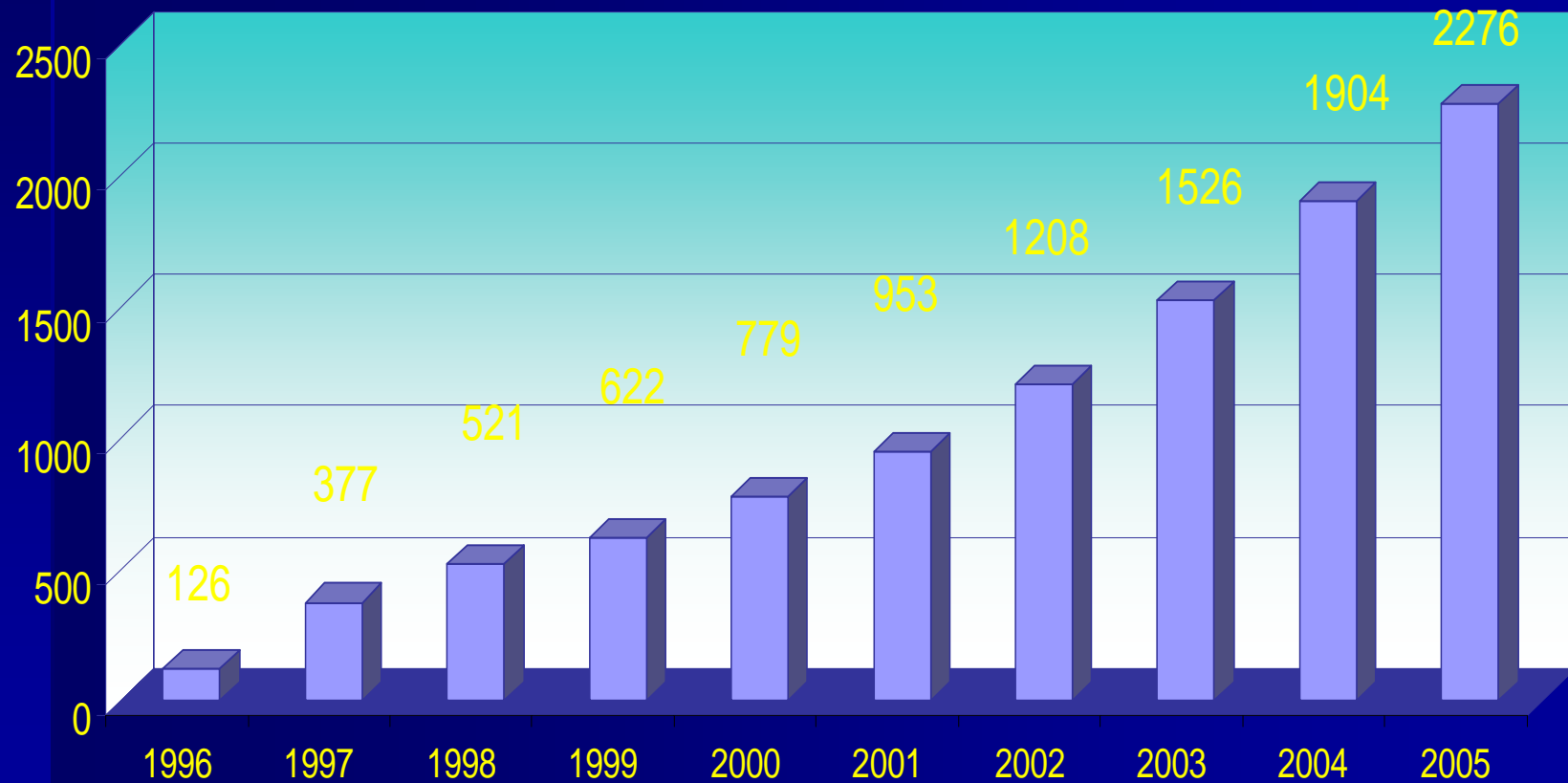


Use of Opioids in Hospice Care

- 2/3 hospice patients have pain
- 800,000 patients receive an opioid
- Analgesics account for 50% of drug costs (400 million/year)

ABHPM Diplomates

Cumulative Number of Physicians Certified
Via ABHPM Examination, As of December 2005



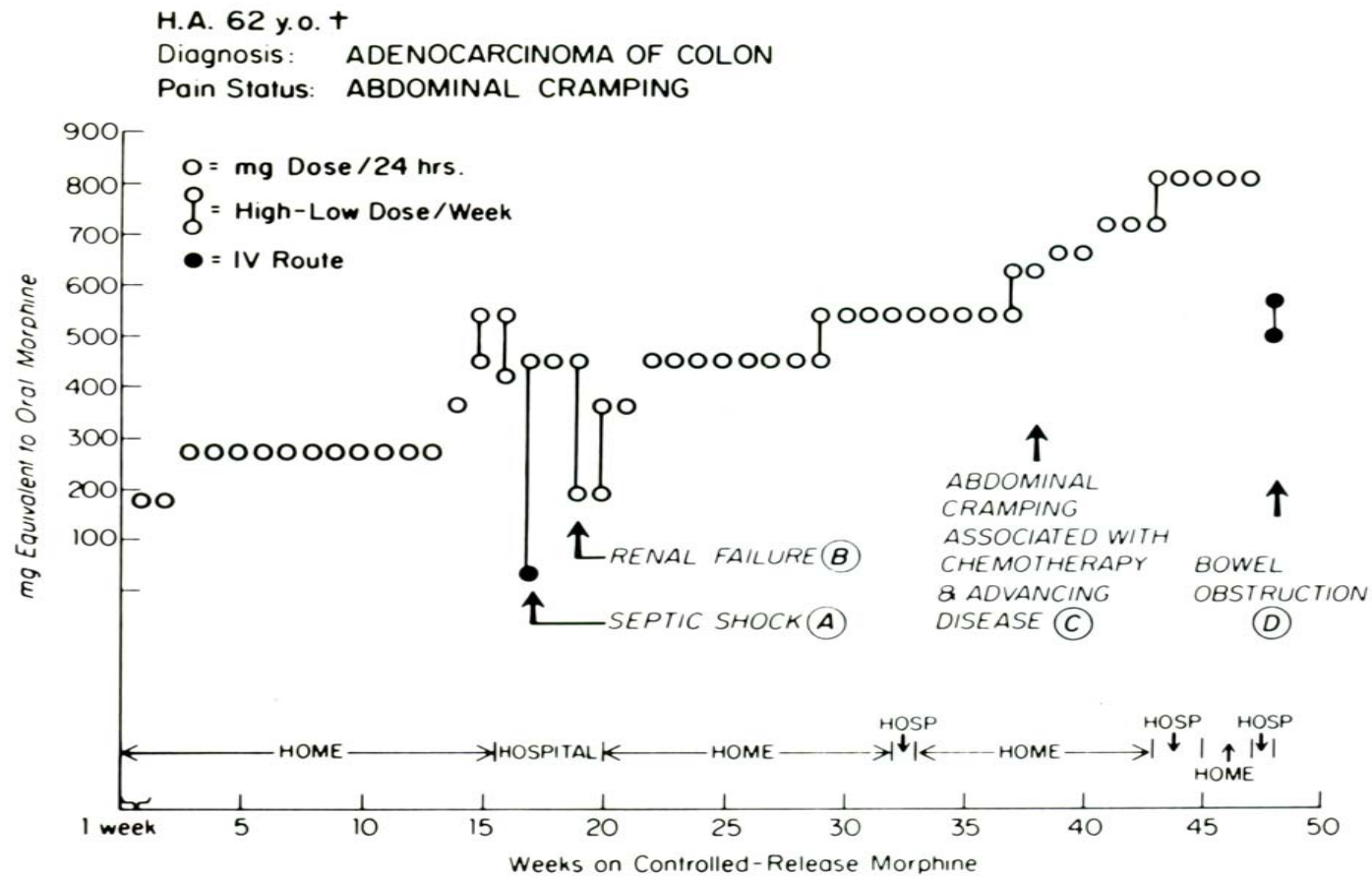
Advances in Cancer Pain 2007

New concepts in opioid
pharmacology

New Concepts in Opioid Pharmacology

- pain stimulus not tolerance dictates opioid requirements

Opioid Dose Escalation in Chronic Pain



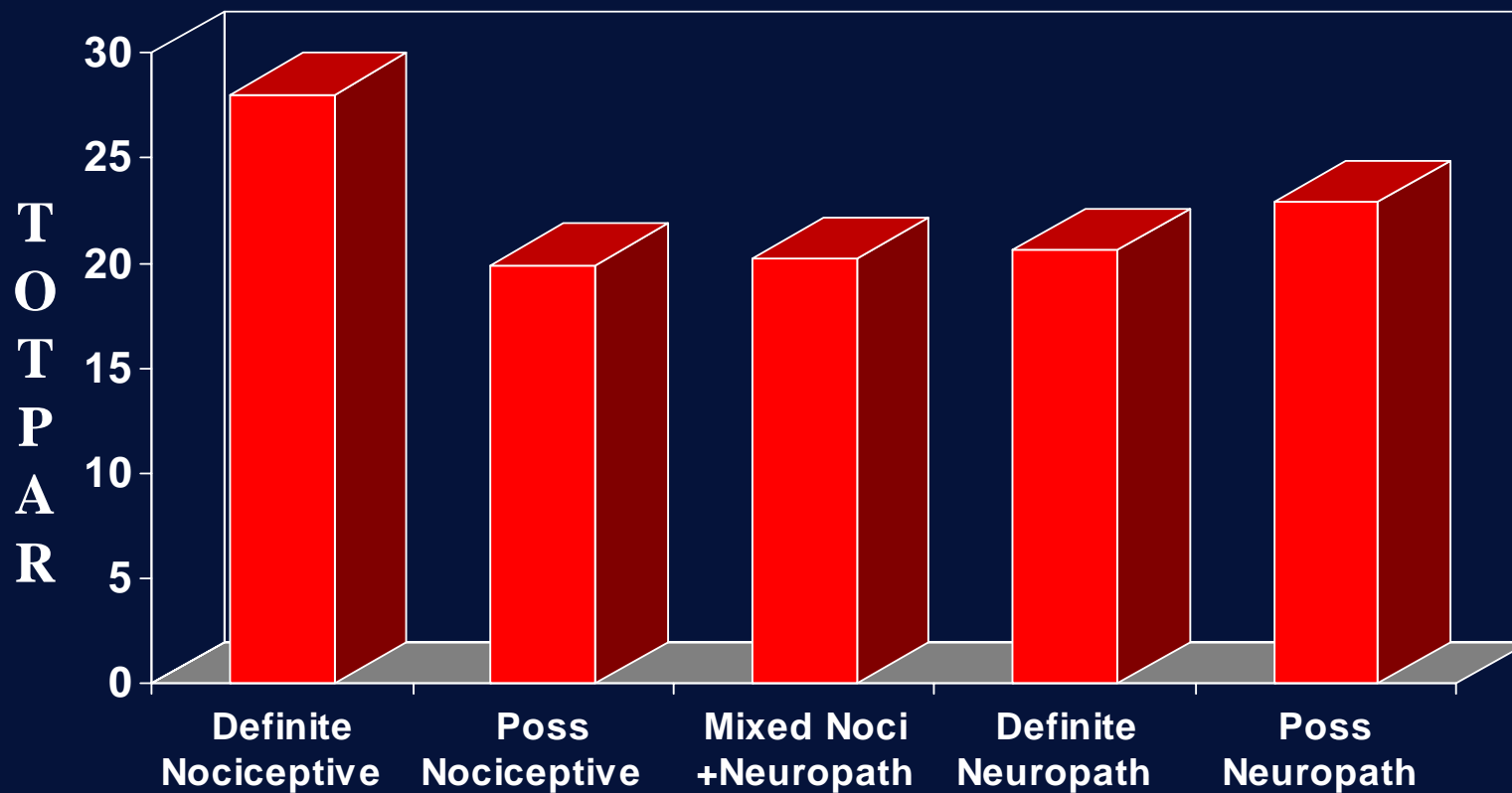
New Concepts in Opioid Therapy

The Concept of Opioid Responsiveness

Neuropathic pain is less responsive than nociceptive pain to opioid analgesia

Opioid Responsiveness Nociceptive vs Neuropathic Pain

Cherney et al. Neurology 1994;44:857-61.

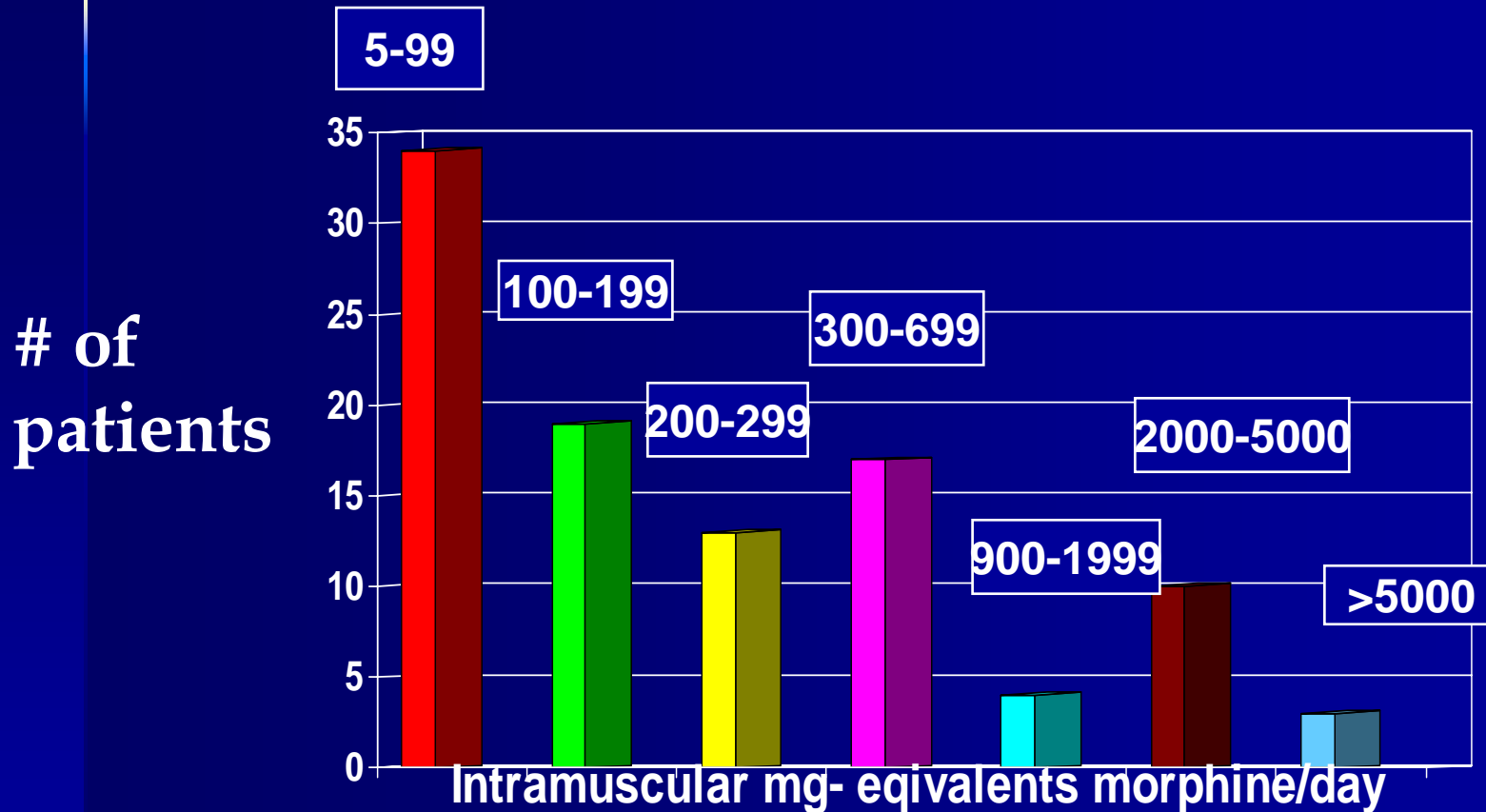


New Concepts in Opioid Pharmacology

- wide interindividual variations in opioid use and response

Peak Opioid Requirements in 24 Hour Period

Foley KM. NEJM. 1985;313:84-95.



New Concepts in Opioid Pharmacology

- cross tolerance is incomplete

Opioid Rotation in Chronic Pain

- Switching opioids in cancer pain*
 - 80% of patients require 1 switch
 - 44% of patients require 2 switches
 - 20% of patients require 3 or more switches

Cherny NI, et al. Cancer 1995;76:1288-93

Opioid Rotation in Cancer Pain

- Why is opioid rotation necessary?
 - Improve efficacy
 - Avoid toxicity
 - <cognitive failure; sedation
 - <hallucinations; myoclonus
 - <pruritus; urinary retention
 - Change route of administration
 - <oral-parenteral
 - transdermal/transmucosal fentanyl

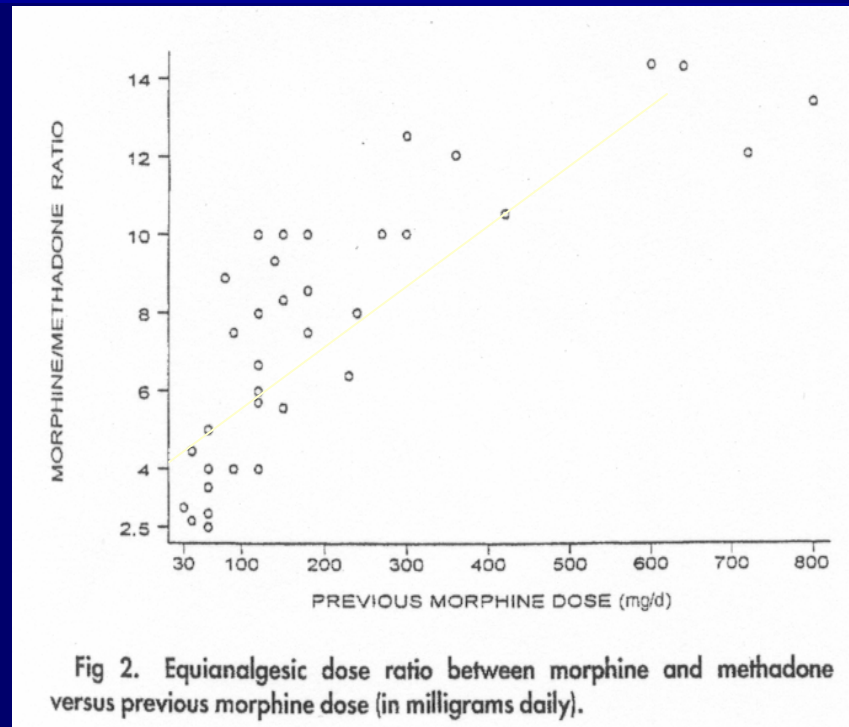
Rotation from morphine to methadone- Estimating the equianalgesic dose conversion ratio

Switching From Morphine to Oral Methadone in Treating Cancer Pain: What Is the Equianalgesic Dose Ratio?

By Carla Ripamonti, Liliana Groff, Cinzia Brunelli, Daniela Polastri, Alessandro Stavrakis, and Franco De Conno

J Clin Oncology 16:3216-3221, 1998

This was a prospective study in 38 cancer patients who were switched from morphine to methadone and the dose titrated until an estimated equianalgesic dose was achieved.



When the estimated equianalgesic dose ratio between morphine and methadone is plotted as a function of the previous morphine dose, a positive linear relationship was obtained.

This rotation approach uses the changing conversion ratio found by Ripamonti to calculate the rotation dose of methadone

Table 1

Suggested Safe and Effective Starting Doses When Rotating Patients from Oral Morphine to Oral Methadone^{7,27}

MORPHINE DOSE	CONVERSION RATIO	EXAMPLE
30–90 mg	4:1	30 mg morphine ≈ 7 mg methadone
91–300 mg	8:1	300 mg morphine = 35 mg methadone
> 300 mg ^a	12:1	400 mg morphine ≈ 35 mg methadone

^aIf previous morphine dose is *much* higher than 300 mg, the dose ratio will be higher than 12:1.

Manfredi and Houde, 2003
www.SupportiveOncology.net

Thus, a patient receiving 400 mg of oral morphine daily should be started on 35 mg of oral methadone daily. This can be administered in a divided dose from two to three times per day.

Challenges in Pain Research

Pain in Survivors

- Prevalence of persistent pain in cancer survivors
- 10 million cancer survivors
 - Limited data on pain, eg:
 - 20% patients of head and neck cancer patients have pain 2 years post treatment
 - 10-15% women have postmastectomy pain
- Passik, et al. planned study of 600 cancer survivors to assess prevalence of pain, psychological distress and HRQL

Challenges in Pain Research

National Institute of Health grant awards for pain, nausea and dyspnea research:
an assessment of funding patterns in 2003

J Pain, 2005;6(5): 275-6

- 2003 NIH funded 548 grants in pain representing 1% of NIH budget
- No NIH Pain Institute

Specific Controversies in Opioid Therapy

- Does the presence of pain affect opioid use
 - cancer patients maintain analgesia on stable doses for months and years
 - dose escalation is associated with change in pain status
 - tolerance to analgesic does not limit effective use
 - wide interindividual variation in response to opioids

Specific Controversies in Opioid Use

Martin TJ, Kim SA, Buechler NI, et al. *Anesthesiology*,
2007;106:312-322

Animal data to support pain modulating opioid use

- Rats in pain titrate their opioids to relieve pain
- Nerve injury in rats reduced the reinforcing effects of low doses of opioids. Only doses of each opioid that reduced mechanical hypersensitivity maintained self-administration.

Specific Controversies in Opioid Drug Therapy

- the long term efficacy of opioids in neuropathic pain
- the assessment of societal risk of opioid availability

Long-term efficacy of opioids in neuropathic pain

Foley, NEJM 2003

- 4-17% remain on opioids at one year
- Lack of evidence of long-term efficacy of opioids for chronic neuropathic pain

Specific Controversies on Opioid Therapy for Patients with Pain

- What percent of the population is at risk of prescription abuse when an opioid is prescribed appropriately for severe pain

Trends in medical use and abuse of opioid analgesics.

Joranson DE, Ryan KM, Gilson AM, Dahl JL. JAMA. 2000 Aug 2;284(5):564.

Pain and Policy Studies Group, Comprehensive Cancer Center,
University of Wisconsin Medical School, Madison, USA.
joranson@facstaff.wisc.edu

Use of oral morphine at home in Kerala, India

- 1723 patients studied over two years
- No instance of abuse or diversion

The Lancet 2001; 358: 139-43

A reassessment of trends in the medical use and abuse of opioid analgesics and implications for diversion control: 1997–2002

Aaron M. Gilson PhD- , Karen M. Ryan MA, David E. Joranson MSSW and June L. Dahl PhD · Journal of Pain and Symptom Management, 2004;28(2):176-188

CPDD Position Statement

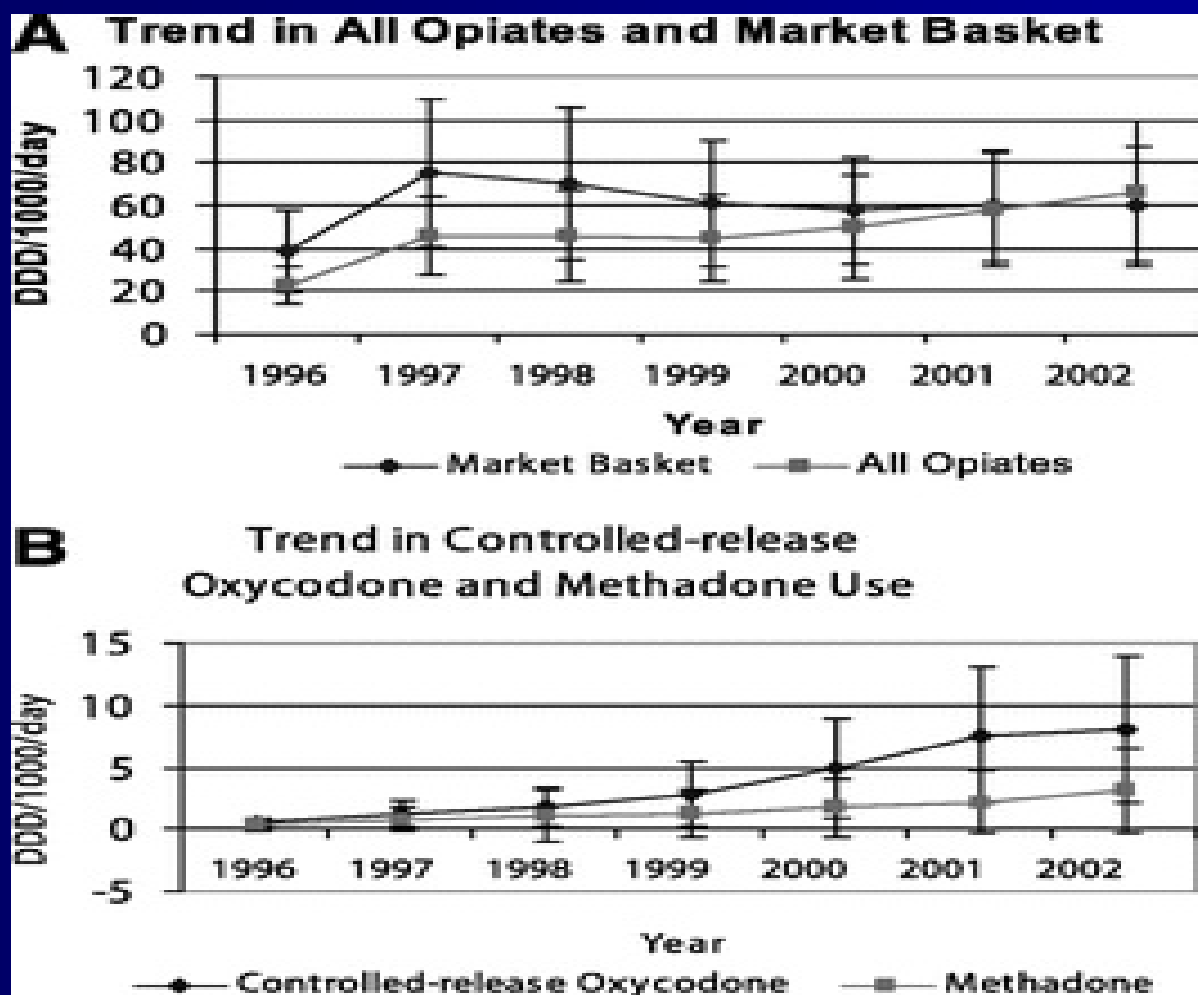
- Position statement: College on Problems of Drug Dependence Task Force on prescription opioid non-medical use and abuse

Drug and Alcohol Dependence 2003;69:215-222

Trends and Geographic Variation of Opiate Medication Use in State Medicaid Fee-For-Service Programs, 1996 to 2002

Zerzan, Judy T. MD, MPH*; Morden, Nancy E. MD†; Soumerai, Stephen ScD‡; Ross-Degnan, Dennis ScD‡; Roughead, Elizabeth PhD§; Zhang, Fang PhD‡; Simoni-Wastila, Linda PhD¶; Sullivan, Sean D. PhD. *Medical Care*, 2006;44(11):1005-1008.

Trends and Geographic Variation of Opiate Medication Use in State Medicaid Fee-For-Service Programs, 1996 to 2002



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