28th Annual Gabor Racz Advanced Interventional Pain Conference and Workshop
Budapest, Hungary August 25-27, 2025

Patient Selection for Interventions for Cancer Pain

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Conflicts of Interest

- None

What are we discussing today?

- Why do we need to do interventions for cancer pain?
  - Incidence and Prevalence of Cancer pain
- Limitations of the WHO ladder
- The journey of a cancer patient
- How to select patients?
- How to select interventions?
- What patients want?
- Summary

Cancer Pain: Introduction

- Pain is the **most feared symptom** of cancer
- Pain announces disease progression and shortening of life expectancy
- Pain is **undertreated** in 31.8% of patients
- How long do different cancer populations suffer from significant pain ? – Data insufficient

Greco MT et al J Clin Oncol 2014

original article

Annals of Oncology 20: 1420–1433, 2009
doi:10.1093/annonc/mdp001
Published online 24 February 2009

Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes

H. Breivik[1]*, N. Cherny[2], B. Collett[3], F. de Conno[4], M. Filbet[5], A. J. Foubert[6], R. Cohen[7] & L. Dow[7]

[1]*Faculty of Medicine, University of Oslo and Department of Anaesthesiology, Rikshospitalet University Hospital, Oslo, Norway;* [2]*Cancer Pain and Palliative Medicine Services, Shaare Zedek Medical Center, Jerusalem, Israel;* [3]*The Pain Management Service, University Hospitals of Leicester NHS Trust, Leicester, UK;* [4]*Rehabilitation and Palliative Care Unit, National Cancer Institute (Foundation), Milan, Italy;* [5]*Centre de soins palliatifs, Centre hospitalier Lyon sud, HCL CHU de Lyon, Pierre Benite, France;* [6]*Departement Gezondheidszorg, Erasmushogeschool, Brussels, Belgium and* [7]*Mundipharma International Ltd, Cambridge Science Park, Cambridge, UK*

Received 29 May 2008; revised 21 October 2008; accepted 22 December 2008

UK
France
Norway
Italy
Sweden
Finland
Czech Republic
Denmark
Romania
Switzerland
Ireland
Israel

www.EPICsurvey.com

n=322

HCP with main responsibility for managing pain:

Severe to most-severe pain

42%
Medical Oncologist

19%
General Practitioner

70% have never been referred to a pain specialist or pain clinic

Prevalence of pain in patients with cancer: a systematic review of the past 40 years

Meta-analysis of 54 studies > 6000 patients (1966 to 2005)

Prevalence of pain

- after curative treatment, **33%**
- during anticancer treatment, **59%**
- with advanced disease,metastatic, terminal **64%**
- all disease stages, **53%**

>33% grade pain as moderate or severe

Despite WHO recommendations, cancer pain still is a major problem.

Annals of Oncology, 2007, MHJ van den Beuken-van Everdingen

Prevalence of pain in patients with cancer: update on previous data

Meta-analysis of 122 studies (Sept 2005 – Jan 2014)
(PubMed, EMBASE, CINAHL, Medline and Cochrane)
4117 titles – 117 studies on pain (n=63,533) and 52 studies on pain severity (32,261)

Prevalence of pain

- after curative treatment, **39.3%**
- during anticancer treatment, **55%**
- with advanced disease, metastatic, terminal **66.4%**

>38% grade pain as moderate or severe

J Pain Symptom Manage. 2016 Jun;51(6):1070-1090.e9. doi: 10.1016/j.jpainsymman.2015.12.340. Epub 2016 Apr 23.

Update on Prevalence of Pain in Patients With Cancer: Systematic Review and Meta-Analysis.

van den Beuken-van Everdingen MH[1], Hochstenbach LM[2], Joosten EA[3], Tjan-Heijnen VC[4], Janssen DJ[5].

Undertreatment of Pain/ What does patients feel

Prevalence of under-treatment in cancer pain: A review of published literature

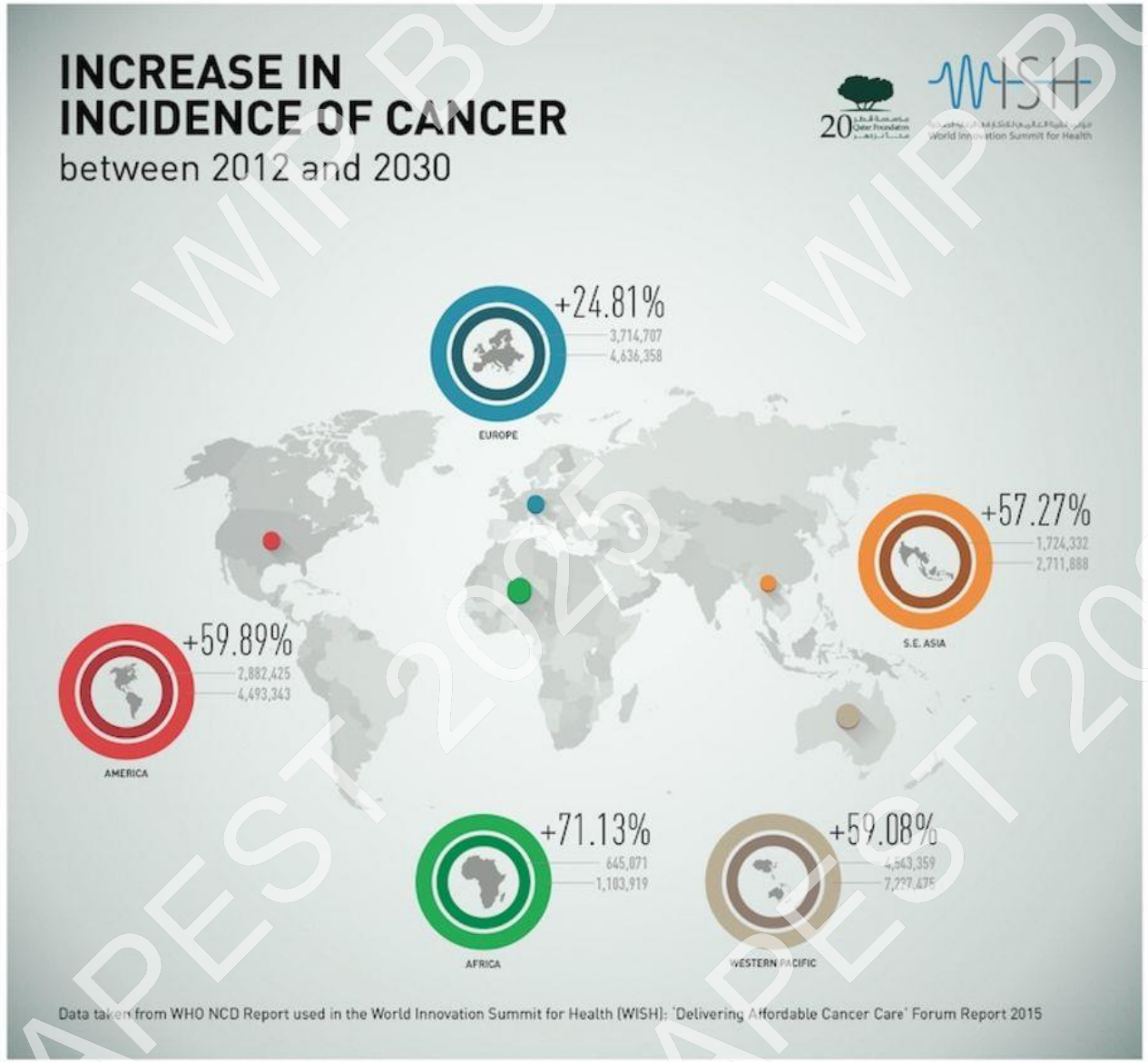
Annals of Oncology, 2008 Dec;19 (12) S. Deandrea

26 studies, >1500 patients **Pain Management Index:** negative score in **43%**

Nearly one out of two patients with cancer pain is undertreated.

Cancer Patient Experience Survey *DoH Dec 2010*

- 67,000 patients, any cancer, surveyed in 2010
- 74 multiple choice questions
- **85% of patients were satisfied that their doctors did everything they could for pain**



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50% survive cancer for 10 years

By PRESS ASSOCIATION

PUBLISHED: 00:24, 3 December 2014 | **UPDATED:** 00:25, 3 December 2014

Share

Half of all cancer patients in England and Wales can now expect to survive at least 10 years after diagnosis, new research has shown.

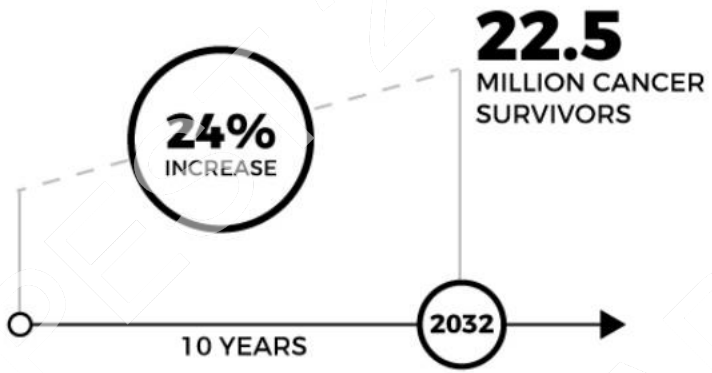
Four decades ago, in the early 1970s, only a quarter of people with cancer were likely to live that long.

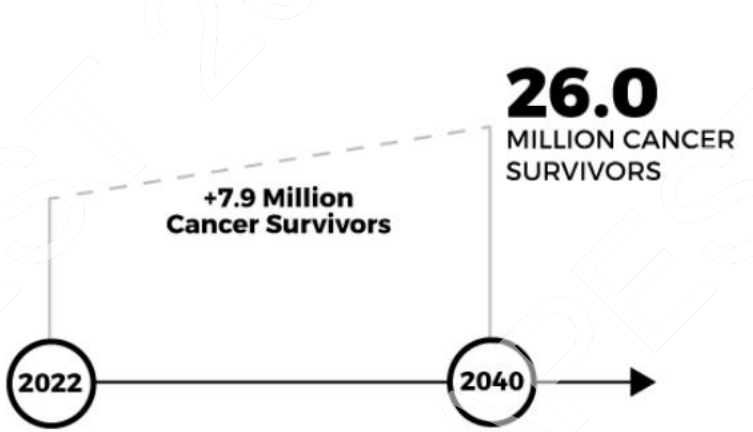
But the positive overall trend masks poor progress in the the fight against certain cancers. Even today, a mere 1% of pancreatic cancer patients manage to reach the 10-year survival mark.

Cancer Survivorship

https://www.cancer.net/survivorship/what-cancer-survivorship

- About 67% of cancer survivors have survived 5 or more years after diagnosis.
- About 18% of cancer survivors have survived 20 or more years after diagnosis.
- 64% of survivors are age 65 or older.



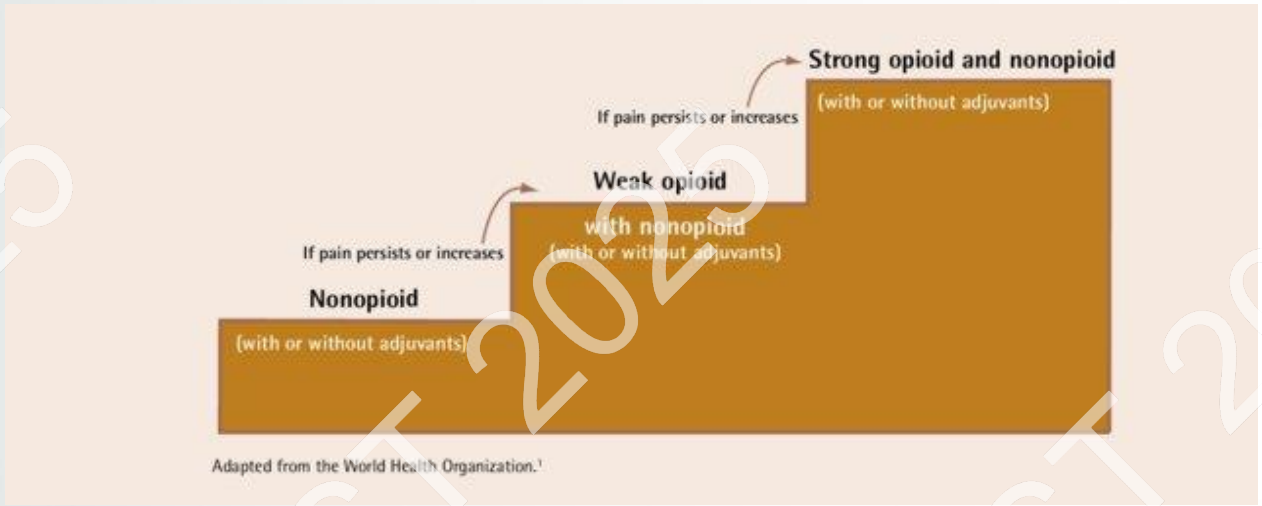


Cancer Survival

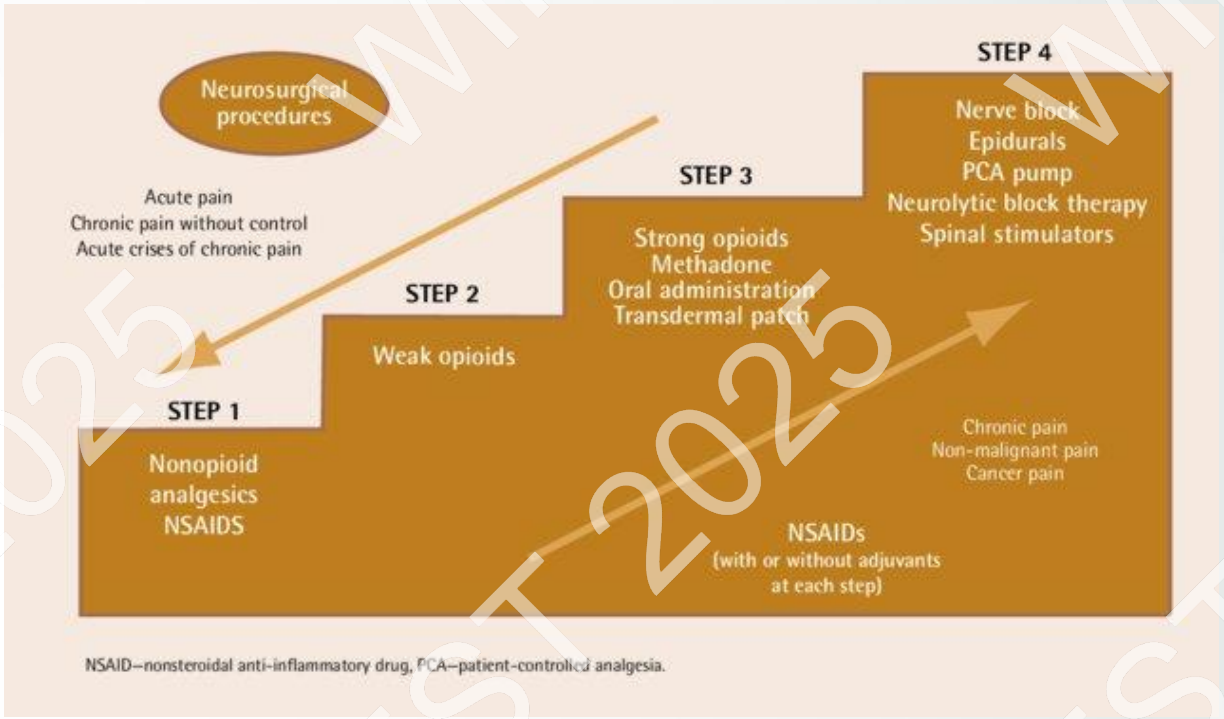
- Half (50%) of people diagnosed with cancer in England and Wales survive their disease for ten years or more (2010-11).
- Cancer survival is higher in women than men.
- Cancer survival is improving and has doubled in the last 40 years in the UK.
- Cancer survival is generally higher in people diagnosed aged under 40 years old, with the exception of breast, bowel and prostate cancers, where survival is highest in middle age.

CANCER RESEARCH UK

WHO Ladder



Adapted from the World Health Organization.[1]

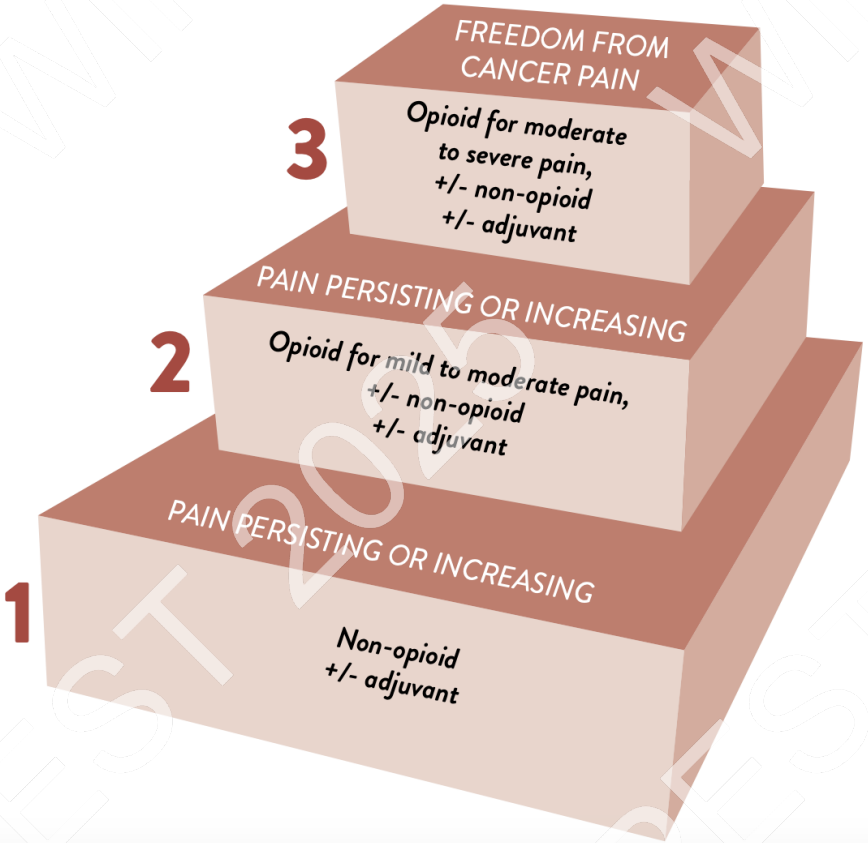


NSAID–nonsteroidal anti-inflammatory drug, PCA–patient-controlled analgesia.

Updated WHO Guidelines

World Health Organization

WHO GUIDELINES FOR THE PHARMACOLOGICAL AND RADIOTHERAPEUTIC MANAGEMENT OF CANCER PAIN IN ADULTS AND ADOLESCENTS



ISBN 978-92-4-155039-0

Recommended Medications

Table 2. Groups and classes of medicines for cancer pain management and specific examples

MEDICINE GROUP	MEDICINE CLASS	EXAMPLE MEDICINES
Non-opioids	Paracetamol	Paracetamol oral tablets and liquid. Rectal suppositories, injectable
	NSAIDs	Ibuprofen oral tablets and liquid Ketorolac oral tablets and injectable Acetylsalicylic acid oral tablets and rectal suppositories
Opioids	Weak opioids	Codeine oral tablets and liquid and injectable
	Strong opioids	Morphine oral tablet and liquid and injectable Hydromorphone oral tablets and liquid and injectable Oxycodone oral tablets and liquid Fentanyl injectable, transdermal patch, transmucosal lozenge Methadone oral tablet, liquid, injectable

WHO and Interventions

5.1. THE GOAL OF OPTIMUM MANAGEMENT OF PAIN IS TO REDUCE PAIN TO LEVELS WHICH ALLOW AN ACCEPTABLE QUALITY OF LIFE

While as much as possible should be done clinically to relieve a patient's pain from cancer, it may not be possible to eliminate pain completely in all patients. The goal of pain management, therefore, is to reduce pain to a level that allows for a quality of life that is acceptable to the patient. The benefit of pain relief must be balanced against the risk of adverse effects and overdose that may result in respiratory depression.

A diagnosis of "refractory pain" should not be made too early as apparently "refractory pain" may simply be due to a lack of access to state-of-the-art pain treatment. Invasive interventions for pain, such as nerve blocks, may be unnecessary when pain management guidelines are followed.

Pit-falls not updated

5.6. ADMINISTRATION OF ANALGESIC MEDICINE SHOULD BE GIVEN "BY MOUTH", "BY THE CLOCK", "FOR THE INDIVIDUAL" AND WITH "ATTENTION TO DETAIL"

5.7. CANCER PAIN MANAGEMENT SHOULD BE INTEGRATED AS PART OF CANCER CARE

Cancer pain management should be integrated into cancer treatment plans throughout the care continuum, including when a patient's disease is not terminal, as necessary. Treatment should begin by giving the patient an understandable explanation of the causes of the pain. Anti-cancer treatment and pharmacotherapy for cancer pain relief should be given concurrently if the patient is in pain.

Flimsy Evidence is good enough for WHO

Summary of the evidence

A single small RCT (n = 68) compared analgesics specifically for management of breakthrough pain in an older population with multiple cancer types (*42*). The trial provided low strength of evidence that the choice between sustained-release and immediate-release morphine may make no difference to prevent breakthrough pain or to reduce pain. The trial did not report on pain relief speed, pain relief maintenance, quality of life, functional outcomes or respiratory depression. The trial provided very low strength of evidence regarding differences between sustained-release and immediate-release morphine to avoid confusion. In the crossover study, two patients developed confusion while taking immediate-release morphine, but the confusion was not attributed to the opioids.

Withdrawing Opioids

6.3. CESSATION OF OPIOID USE

If the cause of cancer pain is effectively addressed by anti-cancer treatment (e.g. surgery or chemotherapy), it follows that the use of opioids is no longer necessary and an opportunity exists to decrease or stop opioid use. The GDG developed a clinical question regarding the optimal tapering regimens of interventions to effectively and safely cease use of opioids specifically in patients who have received opioids for cancer pain (see **Annex 4** for detailed questions).

Best Practice statement

If patients have developed physical dependence on opioids over the course of the management of their pain, opioid dosages should be decreased gradually to avoid withdrawal symptoms.

Summary of the evidence

No eligible studies were found that address this question.

Millionaires and Millionaires

- The USD to IRR operational rate of exchange is 371,992, meaning that one U.S. dollar equals 371,922 Iranian rials.
- 2 British Sterling Pounds or 3 US Dollars or 3 Euros wil make you a millionaire in Tehran

- Over 3 US Dollars or 3 Euros or 2 British Sterling Pounds would get you just 1 Kuwaiti Dinar

- Where would you rather be?

Opioids vs. Interventions

Cordotomy for treatment of cancer-related pain: patient selection and intervention timing

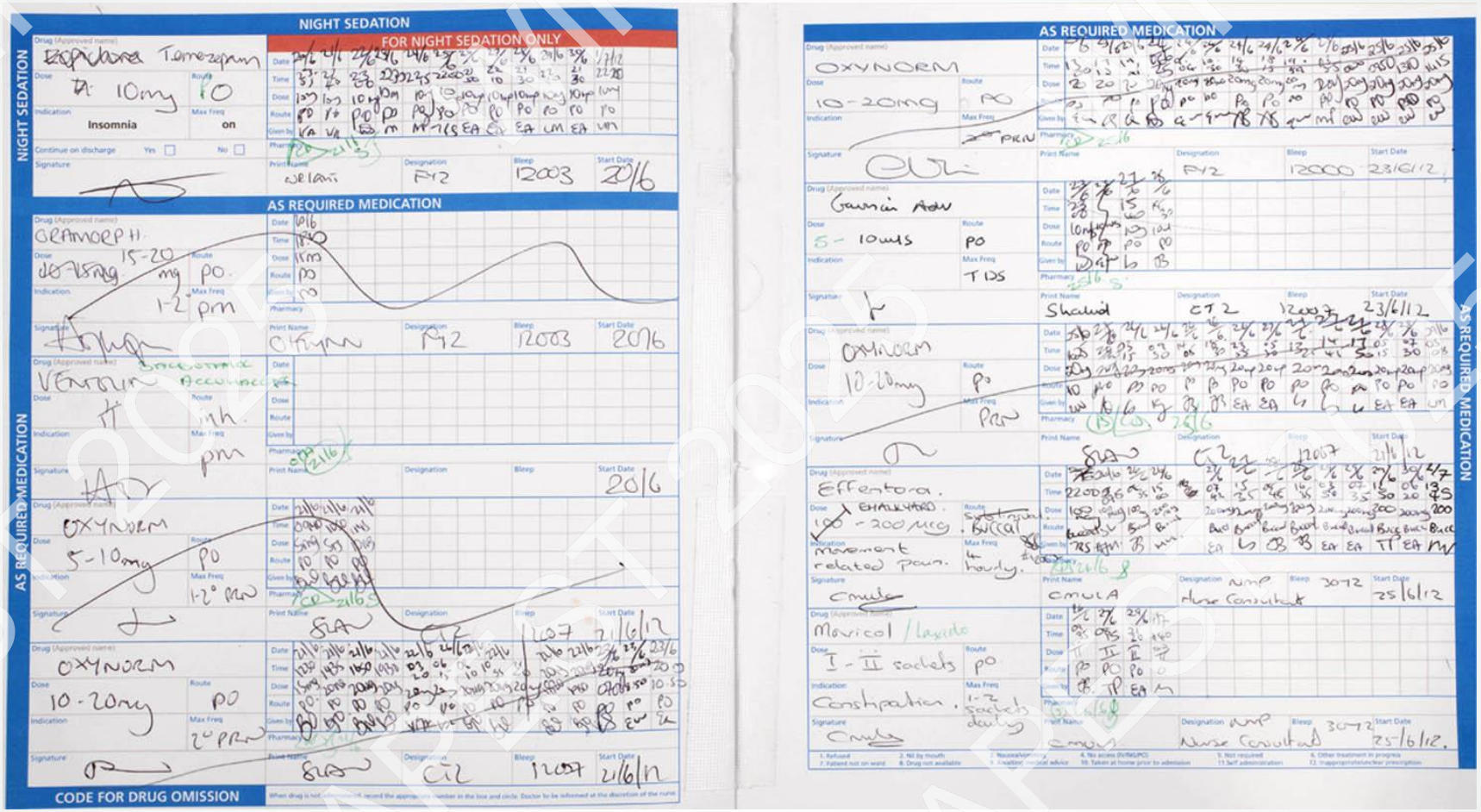
Ashwin Viswanathan, M.D.,[1] and Eduardo Bruera, M.D.[2]

Departments of [1]Neurosurgery and [2]Palliative Care & Rehabilitation Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas

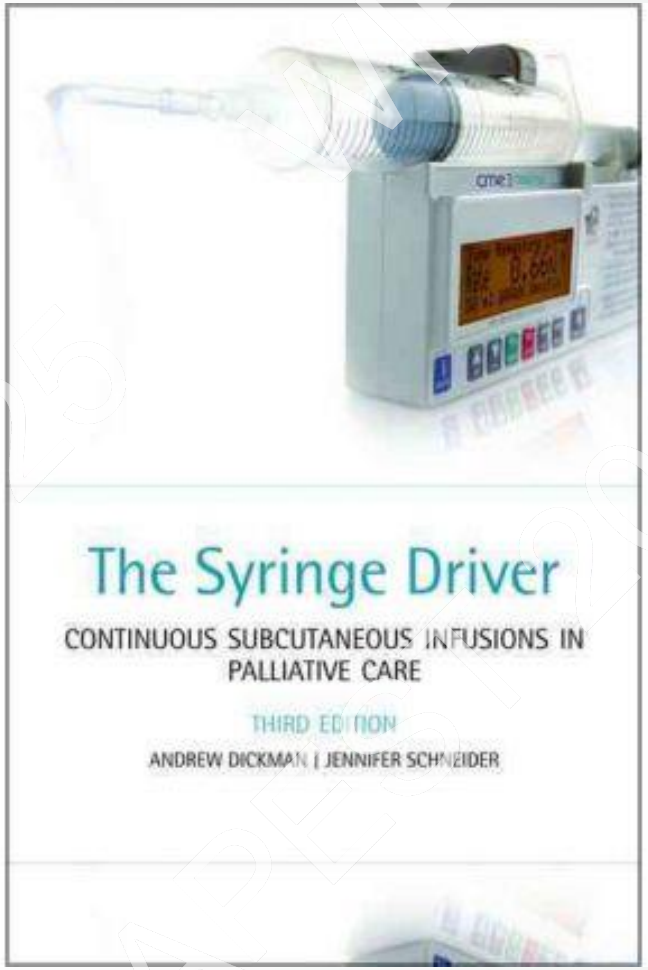
Data from a large tertiary cancer care center emphasize that adequate pain management for cancer patients requires time and dedication from the treatment team.[11] Of 1612 patients consecutively seen at an outpatient supportive care center, 45% had achieved pain relief by their first follow-up visit. These patients would probably never need a procedural intervention because of their prompt and effective response to opioids. However, at the first follow-up visit, 31% of patients continued to have pain scores of 4 and above, and 32% of patients who initially reported mild pain reported worsened pain at their first follow-up visit. These patients might benefit from an early neurosurgical evaluation and possible intervention.

Neurosurg Focus 35 (3):E6, 2013

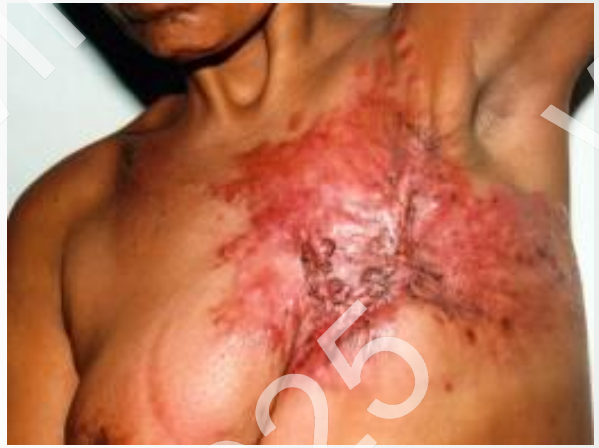
Palliative care and Medication Management

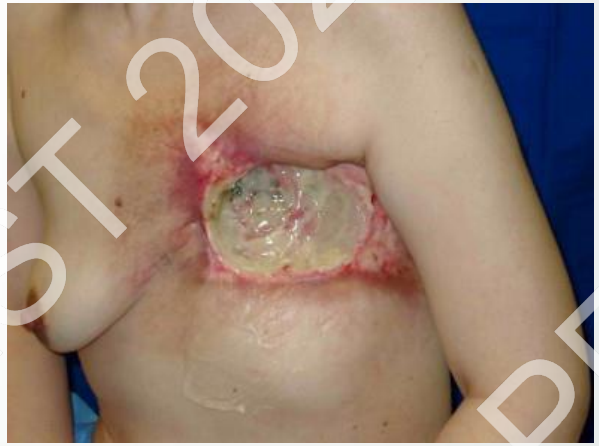


Palliative care and Interventions

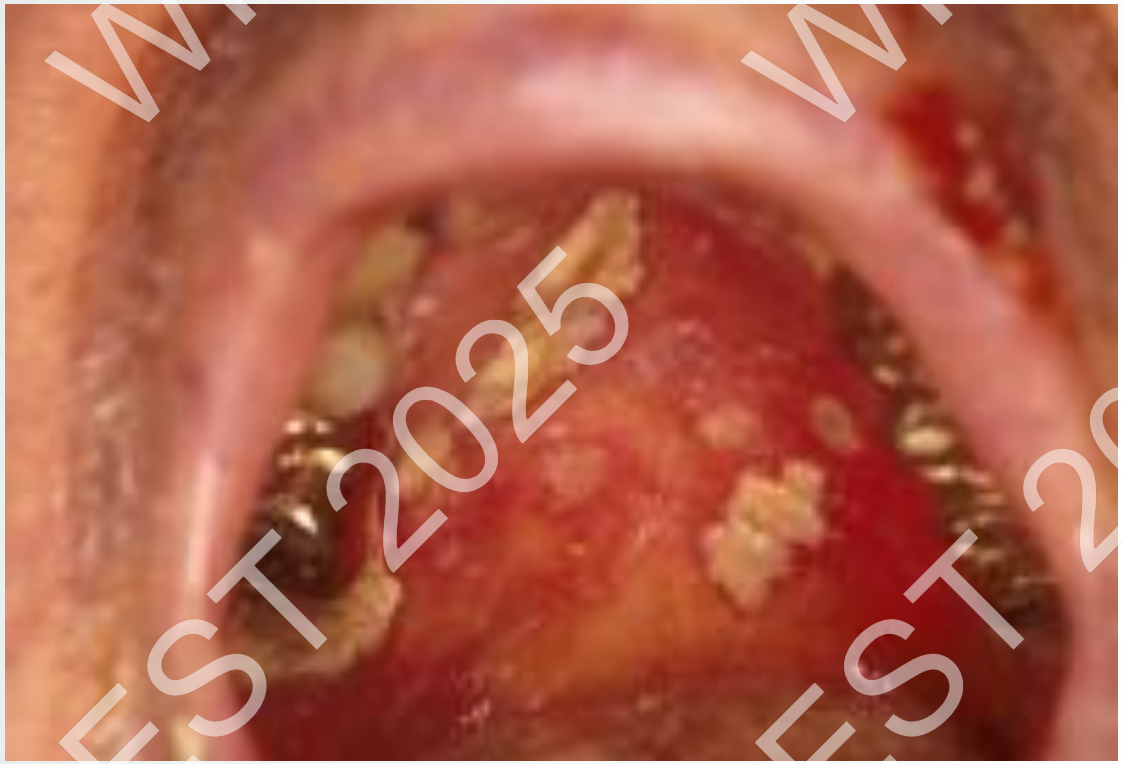


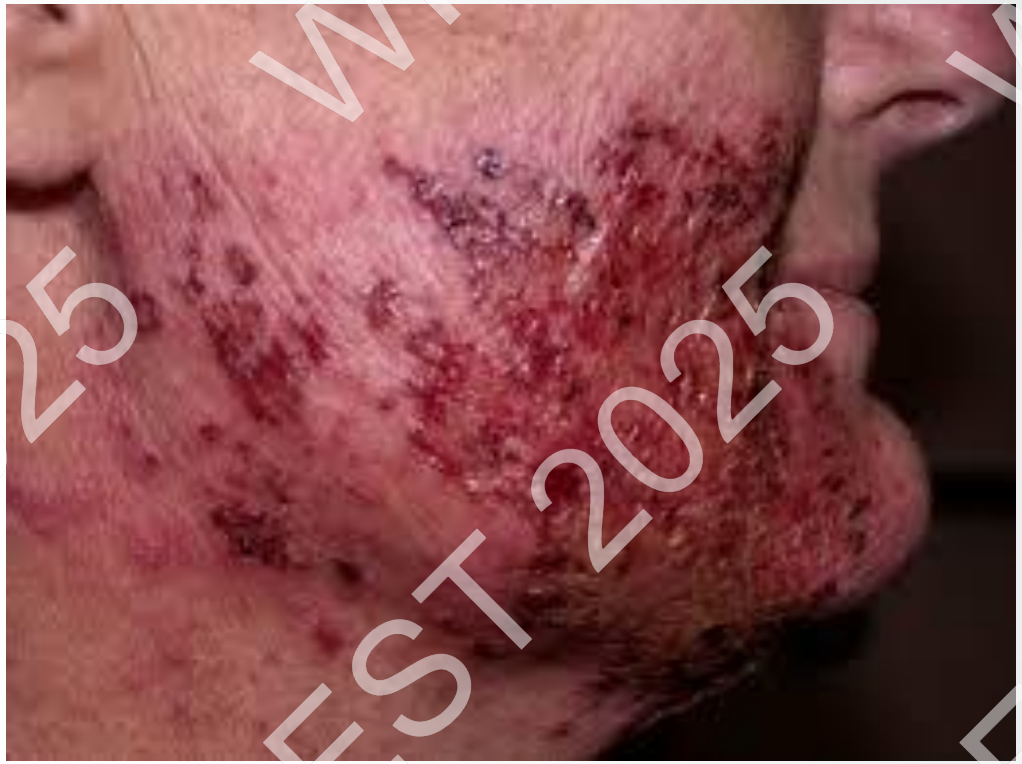
Acute Pain – Surgery/ Radiotherapy





Acute Pain - Mucositis





Chemotherapy-induced Neuropathy

Management of Breakthrough Pain

- Rescue Analgesia
  - Immediate release opioids
  - Oral Transmucosal Fentanyl preparations
  - Ketamine
  - Methadone
- Neuropathic agents
  - Systemic: Pregabalin, Gabapentin, Duloxetine, Amitritptyline
  - Topical: 5% Lidocaine plasters, 8% Very High Dose Capsaicin patch
- Pain Interventional procedures
- Neuromodulation

Unseen Problems due to Opioids

- **Tolerance**
- **Opioid-induced Hyperalgesia**
- **Dependence**
- **Addiction**

- Toxic metabolites
- Opioid-induced Immunosuppression
- Opioid-induced Osteoporosis – contributes towards bone demineralisation
- Significant ↓ HDL; ↑ TG & ↑ Cholesterol
- Cognitive disturbances

Praveen, K. T., et al. (2011)
(Manchikanti, Fellows et al. 2010)

Hormonal Problems due to Opioids

- Opioid-induced Endocrinopathy
  - Hypothalamo-pituitary-adrenal axis
  - Decreased Se Cortisol levels (? Tolerance development)
  - Oedema due to increased vasopressin release
  - Opioid-induced Hyperglycemia
  - ↑ ADH; ↑ ACTH; ↑ PRL
  - ↓ GH; ↓ TSH; ↓ Testosterone; ↓ Cortisol
- Opioid-induced Hypogonadism
  - Hypogonadotropic hypogonadism
- OPIAD– opioid-induced Androgen deficiency
  - Reduced testosterone levels

Ballantye, J (2004)
Banta-Green, C. J., et al. (2009)
Juurlink, D. N. and I. A. Dhalla (2012)

Opioid Tolerant: FDA definition

- Patient who are taking for **one week or longer** at least:
  - **60 mg/day** PO Morphine
  - **30 mg/day** PO Oxycodone
  - 25 mg/ day PO Oxymorphone
  - **8 mg/day** PO Hydromorphone
  - **25 mcg/hr** TD Fentanyl patch
  - Or equianalgesic dose of other opioids

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics 12/2014

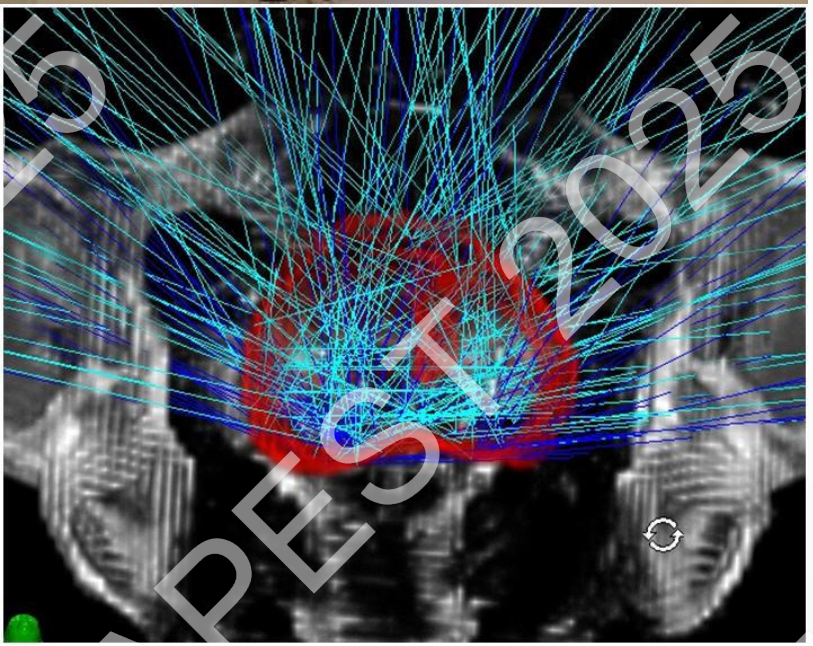
Executive Summary

- No data demonstrating sustained analgesic efficacy in the long term with opioids
- Complete relief of pain is rarely achieved
- 80% of patients in opioids will experience at least one side-effect
- Patients must be aware of the effects on endocrine and immune function
- Opioids should **NOT** be used as first line pain therapy
- Injectable opioids should **NOT** be used in persistent pain
- If patients do not achieve useful relief of pain when titrated to doses between **120-180 mg morphine equivalent per 24 hours**, referral to a pain specialist is strongly recommended

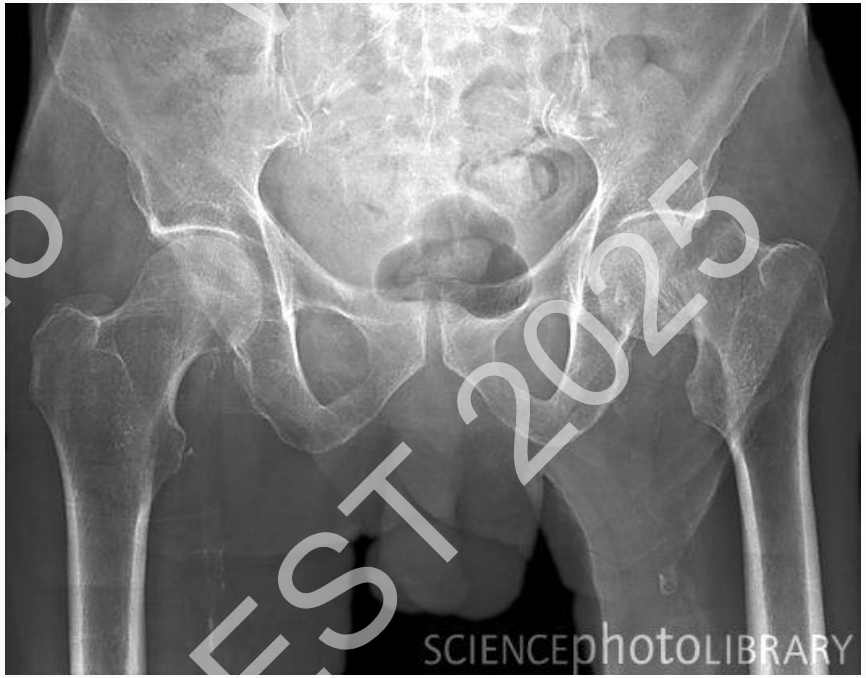
Late referral to Pain services

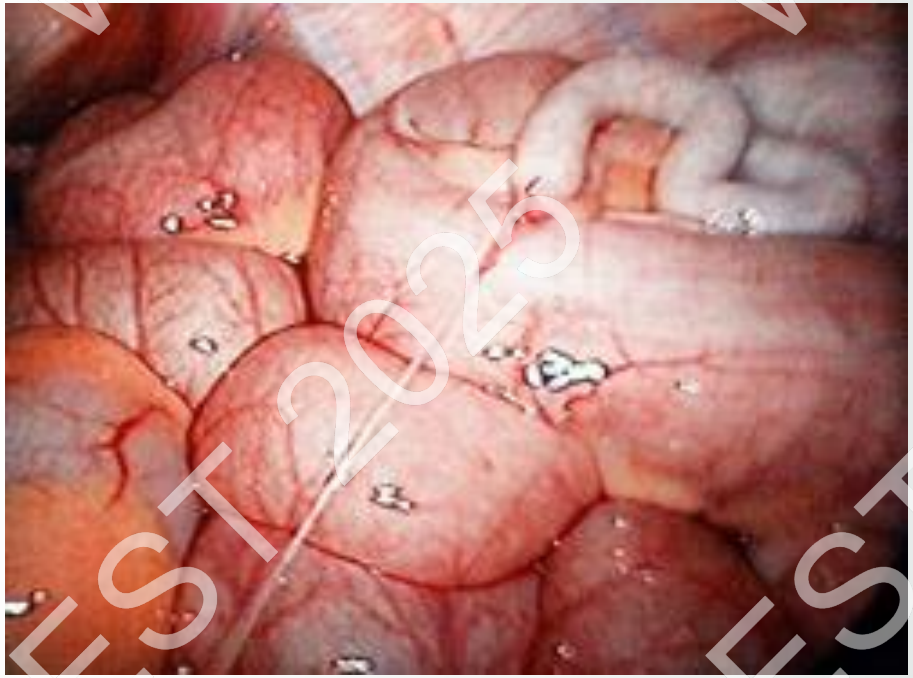
WE ARE MACMILLAN.
CANCER SUPPORT

Why Why Why?



Timing of Interventions





Who benefits from interventions?

- Complex pain with Increasing analgesic requirements
- Frequent episodes of breakthrough pains
- Large differences between analgesic requirement for rest pain and incident pain
  - Pathological fractures
  - Bone pain – spinal metastasis
  - Plexopathies – Brachial, Lumbo-sacral
- Further dose escalation not possible due to:
  - Opioid toxicity
  - Opioid-induced Hyperalgesia
  - Unacceptable side-effects
- **Managing the QUALITY OF LIFE ISSUE**

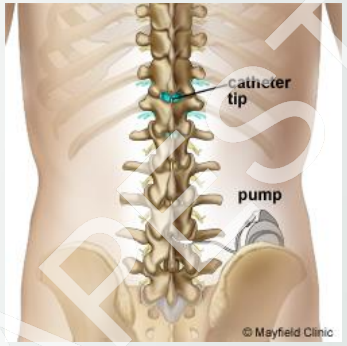
Intrathecal Drug Delivery

- Smith TJ, Staats PS, Deer T, Stearns LJ, Rauck RL, Boortz-Marx RL, Buchser E, Catala` E, Bryce DA, Coyne PJ, Pool G E. **Implantable drug delivery systems study group. Randomised Clinical Trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain; impact on pain, drug related toxicity and survival**. Journal Clinical Oncology 2002;20: 4040-9.
- Smith TJ, Coyne PJ, Staats PS, Deer T, Stearns LJ, Rauck RL, Boortz-Marx RL, Buchser E, Catala` E, Bryce DA, Cousins M, Pool GE. **An implantable drug delivery system (IDSS) for refractory cancer pain provides sustained pain control, less drug related toxicity and possibly better survival compared with comprehensive medical management (CMM).**Annals of Oncology 2005;16:825-833.
- Prager, J, Deer, T, Levy, R, Bruel, B, Buchser, E, Caraway, D, Cousins, M, Jacobs, M, McGlothlen, G, Rauck, R,Staats, P, Stearns, L (2014). **"Best practices for intrathecal drug delivery for pain."** Neuromodulation **17**(4): 354-372; discussion 372.

Neuromodulation. 2017 Feb;20(2):96-132. doi: 10.1111/ner.12538. Epub 2017 Jan 2.

The Polyanalgesic Consensus Conference (PACC): Recommendations on Intrathecal Drug Infusion Systems Best Practices and Guidelines.

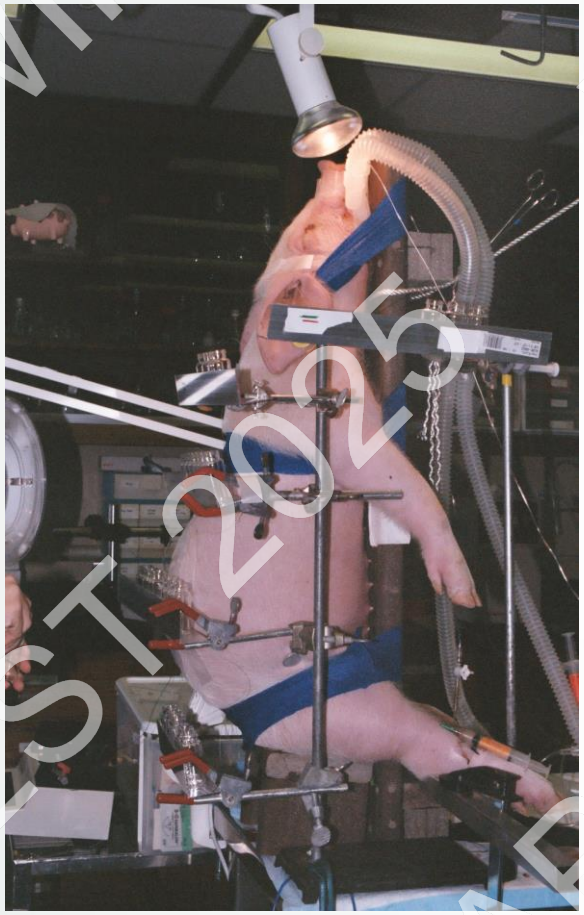
Deer TR[1], Pope JE[2], Hayek SM[3], Bux A[4], Buchser E[5], Eldabe S[6], De Andrés JA[7], Erdek M[8], Patin D[9], Grider JS[10], Doleys DM[11], Jacobs MS[12], Yaksh TL[13], Poree L[14], Wallace MS[15], Prager J[16], Rauck R[17], DeLeon O[18], Diwan S[19], Falowski SM[20], Gazelka HM[21], Kim P[22,23], Leong M[24], Levy RM[25], McDowell G II[26], McRoberts P[27], Naidu R[28], Narouze S[29], Perruchoud C[30], Rosen SM[31], Rosenberg WS[32], Saulino M[33], Staats P[34,35], Stearns LJ[36], Willis D[37], Krames E[38], Huntoon M[39], Mekhail N[40].

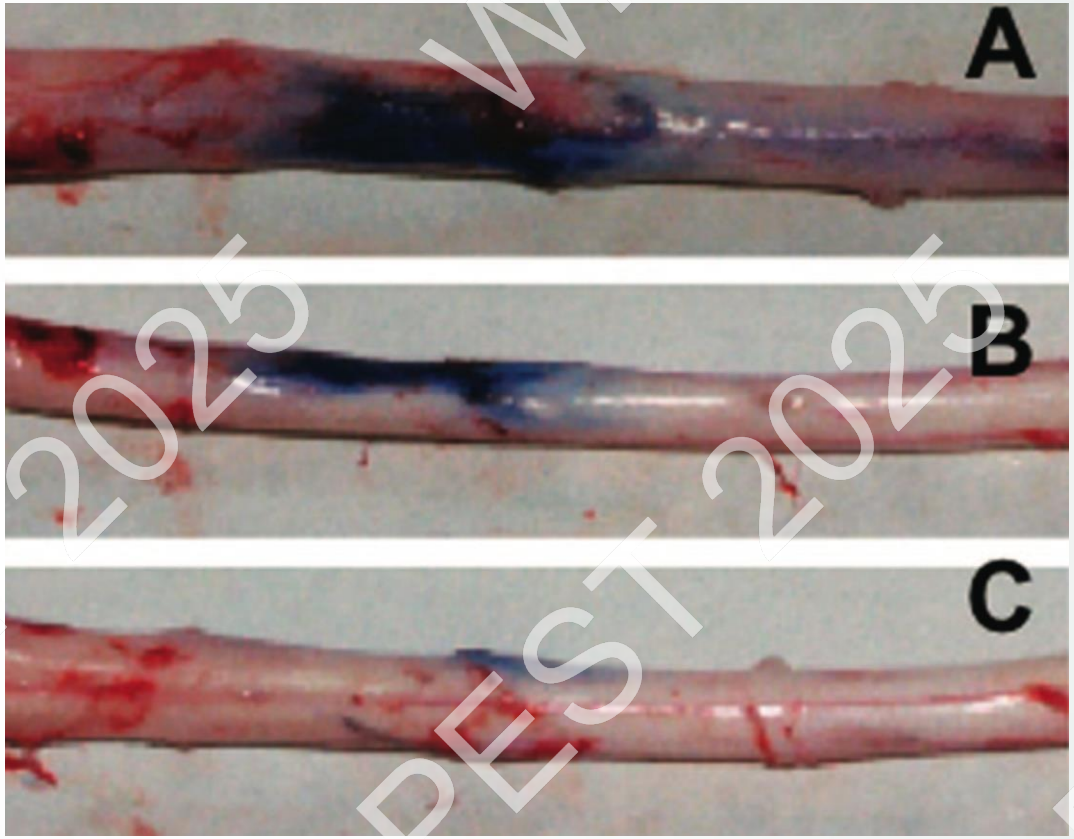


INTRATHECAL DRUG TRIAL

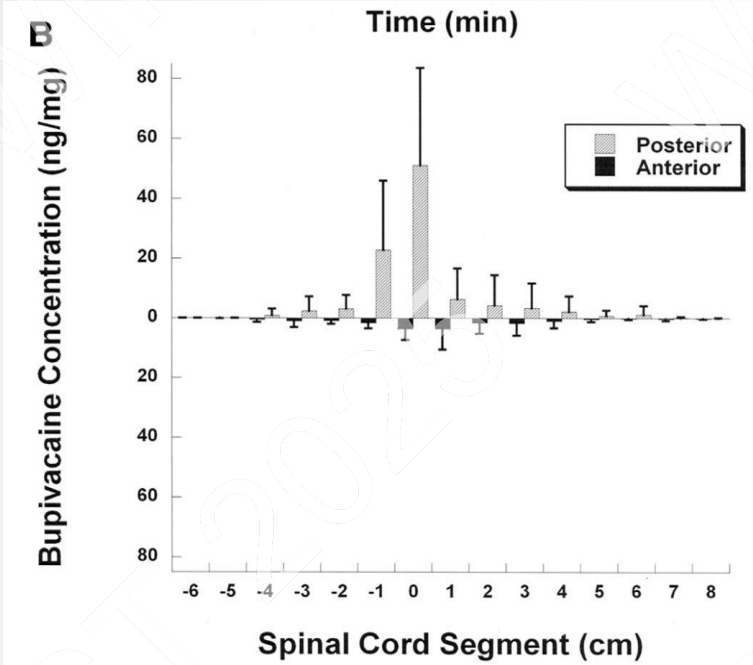
Do Trials Predict Long Term Outcome ?

CSF Circulation

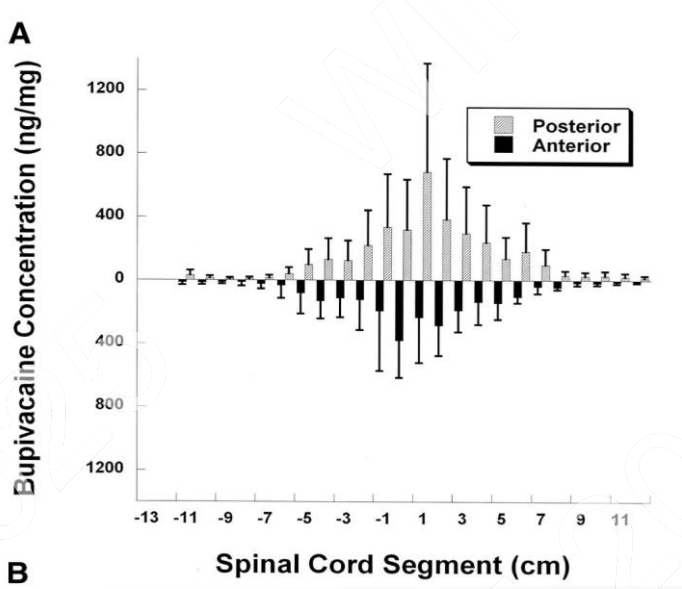




Drop in Effect: an explanation



Infusion 20 ⌈ l/ hr



Infusion of 1000 ⌈ l over 5 min

Christopher M. Bernards. Cerebrospinal fluid and spinal cord distribution of baclofen and bupivacaine during slow intrathecal infusion in pigs..Anaesthesiology.2006;105:169-78

ITDD: Predictors of Poor Response in Cancer pain

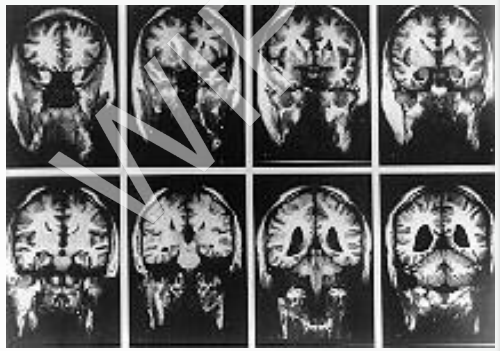
- In-effective in 1/3rd of patients
- Neuropathic pain
- Incident pain
- Mucocutaneous ulcers

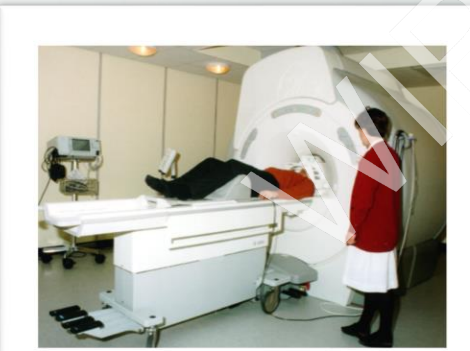
- Psychological distress
- Chemical coping
- Delirium

Escalating opioid therapy

Limitations of Neuromodulation

White, Carolyn W. MSN, FNP-BC, GNP-BC, APRN, ACHPN Spinal Cord Stimulation for Cancer-Related Pain in Adults, Cancer Nursing: 7/8 2017 - Volume 40 - Issue 4 - p 339-340
doi: 10.1097/NCC.0000000000000473





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Better health.

Cochrane Database of Systematic Reviews

[Intervention Review]

Spinal cord stimulation for cancer-related pain in adults

Lihua Peng[1], Su Min[1], Zhou Zejun[1], Ke Wei[2], Michael I Bennett[3]

[1]The Department of Anaesthesia and Pain Medicine, The First Affiliated Hospital, Chongqing Medical University, Chongqing, China. [2]Department of Anaesthesia and Pain Medicine, The First Affiliated Hospital, Chongqing Medical University, Chongqing, China. [3]Leeds Institute of Health Sciences, University of Leeds, Leeds, UK

Journal of Pain Research
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REVIEW

Current Perspectives on Spinal Cord Stimulation for the Treatment of Cancer Pain

This article was published in the following Dove Press journal:
Journal of Pain Research

Jonathan M Hagedorn
Thomas P Pittelkow
Christine L Hunt
Ryan S D'Souza
Tim J Lamer

Department of Anesthesiology and Perioperative Medicine, Division of Pain Medicine, Mayo Clinic, Rochester, MN, USA

Abstract: Cancer and cancer treatment-related chronic pain affect a significant number of patients. The etiology of this pain is diverse and may include nociceptive and/or neuropathic characteristics. Treatment is often multifactorial and may require advanced interventional techniques, such as spinal cord stimulation (SCS). This narrative review provides a thorough overview of cancer-related pain mechanisms and the use of SCS for cancer-related pain. Additionally, a review of the precautions that should be considered when caring for this patient population is provided with recommendations for safe care when utilizing these techniques.

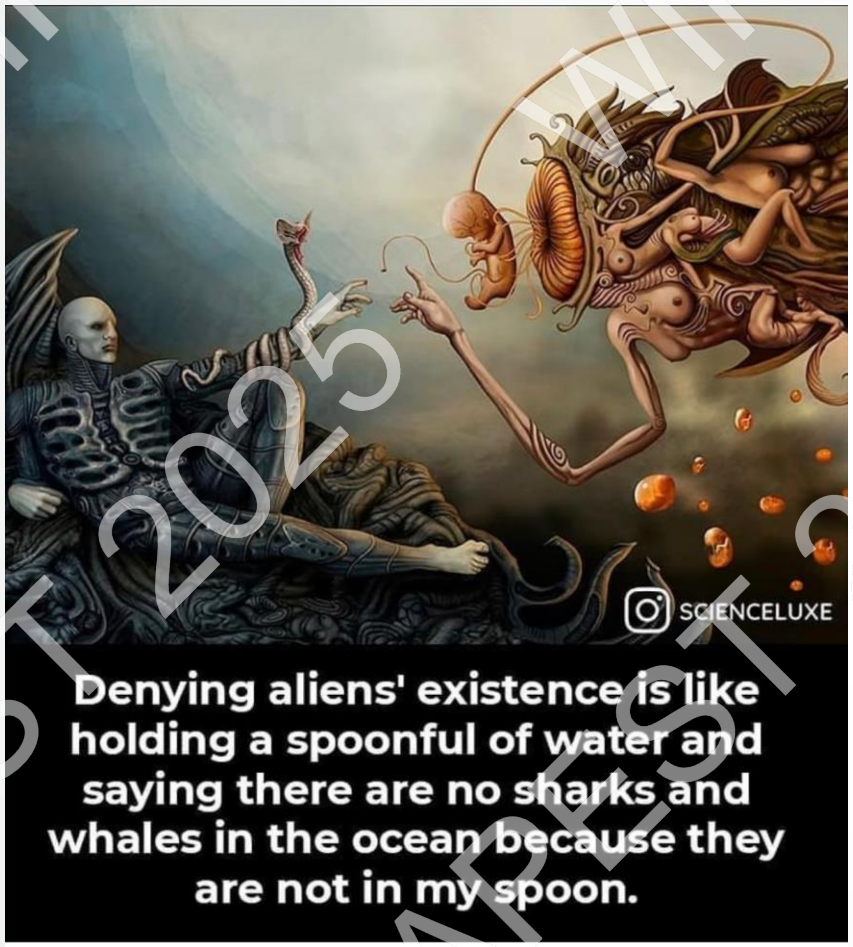
Keywords: spinal cord stimulation, cancer pain, neuromodulation, radiation, chemotherapy, surgery

Neuroablative Procedures

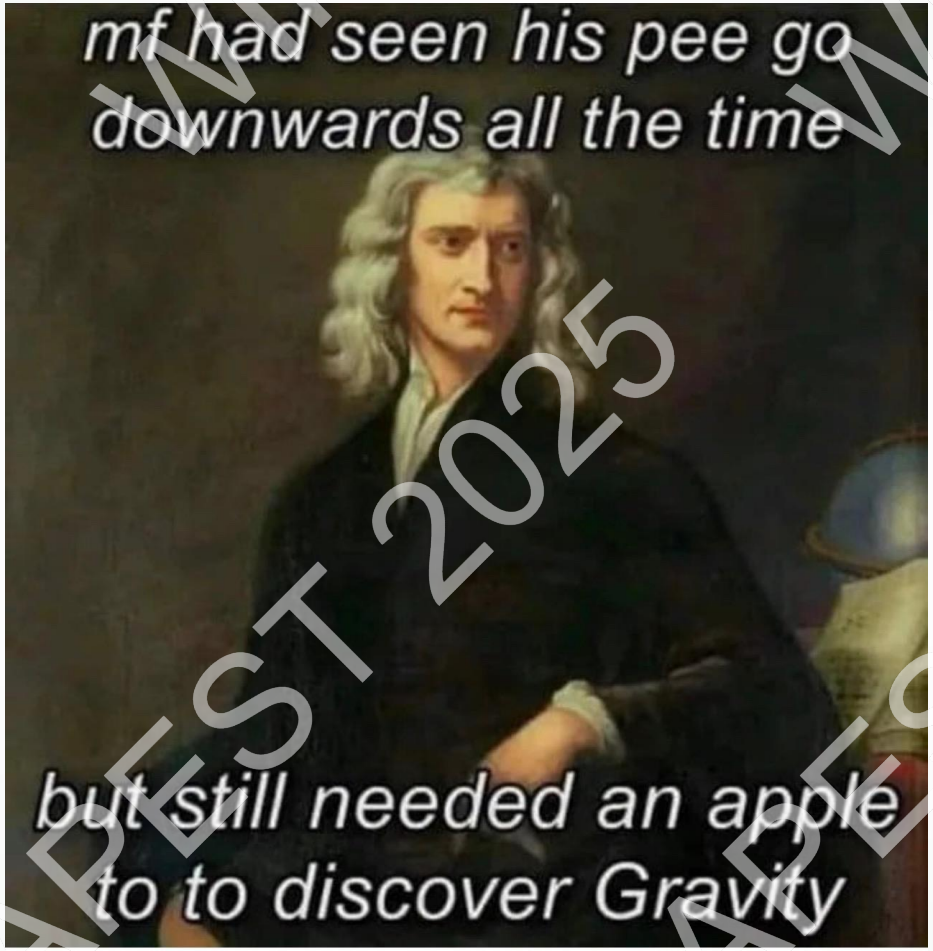
- **Intrathecal**
- **Epidural**
- **Paravertebral**
- **Cervical cordotomy**
- **Inter-pleural**
- Coeliac plexus
- Lumbar sympathetic
- Superior Hypogastric
- Inferior Hypogastric
- Ganglion Impar
- **Trigeminal Ganglion**
- **Peripheral nerve blocks**

- Chemical
  - Alcohol (hypobaric)
  - Phenol (hyperbaric)
  - Glycerol
- Radiofrequency
  - Thermal
  - Pulsed
  - Cooled
- Surgical
  - DREZ lesions

Hiding Behind "Lack of Evidence"



Evidence may be Self-evident



Need for Placebo-controlled studies

And the Statistics can be manipulated…

"Perfect! Six feet two inches and 195 lbs."

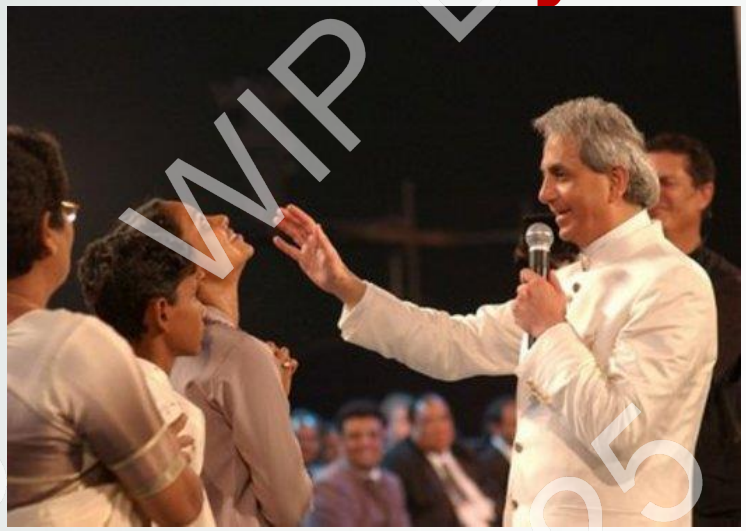
2,770
Coronavirus deaths this year

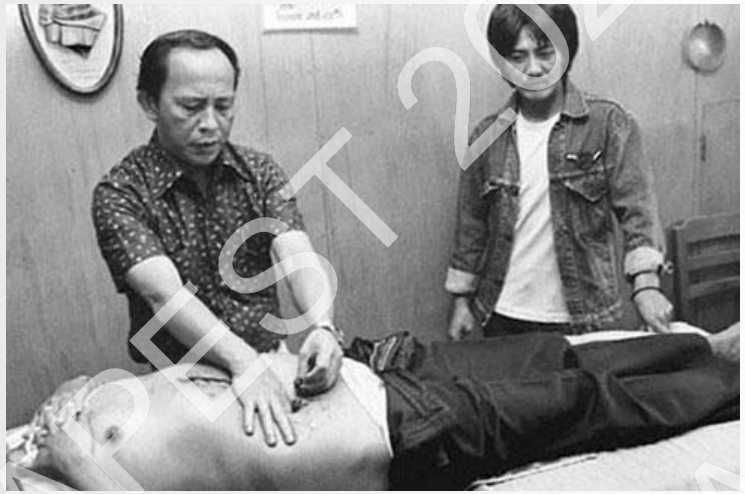
75,636
Seasonal flu deaths this year

751,039,737
Obese people in the world

25,925
People who died of hunger today

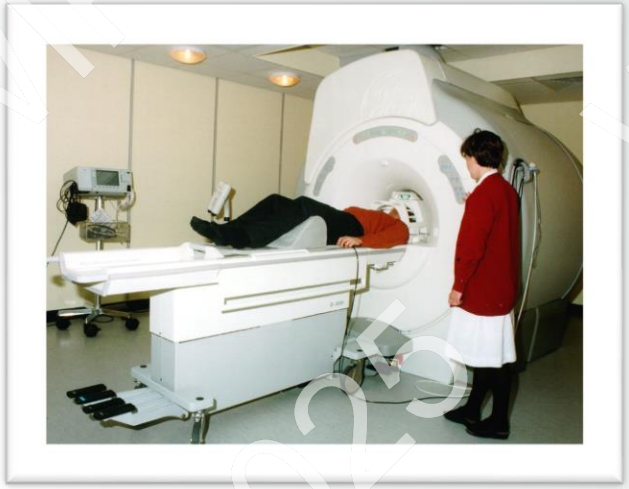
Never say NO to Further Supportive Treatment

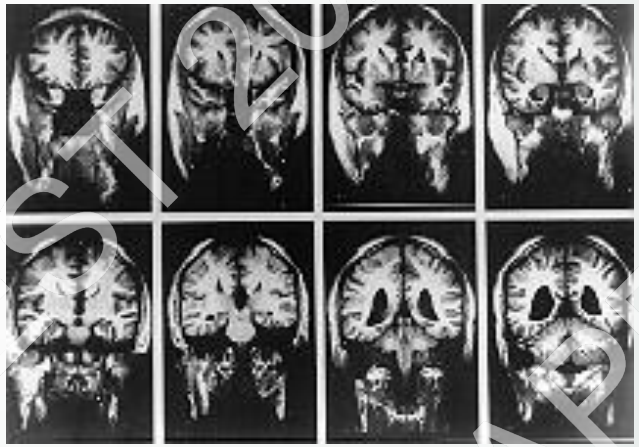




Sometimes we may have to do Something…

But Do Nothing if that is more relevant





Summary recommendations

- Patients taking over a certain amount of Morphine equivalent should be reviewed by a pain specialist
- Patients having more than a certain number of breakthrough pain episodes or requiring rescue analgesia
- Patients whose oncological treatments are being compromised
- Most cancer patients have flare-up of pre-existing pains
- Cancer survivors and those in long term remission may benefit from interventions and neuromodulation to come off opioids
- Better collaboration of pain medicine with palliative care and oncology colleagues at a formal level

Agree on realistic goals.....

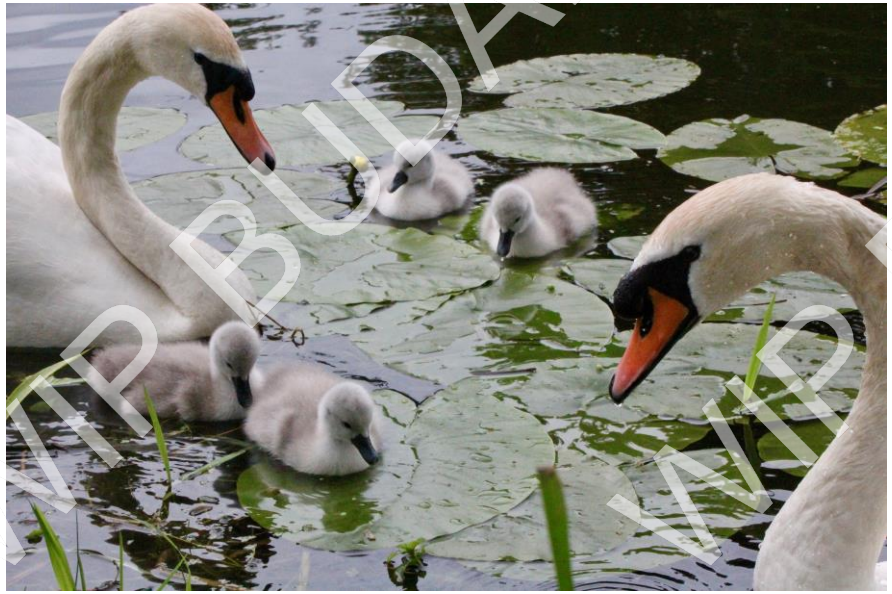
Try to be involved early.....

Stay on track.....

Try to be collaborative……..

Timing is very important……..

Have a contingency plan.....



THANK YOU

WORLD INSTITUTE OF PAIN®

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Budapest, Hungary August 25-27, 2025