

PAIN MANAGEMENT.

Chronic Pain and Prescription abuse.

PENNY BRISCOE.

RAH PAIN MANAGEMENT UNIT.

ROLE PAIN MEDICINE SPECIALIST.

- Manage & R_x
 - Acute, Chronic & Cancer Pain.
- Educate & advise.
 - Students, colleagues, public and patients.
- Provide Expert opinion.
 - Patients, Medical Boards, DHS & Lawyers.
- Set & maintain appropriate standards.
 - Training, Study guides, Examinations.
- Governance.
 - Promote the Specialty of Pain Medicine.

PAIN RELIEF –

A Basic Human Right!

M J COUSINS, F BRENNAN: PAIN: 2004: 112: 1-4

AUSTRALIAN GOVERNMENT

PAIN → *TOP 3*

cost

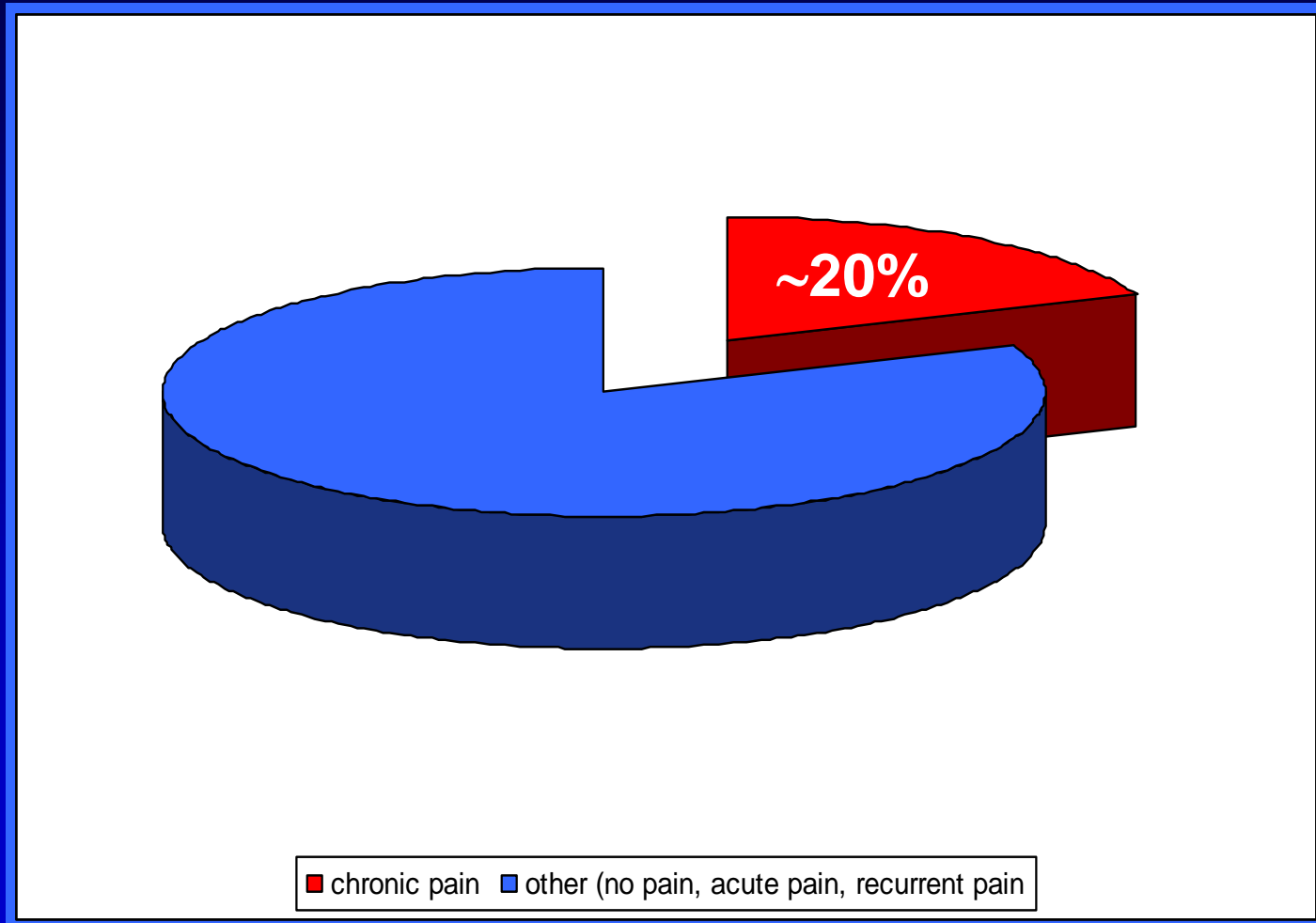
Australian health care

- Diabetes / Asthma.

MJA: 167:1:9:1997

Burden chronic pain* - Australia.

(Blyth et al, Pain 2001)



*daily pain for at least 3 months in a 6 month period

Chronic pain
more common
than any other chronic condition.

- Diabetes, Hypertension, Asthma.

BLYTH 2001

3.2 million Australians.

Message - population studies.

- Chronic pain is common.
- Recurrent pain is more common.
- Persistent pain is a disease entity.

Message - population studies.

- Pain one site - predisposes individuals other pain problems.
- Persistent pain can interfere daily activities – can affect all areas of life

PAIN IS :

Sensory and emotional experience.

- Difficult to measure.
- What the patient says *hurts*.

TYPES OF PAIN.

ACUTE.

CHRONIC (Persistent).

CANCER.

Chronic pain ≠ Acute pain!!

CHRONIC PAIN

-

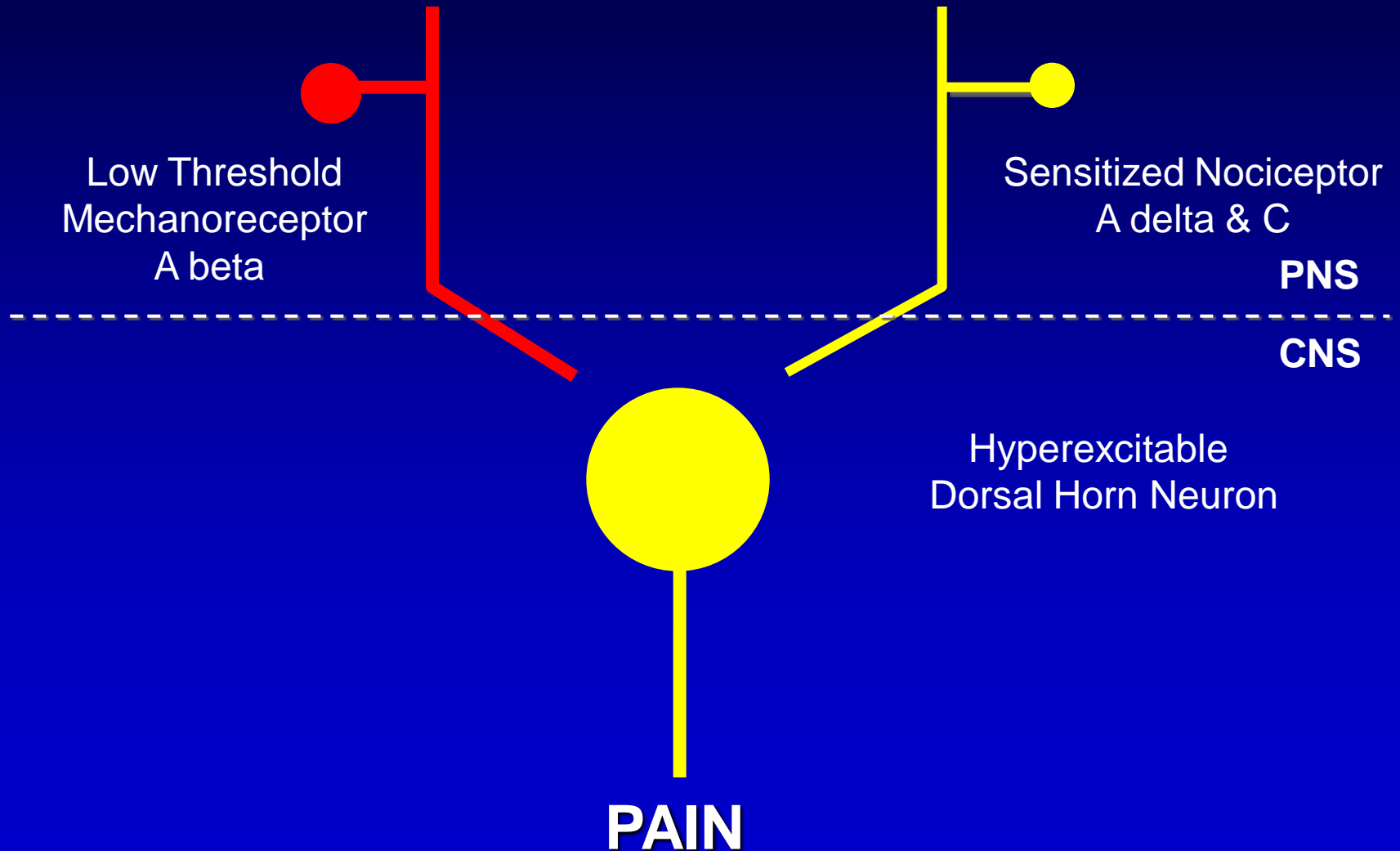
A DISEASE ENTITY.

CHRONIC PAIN

“Pathological??”

Pathological Pain.

Low Intensity Stimulus



Evidence

SENSITIZATION -

show chronic pain

not

psychological problem.

**Genetic & immune factors
now implicated!**

**Are patients who develop
chronic / persistent symptoms
*pre-determined?***

**By severity injury, psychosocial factors,
or
a combination ?**

Genetic factors?

PAINFUL FAMILIES.

Many types of pain problems aggregate or cluster in families.

Transmission of pain could occur through biological or psychological mechanisms.

GOODMAN, MCGRATH: PAIN: 1991

IMPROVING MANAGEMENT .

- Educating - “no blame”
- Early recognition and referral.
- Listen, examine and explain.
- Treat neuropathic pain.
- Focus on functional restoration.

Sleep pattern

Physical activity

Time heals mostif detected early

TYPES OF PAIN.

NOCICEPTIVE

NEUROPATHIC.

NEUROPATHIC PAIN.

Lesion or disease

somatosensory

nervous system.

**“Burning
Stabbing, stinging
Shooting
Dysaesthetic
Electric shock-like quality
Allodynia”.**

TREATMENTS.

RAH PAIN MANAGEMENT UNIT

Multi disciplinary clinic.

ROLE PAIN MANAGEMENT UNIT

- **Diagnosis pain mechanisms.**
- **Reassurance “pain is real”.**
- **Education.**

MULTI-DISCIPLINARY R_x

- **PHYSICAL**

- Drugs
- Procedures
- Physical therapy

- **Active** / ~~Passive~~

- **PSYCHOLOGICAL**

- Cognitive
- Behavioral
- Relaxation / Hypnotherapy

PAIN TREATMENTS

- **Drugs.**
 - Analgesics - Simple / opioid.
 - Adjuvant analgesics.
- **Nerve blocks.**
 - Diagnostic
 - Therapeutic
- **Physiotherapy - ~~passive~~ / ACTIVE.**
- **Hydrotherapy.**
- **TENS.**

PAIN TREATMENTS

- **Psychotherapy / Behavioral therapy.**
 - Pain Management Program
 - Relaxation / hypnosis
- **Acupuncture.**
- **Implantable therapy - Intrathecal.**
- **Neurolytic blocks.**
- **DCS / Peripheral nerve stimulation.**

ASSESSING TREATMENTS.

- **Aim — reduce pain.**
- **Improve functioning.**
- **Rationalise medication.**

IMPROVE QUALITY OF LIFE.

MANAGEMENT OF PAIN.

RESPONSIBILITY

OF

PATIENT!

DRUGS

PAIN SPECIALISTS

recognise

current drugs

have

limited role,

managing

Chronic Pain.

Opioids - ↓ pain 30% in 1/3rd .

NSAID'S – asthma / gut / kidney / PLE.

Paracetamol CR ???

Adjuvants?

ADJUVANT DRUGS.

anticonvulsants

antidepressants

antihistamines

steroids

benzodiazepines

α_2 agonists

baclofen

major tranquilizers

ADJUVANT ANALGESICS

Need to explain:-

- Why drugs are used.
- Side effects common.
- Tolerance develops.
- Start one drug only, add others later.

ADJUVANT ANALGESICS

“START LOW, GO SLOW”.

Up to 4 weeks for full effect.

Push dose until effects / side-effects

ANTIDEPRESSANTS.

TCA's

SSRI's

SNRI,s

MAOI's

Lithium

TCA's studied: best analgesic effect.

NNT 2.4

TCA's in optimal dose -
most efficient treatment
Neuropathic Pain.

Other treatments may be better
tolerated.

SINDRUP: PAIN: 83: (1999): 389-400.

ANTIDEPRESSANTS.

TCA's

high

side effect profile.

ANTIDEPRESSANTS.

Unwanted effects:

- **Sedation.**
- **Anti-cholinergic:**
 - dry mouth, blurred vision, palpitations, constipation, hesitancy
- **Postural hypotension.**

8% major / 33% minor side-effect.

ANTIDEPRESSANTS.

Action *independent* antidepressant effects.

Speed onset days faster.

Effective dose lower.

ANTICONVULSANTS.

All older anticonvulsants

potential

serious adverse events.

ANTICONVULSANTS.

CARBAMAZEPINE, PHENYTOIN, VALPORATE

→ hepatic dysfunction / blood dyscrasias.

CLONAZEPAM → physical dependence.

All → impaired mental & motor function.

ANTICONVULSANTS.

Idiosyncratic side-effects.

Stevens Johnson's syndrome

Aplastic anaemia

Hepatotoxicity

SLE

ANTICONVULSANTS.

Affect pain indirectly : ↑ sleep & mood.

- Carbamazepine

70% Trigeminal neuralgia improve._[level 1]

30% diabetic neuropathy

No better placebo: post-stroke pain.

- PHENYTOIN, VALPORATE, CLONAZEPAM /
NO GOOD EVIDENCE

GABAPENTIN.

- potential usefulness - diabetes / PHN.
- ↓ serious adverse reactions.
- Drowsiness, confusion, ataxia.
- OK hepatic impairment.
- ↓ dose renal disease.

GABAPENTIN.

No active metabolites.

Does not interact with other drugs.

Well tolerated, wide safety margin.

Overdose 49 gms reported

NNT 3.2

PREGABLIN.

Analogue GABA

Trials only against inactive treatments.

Lowers pain scores 1.2 - 2.5.

300mg/day- 30% dizziness, 24% somnolence.

Ataxia, altered coordination & vision.

Oedema, weight gain, dry mouth.

↓ dose renal disease.

NNT 3

KETAMINE.

- Noncompetitive NMDA antagonist.
- Inhibits excitatory amino acid glutamate.
- Oral Ketamine – 25% good analgesia.
- 50% cease due intolerable side effects.
- Prevent tolerance opioids.
- ABUSE POTENTIAL.

NNT 1.9 (dextromethorphan : diabetic neuropathy)

LIGNOCAINE

- 1b anti arrhythmic
- Local anaesthetic
- Sodium channel blocker

Various pains: (peripheral neuropathy).

5mg/kg - ↓ allodynia 45 mins

MEXILETINE

- Structurally similar lignocaine
- Class 1b antiarrhythmic
- Local anaesthetic
- Sodium channel blocker

Adverse effects common / dose related.

NNT 10 (diabetes)

WHAT DOES WORK?

**A GOOD
DOCTOR - PATIENT
RELATIONSHIP
IS CRITICAL,
AND IMPROVES
HEALTH OUTCOMES.**

**COGNITIVE
BEHAVIORAL
THERAPY.**

CBT

Pain influenced by:

- Physiological / pathological conditions.
- Physical state. (external / internal)
- Emotions (stress / happiness etc.)
- “Attention”.
- Thinking / cognitive processes.

CBT

Treatment includes:

- Education.
- Training in relaxation.
- Other coping mechanisms.
 - Pacing
 - Acceptance
- Rehearsal of these skills.
- Relapse prevention.

EXERCISE.

EXERCISE

- Established 20 years ago - integral R_x
- Start below capacity.
- “Start low - Build slow”.
- Improves fitness, self worth.
- Need programs sensitive to needs.

PAIN

IS A

PLACEBO RESPONSIVE

CONDITION.

**“Why is
Chronic Pain
so difficult to treat?”**

WEISBERG 1999: POSTGRADUATE MEDICINE.

CHRONIC PAIN

There are no “magic” bullets.

Pharmacological treatment isolation →
frustration patient / doctor.

Actively treat *physical, social, psychological* factors.

Investigations often normal.

Current treatments unsatisfactory.

R_x may not reduce the pain.

Aim ↓ *suffering.*

**Patients are:
time consuming,
frustrating,
emotionally draining.**

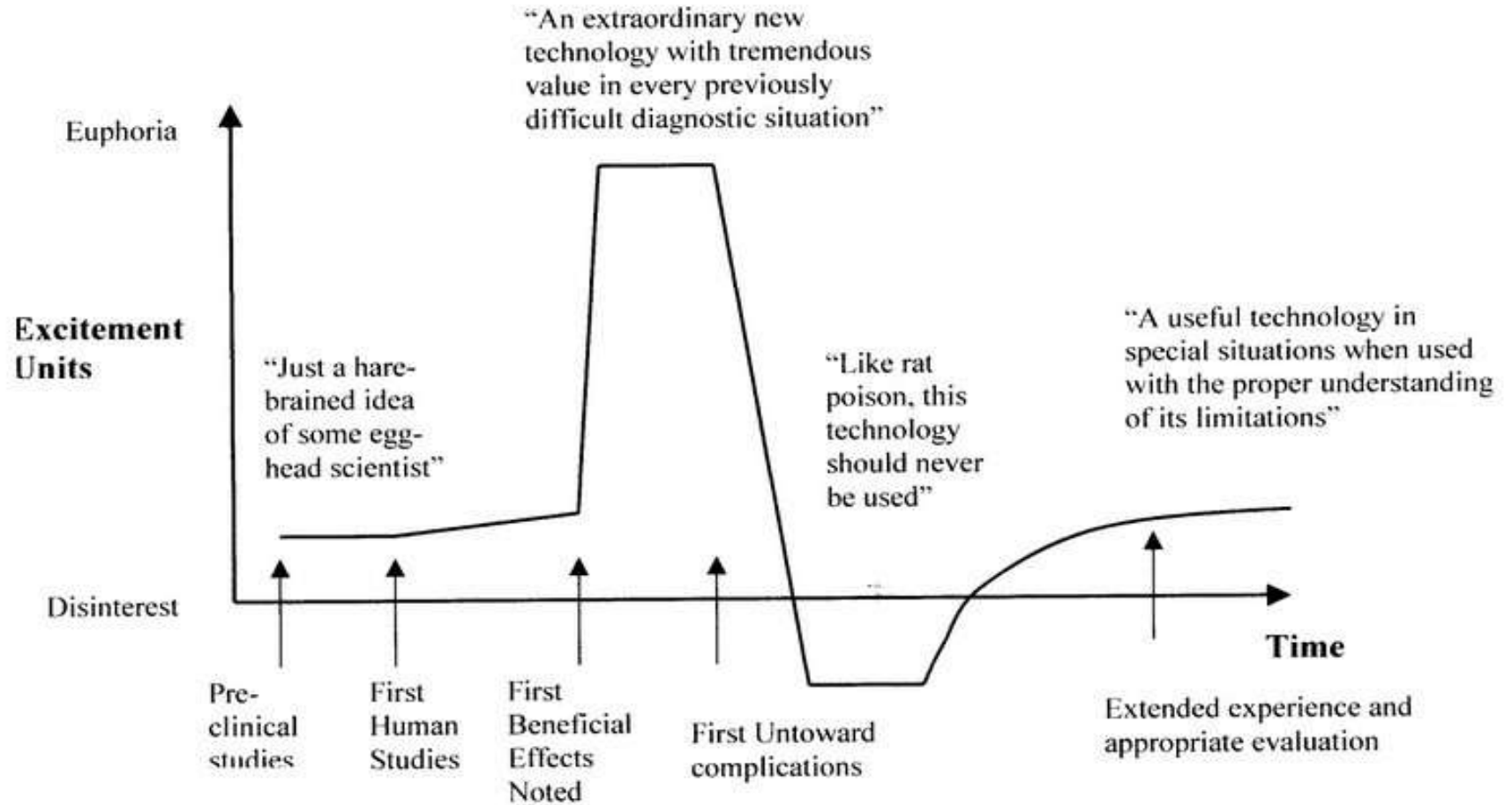
WEISBERG 1999.

DISEASE BURDEN CHRONIC PAIN

- Unemployed for health reasons
- Poor self rated health
- High level psychological distress

**NEW INSIGHTS
WITH
OPIOIDS.**

For Chronic Pain.



The Natural History of a New Device, Drug or Intervention

OPIOIDS –CHRONIC PAIN.

- 1986 Portenoy / Foley-
 - some patients opioids appropriate
 - BUT – not all pains respond!
 - Aim → pain relief – but may not be achievable.
- 1990 Portenoy guidelines.
- 1996 Portenoy revised guidelines.
 - “abberant drug related behaviours”.
- 1997 Goucke/ Graziotti Australian guidelines.

OPIOIDS –CHRONIC PAIN.

- MJA Editorial 1997:
 - “Ideally a comprehensive multidisciplinary assessment should precede the prescription of oral opioids.”
 - Distressed patients receive more oral opioids even in the absence of adequate analgesia,

Perhaps:

“reflecting their doctors sense of helplessness”.

OPIOIDS –CHRONIC PAIN.

2000 - RCPS - Ontario.

- ***FOLLOW COMMON SENSE.***
- Adequate trials non opioids and adjuvants
- Long acting opioids / small dose / short trial.
- Large dose suggest pain -
partially or non opioid responsive.
- Discourage parental - (IM).
- Aim regular doses - limit breakthrough.
- Opioids will not eliminate pain!

OPIOIDS –CHRONIC PAIN.

Do's and Don'ts:

- One prescriber who knows patient well.
- Don't prescribe short acting opioids.
- Don't prescribe injectable opioids - home use.
- Don't prescribe 2 or more different opioids.
- Don't prescribe 2 or more drugs with abuse potential – opioids and benzodiazepines.
- Be aware if patients want prescriptions early.

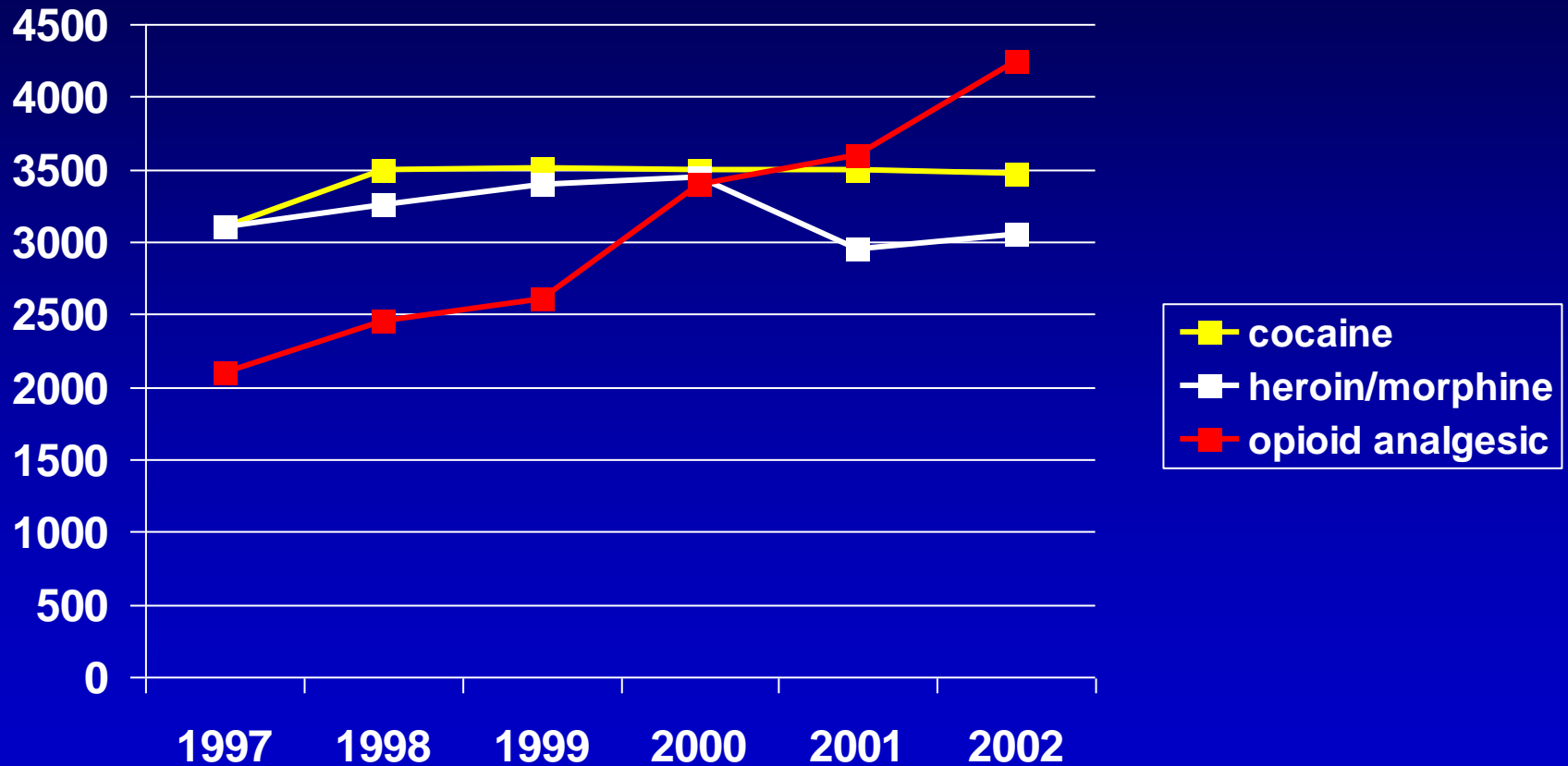
OPIOIDS –CHRONIC PAIN.

Criteria for successful treatment:

- Pain relief that *improves well being*.
- + ve progress towards goals.
- Improve function.
- Improved quality of life.
- Patient copes stable dose at a moderate level

DEATHS ASSOCIATED - DRUG ABUSE

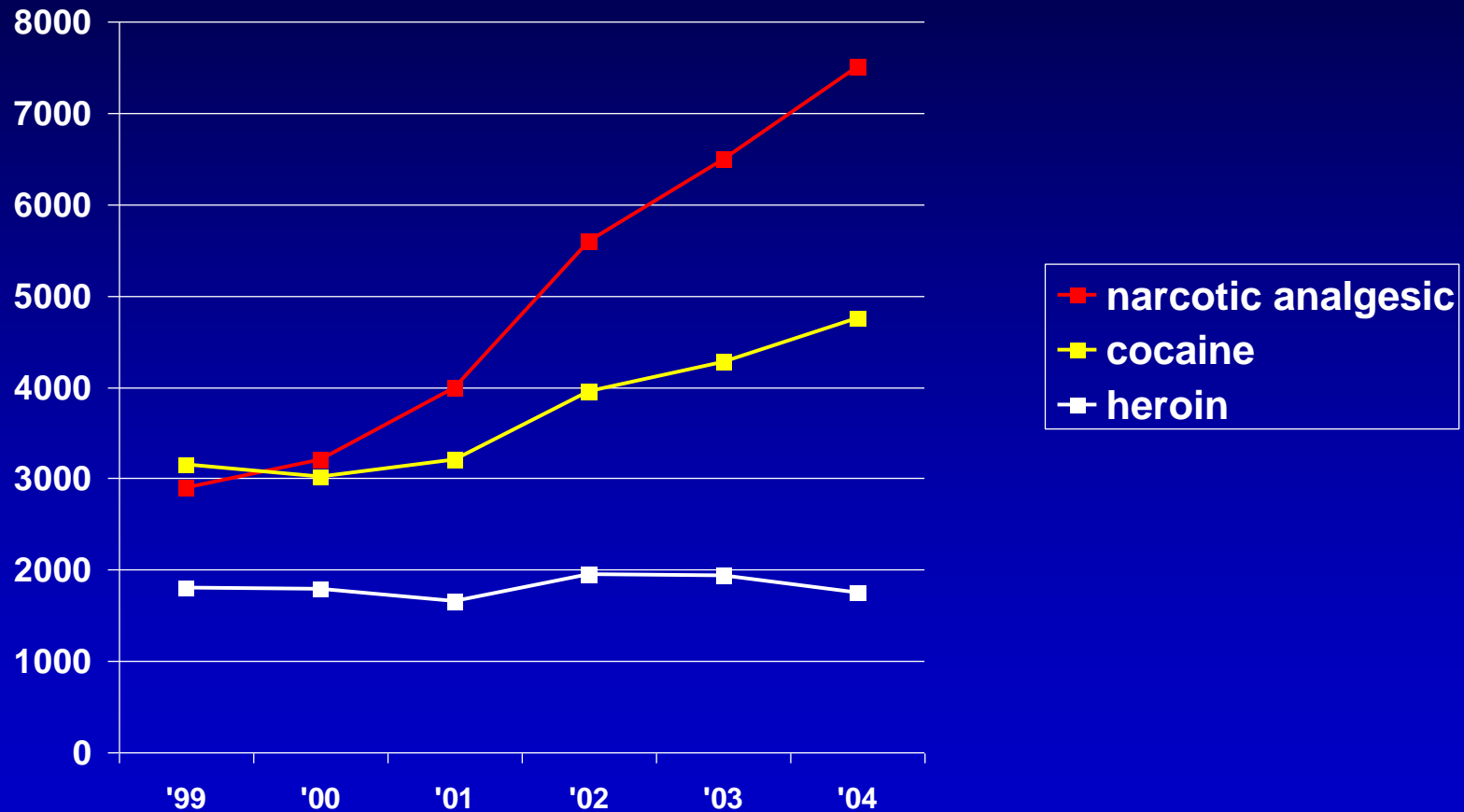
OPIOID DEATHS USA: DOUBLED



PAULOZZI LJ: AMER J PUB HEALTH 2006;96:1755-7.

US DAWN MED. EXAMINER

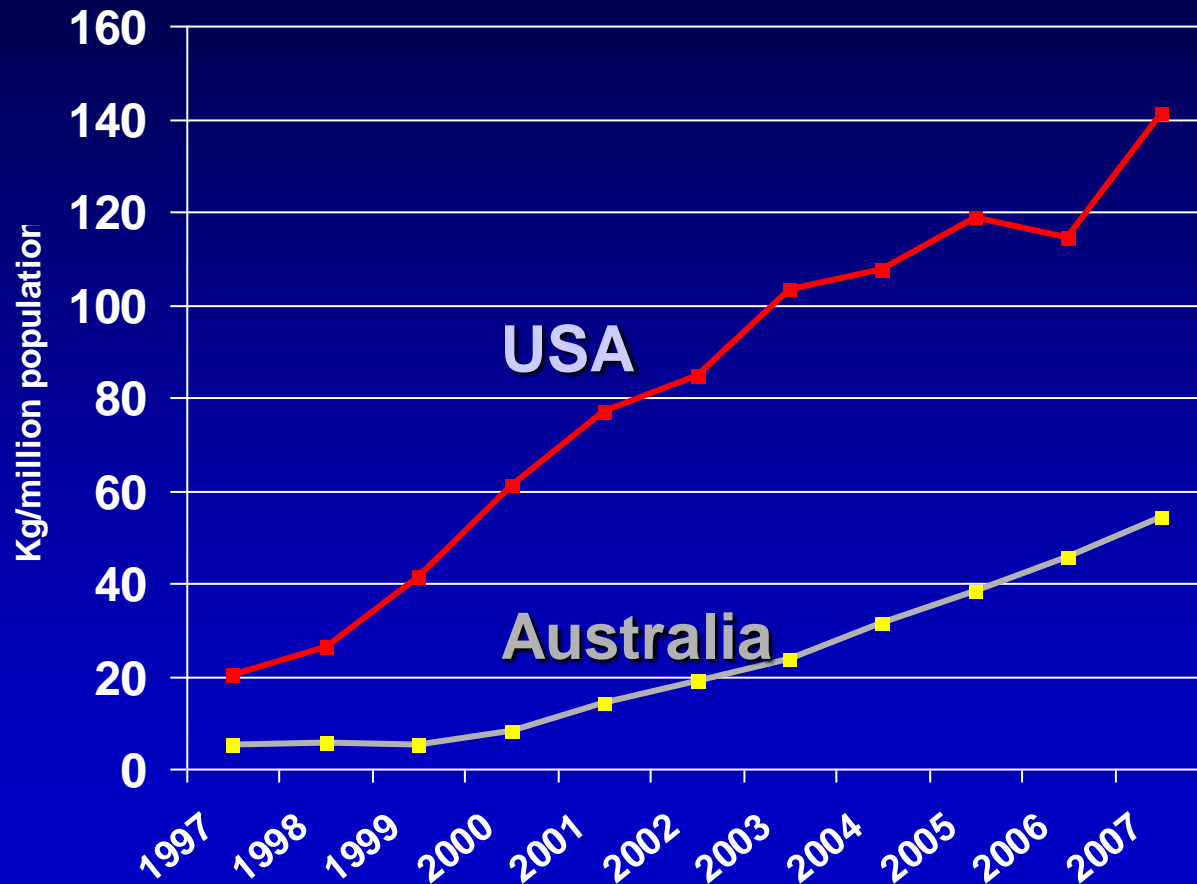
UNINTENTIONAL DEATHS - NARCOTICS & 'OTHER DRUGS' USA - 1999-2004



PAULOZZI: EPIDEMIOLOGY OF UNINTENTIONAL DRUG POISONING: SEOW AUDIO
CONFERENCE, DECEMBER 12, 2007.

[HTTP://WWW.ASTHO.ORG/PUBS/POISON-PAULOZZI.PPT#465,1](http://www.astho.org/Pubs/Poison-Paulozzi.PPT#465,1)

PER CAPITA OXYCODONE BASE SUPPLY: AUSTRALIA & USA: 1997-2007



INCB TABLES REPORTED STATISTICS: 2007: US CENSUS BUREAU INT'L DATABASE

CONSEQUENCES ↑↑ SUPPLY

- **“...very strong correlation between therapeutic exposure to opioid analgesics.....and their abuse”**
 - **CICERO TJ et al: PHARMACOEPIDEMIOLOG DRUG SAF: 2007:16(8): 827-40
RELATIONSHIP BETWEEN THERAPEUTIC USE & ABUSE OPIOID ANALGESICS
IN RURAL, SUBURBAN AND URBAN LOCATIONS IN USA.**
- **“...linear relationship between total opioid analgesic sales and drug poisoning mortality.”**
 - **PAULOZZI LJ, RYAN GW: AM J PREV MED 2006: 31(6): 506-11.
OPIOID ANALGESICS & RATES FATAL DRUG POISONING IN USA:**

PATTERNS OF ABUSE UNINTENTIONAL PHARMACEUTICAL OD DEATHS: WEST VIRGINIA:2006.

- Population: 1.8 million – Appalachia
- 1999- 2004: 550% ↑ unintentional poisoning deaths
- continuing increase
- 2006: 295 unintentional poisoning deaths

PATTERNS OF ABUSE UNINTENTIONAL PHARMACEUTICAL OD DEATHS: WEST VIRGINIA, 2006.

- 63.1% - involved pharmaceutical diversion*
- 21.4% - evidence of doctor shopping
- 94.6% - substance abuse indicators
- Prevalent non-medical routes of exposure
- Prevalent illicit contributory drugs in drug diverters
- 79.3% - multiple contributory substances
- 93.2% - opioid analgesics (of whom only 44.4% had ever been prescribed these drugs)

*** Pharmaceutical diversion**

- Death - prescription drug without prescription
- Prescription for controlled substance from 5+ different doctors

USA

US Figures show *prescription painkillers* are the new drug of choice, overtaking marijuana and cocaine, and opioids.

They cause more overdose deaths in the US than cocaine and heroin combined.

USA

The US Federal Drug Enforcement
Administration

report *7 million Americans*

abuse prescription drugs;

more than the number abusing cocaine,
heroin,

hallucinogens, ecstasy and inhalants
combined

MICHAEL JACKSON

“Concerns had been expressed about Michael Jackson’s abuse of medication over a number of years.

He did not drink alcohol and was outspoken against illegal drugs.

He allegedly abused prescription drugs.”

He used numerous aliases to receive prescriptions.

pethidine, alprazolam, hydrocodine, hydromorphone, oxycontin and a couple of anti-depressant medications.

MICHAEL JACKSON

The alleged cause of his death
was
in fact
intravenous propofol.

AUSTRALIAN EXPERIENCE.

AUSTRALIAN ROYAL COMMISSION. Inquiry into Drugs.

‘that any rational community action to limit the abuse of drugs must embrace all drugs, not merely those classified as illegal.

The case for including legal drugs in any overall strategy aimed at minimising drug abuse is based not only on the seriousness of the problem associated with abuse of legal drugs, but that the abuse of one drug, tends to be “all of a piece” with the abuse of all drugs, legal and illegal alike.”

HONOURABLE JUSTICE WILLIAMS 1980

HEATH LEDGER

The final toxicology report commented –

“Mr Heath Ledger died as a result of acute intoxication, by the combined effects of oxycodone, hydrocodone, diazepam, temazepam, alprazolam and doxylamine.

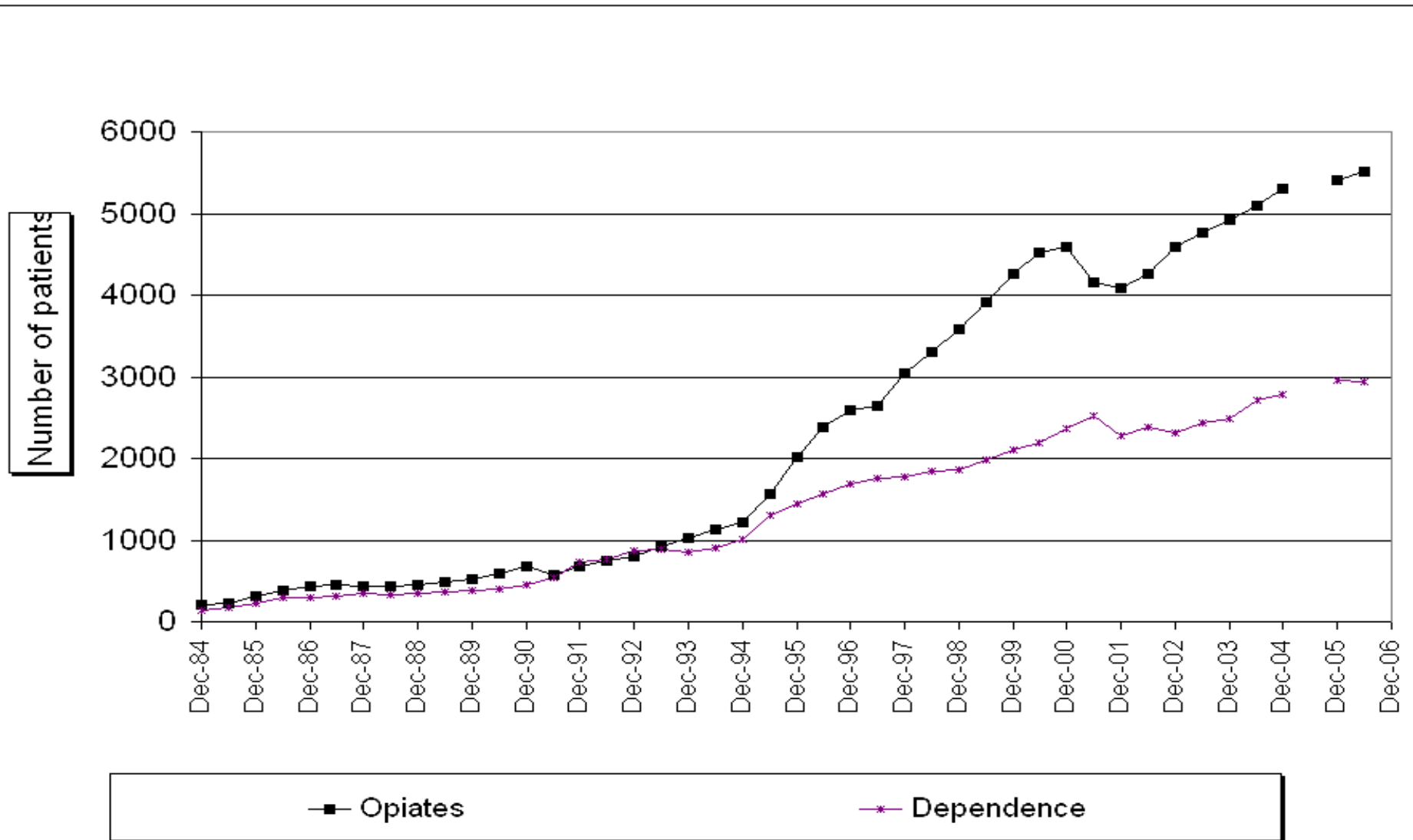
We have concluded that the manner of death
is an accident,
resulting from the abuse of prescription medications.”

HEATH LEDGER

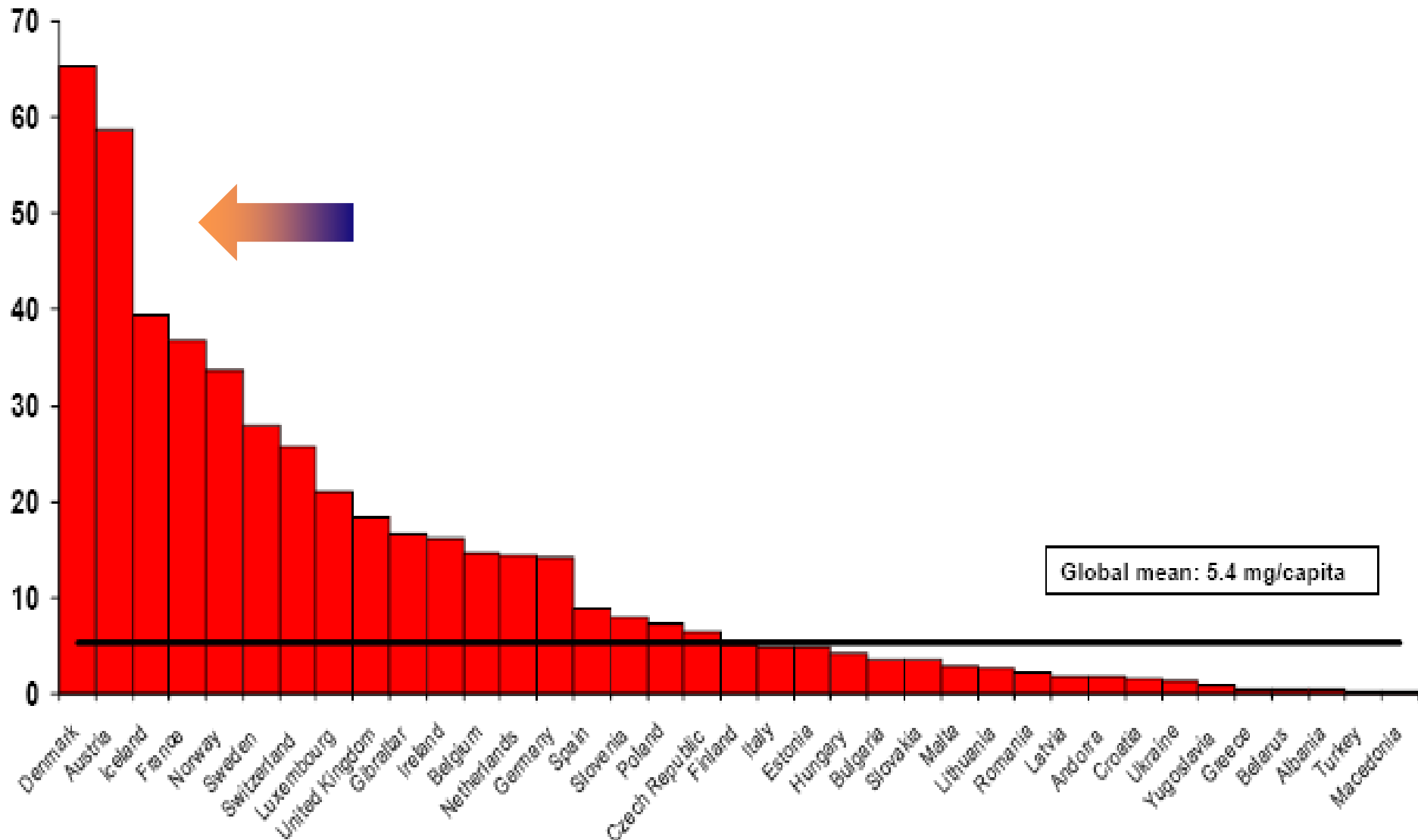
- 3 BENZO's
- 2 OPIOIDS
- 1 SEDATIVE

NO PAIN CONDITION.

Trends SA opioid prescription Chronic pain 1984 - 2006

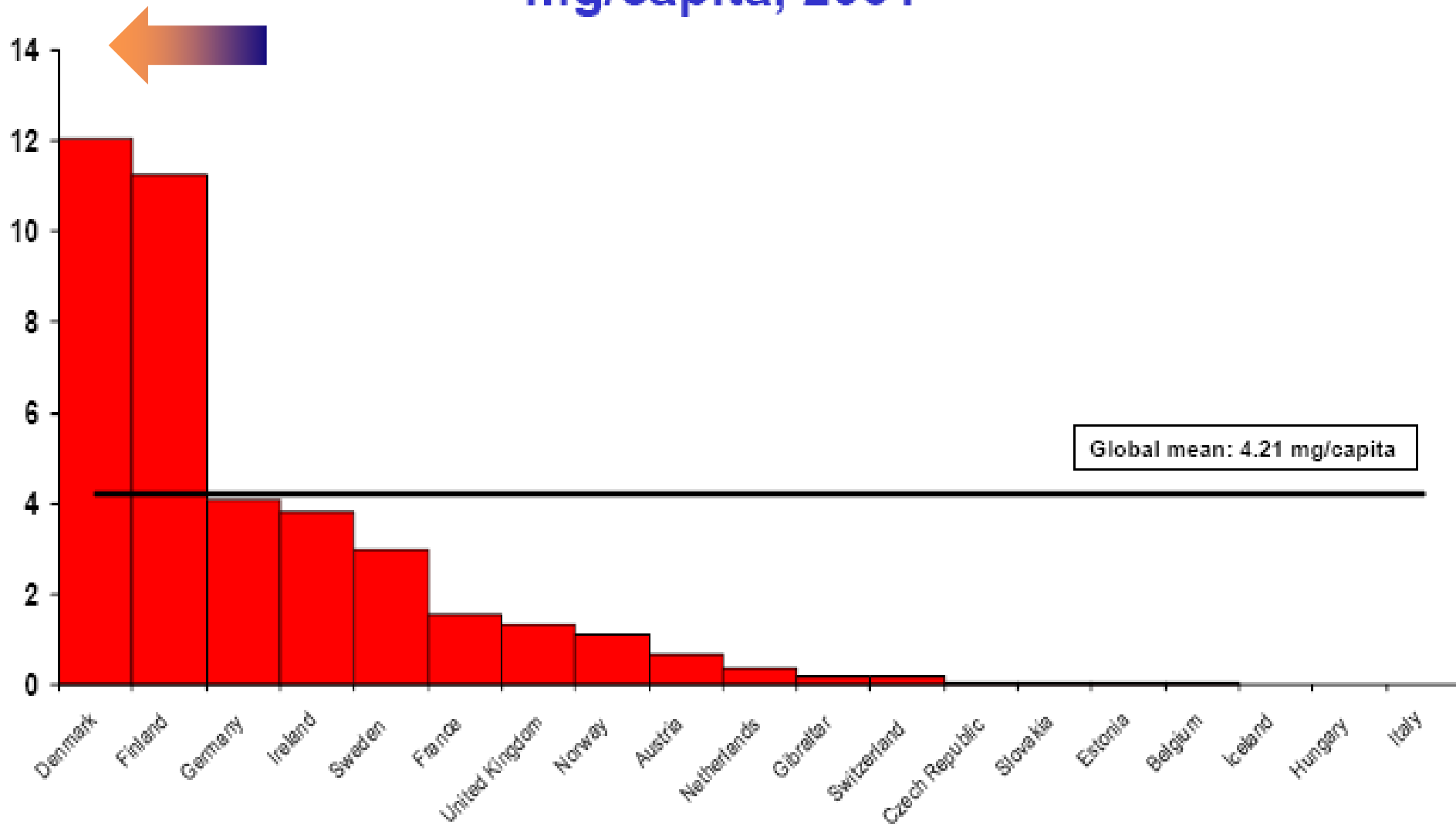


Consumption of Morphine in Europe mg/capita, 2001



Source: International Narcotics Control Board; United Nations Demographic Yearbook
By: Pain & Policy Studies Group, University of Wisconsin/WHO Collaborating Center, 2003

Consumption of Oxycodone in Europe mg/capita, 2001



Source: International Narcotics Control Board; United Nations Demographic Yearbook
By: Pain & Policy Studies Group, University of Wisconsin/WHO Collaborating Center, 2003

RACP: OPIOIDS CHRONIC PAIN

- Use oral morphine tabs ↑ 40X 1990-2006
- Use oxycodone ↑ 4x 1990 – 2003.
- Some parts Australia, prescription opioids are main opioid used illicitly.
- Oxycontin most commonly used drug in Kings Cross safe injecting room.

RACP: OPIOIDS CHRONIC PAIN

Three areas concern:

- Development dependence on prescription opioids by a proportion pts.
- Use prescription opioids by individuals with other drug and alcohol problems
- Management CNMP in opioid dependent individuals

RISKS DEPENDENCE

- SMOKING 25%
- ALCOHOL 16 – 20%.
- ILLICIT DRUGS 6-10%

In Australia over a 12 month period in 2004:
3.1% population (0.6 million) 14 and over reported
using pain killers for non-medical purposes.

Overall 7.6% Australians report using pharmaceutical
drugs for non-medical purposes at least once.

LONG - TERM OPIOID EFFECTS.

- Pharmacogenomics
- Pain relief?
- Quality of life / function.
- Neuro-endocrine effects.
- Immune status
- Tolerance / dependency
- Increased pain sensitivity - “hyperalgesia”.

PHARMACOGENOMICS / OPIOIDS

- **CYP2D6 essential → activate**
 - codeine, oxycodone, tramadol
- **10% Caucasians poor metabolizers**
 - so minimal drug effect.
- **8% Caucasians ultra-rapid metabolizers**
 - massive drug effect??

Unpredictable response ~ 20% patients!!

RCT SUMMARY

- No RCTs - looked opioid treatment CNCP –
in large doses - more than 16 weeks.
- Effect opioids on function / quality of life –
NOT KNOWN!!!!!!.

- 1). Significant placebo effect.
- 2). ↓ pain intensity 30% (15-30% for placebo).
- 3). ↓ Visual Analogue Scale (VAS) 15 /100
- 4). 5-10% withdraw - lack efficacy (20% placebo).
- 5). 50-80% develop - one opioid-adverse effect
(30-60% for placebo).

Only 30% RCT patients
- remain 'long-term' opioid
therapy
for management of pain.

OPIOID NEURO-ENDOCRINE EFFECTS

- Suppression hypothalamic-pituitary axis
- Reduction - fertility, libido, drive.
- Weight-gain / fluid retention.
- Hypo-testosteronism / amenorrhea.
- Reduced lumbar bone mineralisation.

Monitoring by prescribers.

Hormonal screening and replacement.

IMMUNE SUPPRESSION

Acute administration morphine ↓ killer T cell activity, cytokine production, lymphocyte proliferation

- well organisms / volunteers
- central effect, naloxone protects!
- dose related
- high infection rates in drug addicted

BUT

- Having pain is immunosuppressive
- No significant studies in chronic dosing

FAILURE PREVIOUS EFFECTIVE OPIOID THERAPY

- Disease progression
- New disease
- Progression of co-morbidities.
- Opioid tolerance.
- **Opioid-induced pain sensitivity.**
 - **“Hyperalgesia” (OIH) .**

OPIOID INDUCED HYPERALGESIA

1995 Mao recognised morphine *tolerance* & *“hyperalgesia.”*

- ↑ response to a painful stimulus.
- Increasing morphine doses ↑ pain!!!!
- Pts high doses – improve pain relief ↓ dose

2003 Ballantyne- evidence rapidly accumulating
pts high dose - rarely report
satisfactory analgesia or improved function.

OPIOID INDUCED HYPERALGESIA

2003 Ballantyne:

“Evidence - treating patients with chronic pain, opioid doses should be limited in order to maintain efficacy & safety.”

Doses moderate range:

Morphine 120 + mg / day.

Oxycontin 100mg / day.

Methadone 60mg / day.

One patch only!

OPIOIDS - CHRONIC PAIN

- Pain history and examination
- Informed consent
- Exclude harm to individual
- Consider harm to community!
- Neuro-endocrine workup
- Is opioid R_x helping ?
- Is change feasible ?

OPIOIDS CHRONIC PAIN

- Opioid monotherapy *not* supported RCTs
- Improving physical / mental health
essential better outcome.
- Longterm outcomes opioid therapy as
component of multimodal approach.....

“FOLLOW COMMON SENSE.”

Mrs RC (divorcee)
56 years old.

1. Durogesic 25µg /hr (600µg/day)
2. Oxycodone CR 10mg prn.
3. Oxycodone 5mg prn.
4. Prothiaden 100mg nocte.
5. Stelazine 5mg nocte.
6. Temazepam 10mg nocte.
7. Carbamazepine 200mg 5/day (1000mg)

Mrs E.G (RN) 35 years old.
Doctors wife.

1. Anamorph 45mg qid. (180mg morphine/day)
2. Amitriptyline 75mg nocte.
3. Effexor 300mg mane
4. Baclofen 20mg tds.
5. Diazepam 10mg prn.
6. Oxazepam 30mg prn.
7. Coloxyl & senna

Ms JW.

- Cholecystectomy.
- Partial gastrectomy with stricturoplasty.
- Laparotomy with peritonitis.
- DVT left arm.
- PE - anti-coagulated.
- Hypoalbuminemia – albumin 5g/L.
- E. coli septicaemia.
- Hypogammaglobulinaemia.
- Anaemia of chronic disease
- Protein C deficiency / Factor V Leiden heterozygote
- Vitamin B12 deficiency

FOUR “A’S” OF PAIN TREATMENT

- Analgesia (pain relief)
- Activities of daily living (increased)
- Adverse effects (side effects)
- Aberrant drug taking - addiction related outcome

10 POINTS TO KNOW.

1. Pain pathways / “plasticity” CNS:
 - Transition Acute → Chronic
 - Risk factors / prevention?
2. Pain is a *Bio-psycho-social* experience
3. Difference acute/cancer/chronic pain
 - Does this matter??
4. Chronic pain *is* a disease in own right.
5. How assess pain / Pain History.
 - Difficulties extremes age etc

10 POINTS TO KNOW!

6. Different drugs

Acute: short acting drugs, high doses, taper quickly

Chronic: long acting oral drugs, moderate doses.

Cancer: both.

7. Pharmacology medication.

Simple analgesics / NSAID's/ opioids/adjuvants/LA's

Recognition drug interactions – Serotonin Syndrome.

8. Appropriate use medication – acute v's chronic.

9. Different Interventions – acute v's chronic.

10. Management difficult patient

opioid tolerant / dependency issues / co-morbidities

OPIOID RULES.

Acute Pain!

- Not all opioids are the same.
- Variation pharmacology (bioavailability)
– different routes.
- Initial doses *age* based.
- Monitor sedation scores – not RR.
- Do controlled release opioids have role?
- Pethidine no advantage.
- Durogesic patch no place.

OPIOID RULES

Chronic Pain!

- Select appropriate patient.
- Controlled release only.
- Breakthrough medication limited role
 - Patients require re-education to pace.
- Education pts – responsibility / expectations.
- Educⁿ long term effects / hormonal, endocrine.
- Equi-analgesic dose tables:
 - Morphine: methadone varies 3:1 to 20:1

MORPHINE :METHADONE

Morphine < 100mg : 3:1

Morphine 100 - 300mg : 5:1

Morphine 300 - 600mg : 10:1

Morphine 600 - 800mg : 12:1

Morphine 800 - 1000mg : 15:1

Morphine > 1000mg : 20:1

EQUI-ANALGESIC DOSES.

- Morphine 30mg oral \cong 10mg IM.
- \cong Oxycodone 15mg oral.
- \cong Methadone 10mg oral.
- \cong Hydromorphone 4mg oral.
- \cong Codeine 180mg
- \cong Transdermal buprenorphine 15 μ g/hr
- \cong Transdermal fentanyl 8 μ g/hr.

