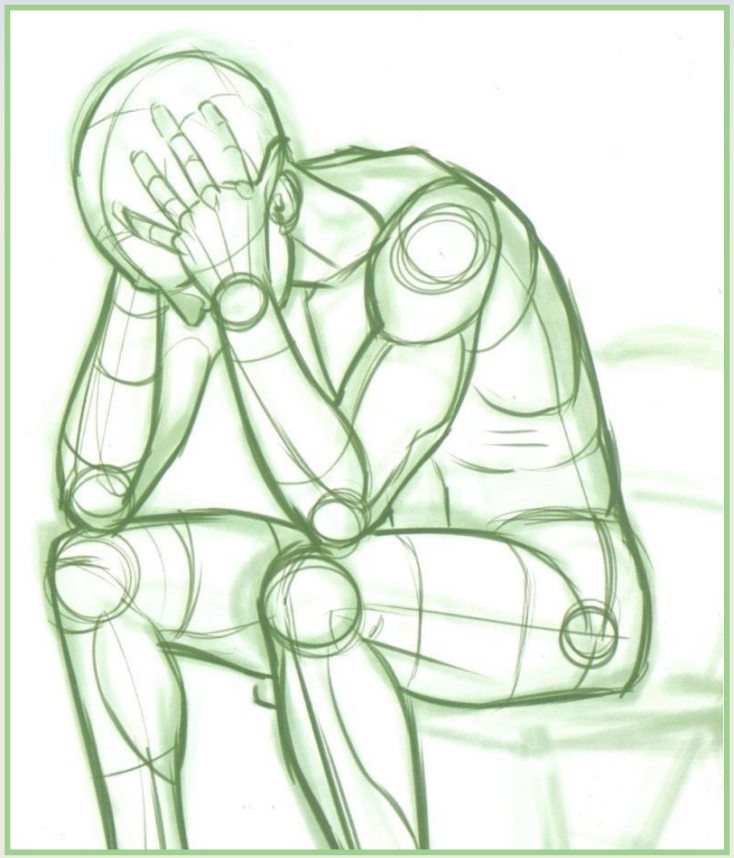
Pain Management

Current perspectives

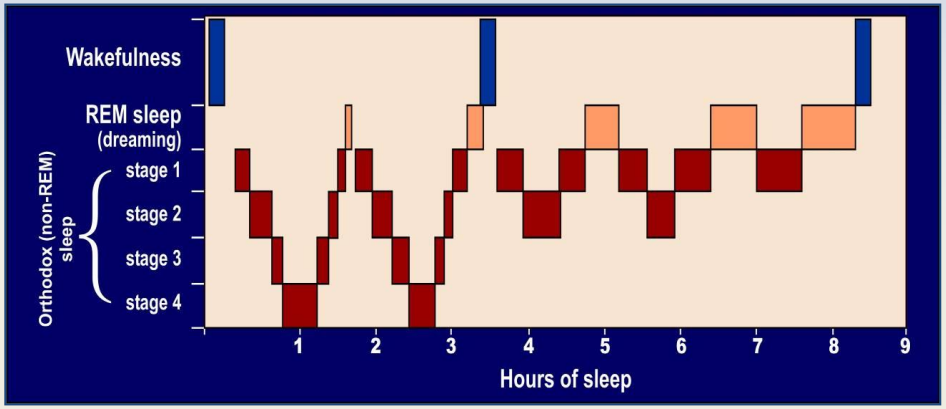


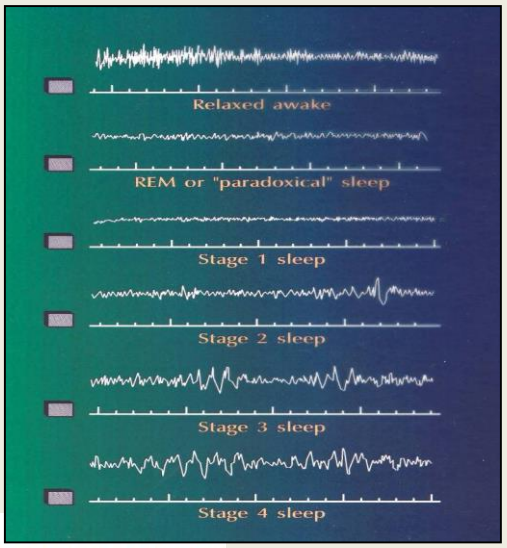
Helgard Meyer FCFP(SA)
Department of Family Medicine
University of Pretoria
Wilgers MR Medical Centre

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA
Denkleiers • Leading Minds • Dikgopolo tša Dihlalefi

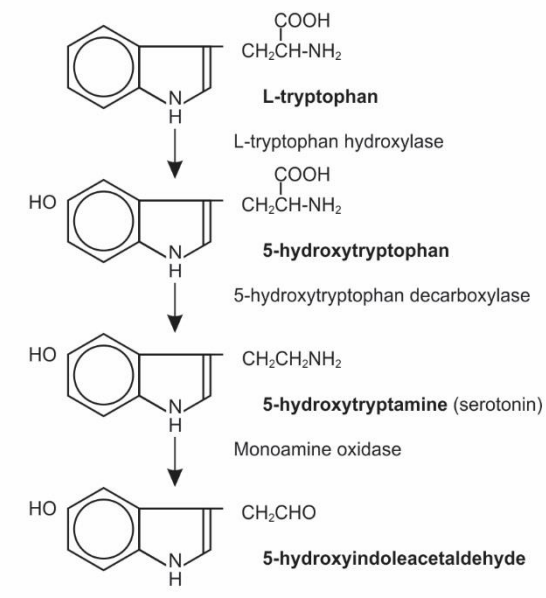
Stress – Depression – Chronic pain relationship

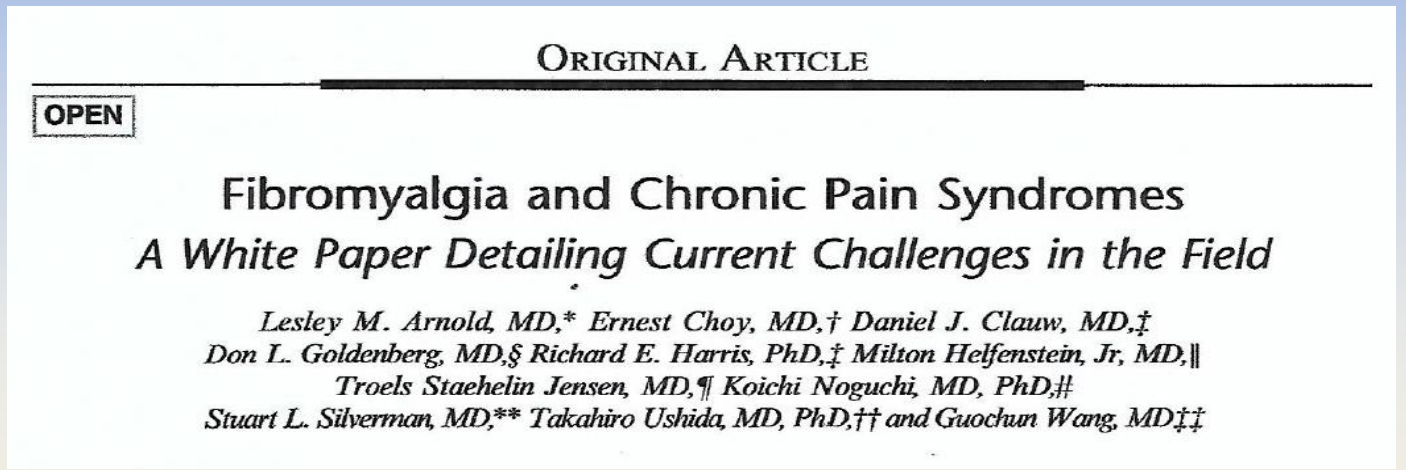
Moldofsky in Arthr Rheum, 1979
Thiagarajah et al in Int J Clin Rheum, 2014





Serotonin Synthesis





ORIGINAL ARTICLE

OPEN

Fibromyalgia and Chronic Pain Syndromes

A White Paper Detailing Current Challenges in the Field

Lesley M. Arnold, MD, Ernest Choy, MD,† Daniel J. Clauw, MD,‡*
Don L. Goldenberg, MD,§ Richard E. Harris, PhD,‡ Milton Helfenstein, Jr, MD,‖
Troels Staehelin Jensen, MD,¶ Koichi Noguchi, MD, PhD,#
*Stuart L. Silverman, MD,** Takahiro Ushida, MD, PhD,†† and Guochun Wang, MD‡‡*

- New knowledge – not reaching clinicians
- Less well understood than nociceptive / neuropathic pain
- Overlaps with OA RA SLE
- Overlaps with *chronic low back pain* and *chronic headaches*

OPEN ACCESS

Diclofenac use and cardiovascular risks: series of nationwide cohort studies

Morten Schmidt,[1,2] Henrik Toft Sørensen,[1,3] Lars Pedersen[1]

[1]Department of Clinical Epidemiology, Aarhus University Hospital, Olof Palmes Allé 43-45, 8200, Aarhus, Denmark

[2]Department of Cardiology, Regional Hospital West Jutland, Herning, Denmark

[3]Department of Health Research & Policy (Epidemiology), Stanford University, Stanford, CA, USA

Correspondence to: M Schmidt
morten.schmidt@clin.au.dk
(ORCID 0000-0001-5646-1314)

Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2018;362:k3426
http://dx.doi.org/10.1136/bmj.k3426

Accepted: 19 July 2018

1 370 832 diclofenac initiators
3 878 454 ibuprofen initiators
291 490 naproxen initiators
768 781 paracetamol initiators
1 303 209 non-initiators of NSAID's

→ Major CVS events at **30 days**

(AF, stroke, MI, cardiac death)

- 50% increase vs non-initiators
- 30% increase vs naproxen
- 20% increase vs ibuprofen / paracetamol

→ 4,5 fold increase in GI bleeding

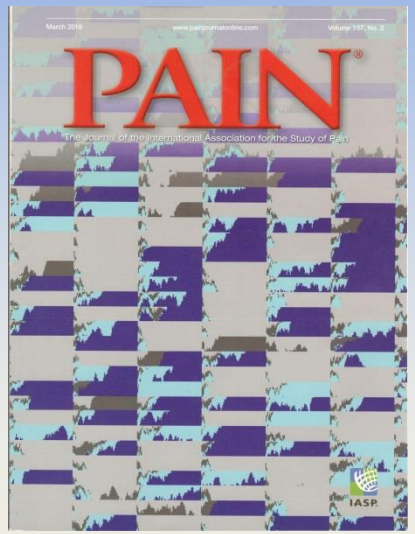
"Its time to acknowledge the potential health risk of diclofenac and reduce its use."

Topical Review

PAIN®

Updating the definition of pain

Williams et al in Pain, 2016



"Pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive, and social components."

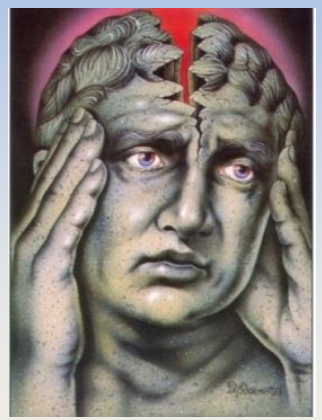
Acute pain

Holdcroft in Core topics in Pain, 2005

- Normal biological response
- Protects / promotes healing
- Unrelieved acute pain:
  - ↑ catecholamines
  - ↑ heart rate
  - Delayed healing
  - Nervous system effects
  - May evolve into chronic pain
- Must be treated and its cause be removed

Chronic pain

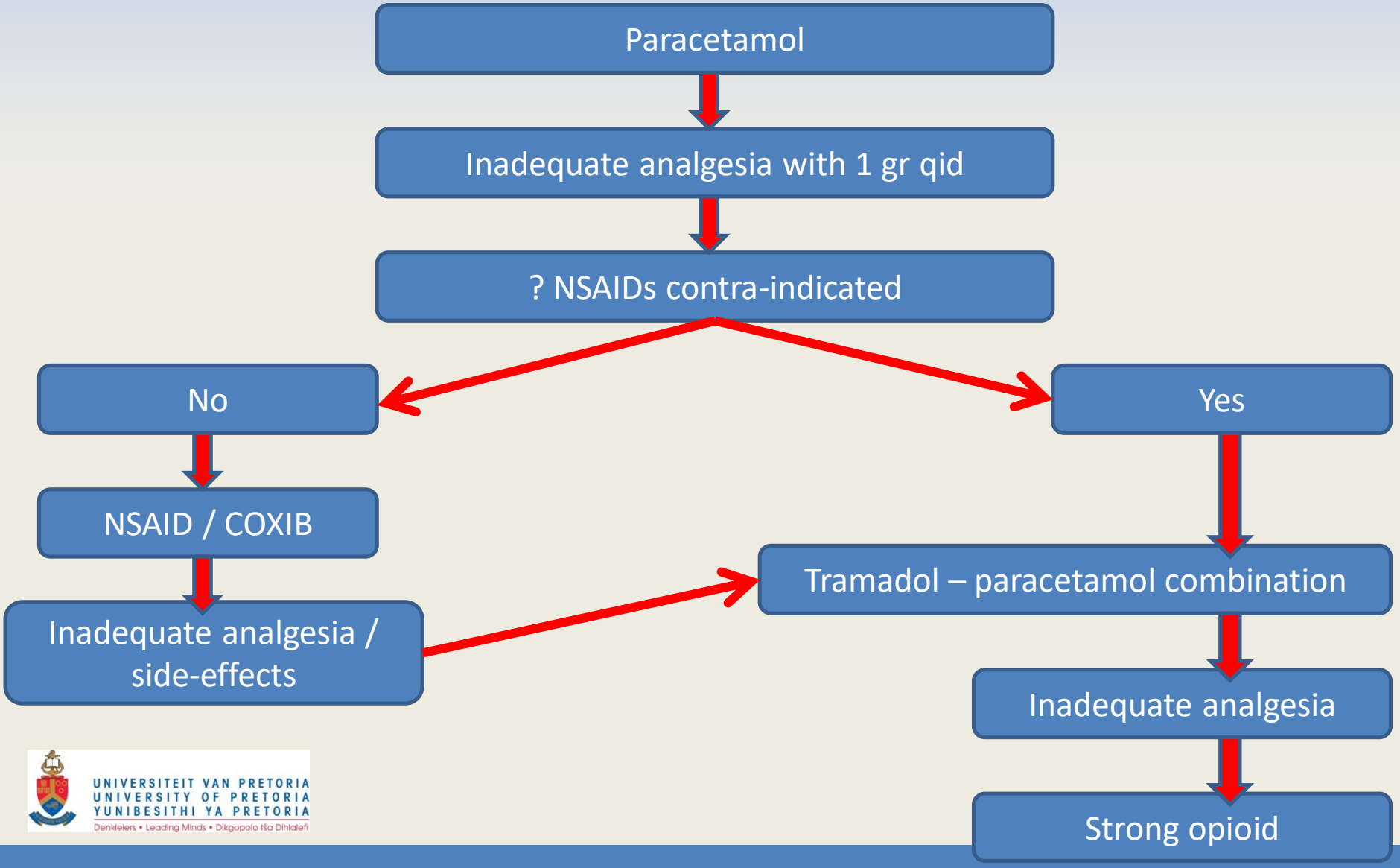
Holdcroft in Core topics in Pain, 2005



- Persists longer than the expected time for healing (>3 months)
- No “warning” function
- Pain becomes the “disease”
- Emotional / psychosocial factors important
- Complex to treat
  - Interdisciplinary approach

Acute non-specific pain

Sachs in Am Fam Phys, 2005



Paracetamol

Nikles in Am J Ther, 2005
Schug in Clin Rheum, 2006
Nikles in Am J Ther, 2005
Schug in Clin Rheum, 2006

Central effect

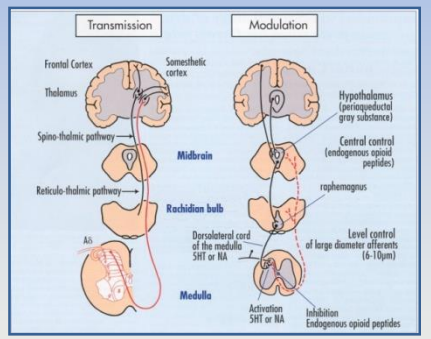
- *No specific binding sites*
- Serotonergic anti-nociceptive pathway
- Endocannabinoid system
- Acute post-op pain *vs* chronic pain

Proven synergy

- **NSAIDs**
- **Tramadol**
- **Opioids**

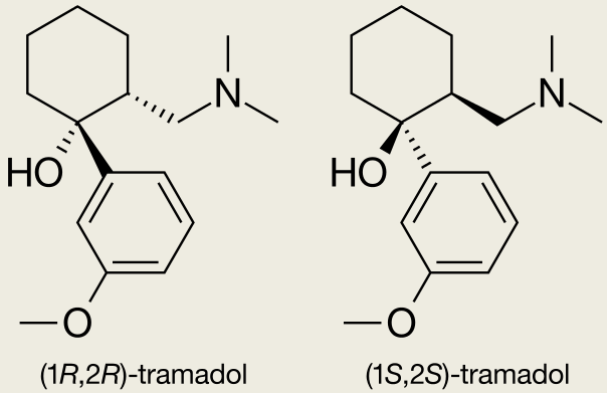
Tramadol

Cicero et al in Drug Alcohol Dep, 1999
Schug in Anaesth Int Care, 2000
Epstein et al in Biol Psych, 2006
Rafa in J Clin Pharm, 2008
Barkin in Am J Therap, 2008
Park et al in Clin Rheum, 2012
Smith et al in Drug Eval, 2013



- Central acting atypical opioid
- Both mono-aminergic and opioid effects
- **Much less opioid receptor affinity than morphine**

Very low abuse potential (< 1/100 000)



(1*R*,2*R*)-tramadol (1*S*,2*S*)-tramadol

Tramadol (37,5mg) / Paracetamol (325mg)

Schug in Clin Rheumtol, 2006
McQuay in Eur J of Anaesth, 2008
Park et al in Clin Rheum, 2012

- Rational combination therapy *(NNT=3)*
- Faster onset and longer duration
- **25% less tramadol - less nausea**
- Triple (+) mechanism of action

➡ *Positive studies in:*

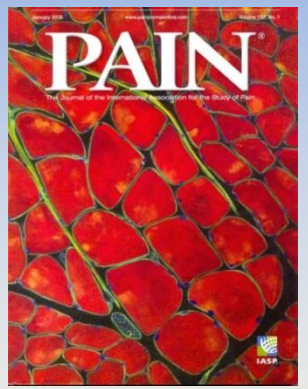
- Post-op pain
- Low back pain
- Fibromyalgia
- Neuropathic pain
- **OA flares**

NB: Mixed nociceptive – neuropathic pain

Warning

Focussing only on pain intensity in the assessment of chronic pain patients

Sullivan in Pain, 2016



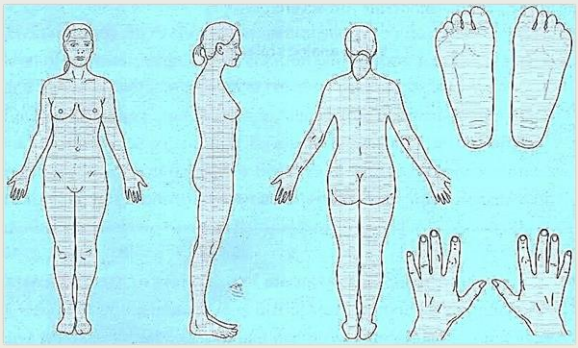
- Results in the strongest analgesics for the wrong patients.

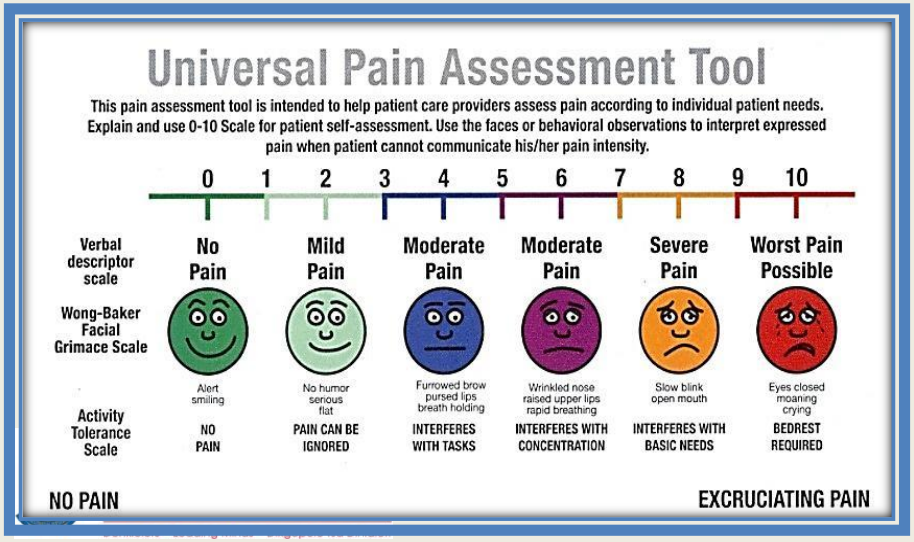
'Higher pain intensity in chronic musculo-skeletal pain mostly indicates more emotional and psychosocial factors."

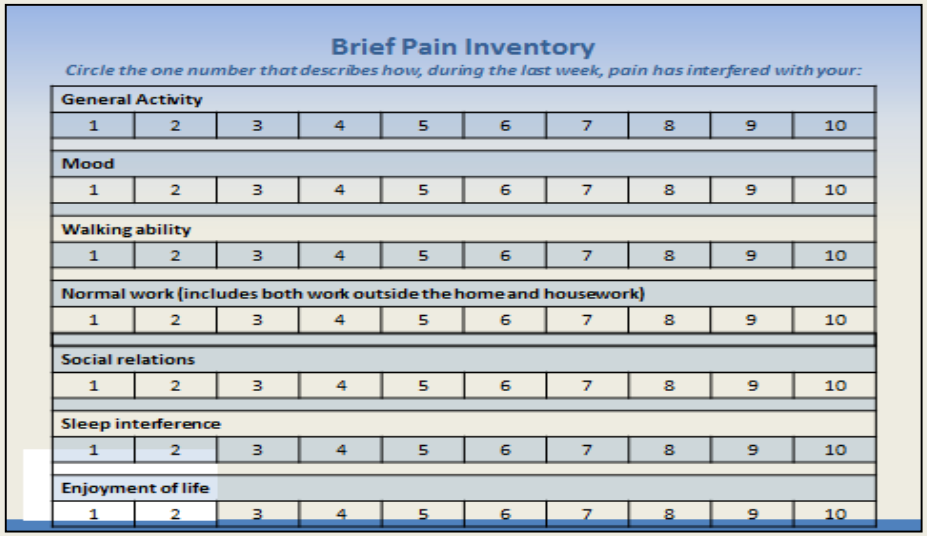
Assessment of patients in chronic pain

Mackichan in Rheum Dis Clin North Am, 2008
Meyer in SA Fam Pract, 2011

- Unique and personal experience
- DN-4 / PHQ-9
- Measure







The Patient Health Questionnaire (PHQ-9)

Over the past 2 weeks, how often have you been bothered by any of the following problems	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3
3. Trouble falling asleep, staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you're a failure of have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or, the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

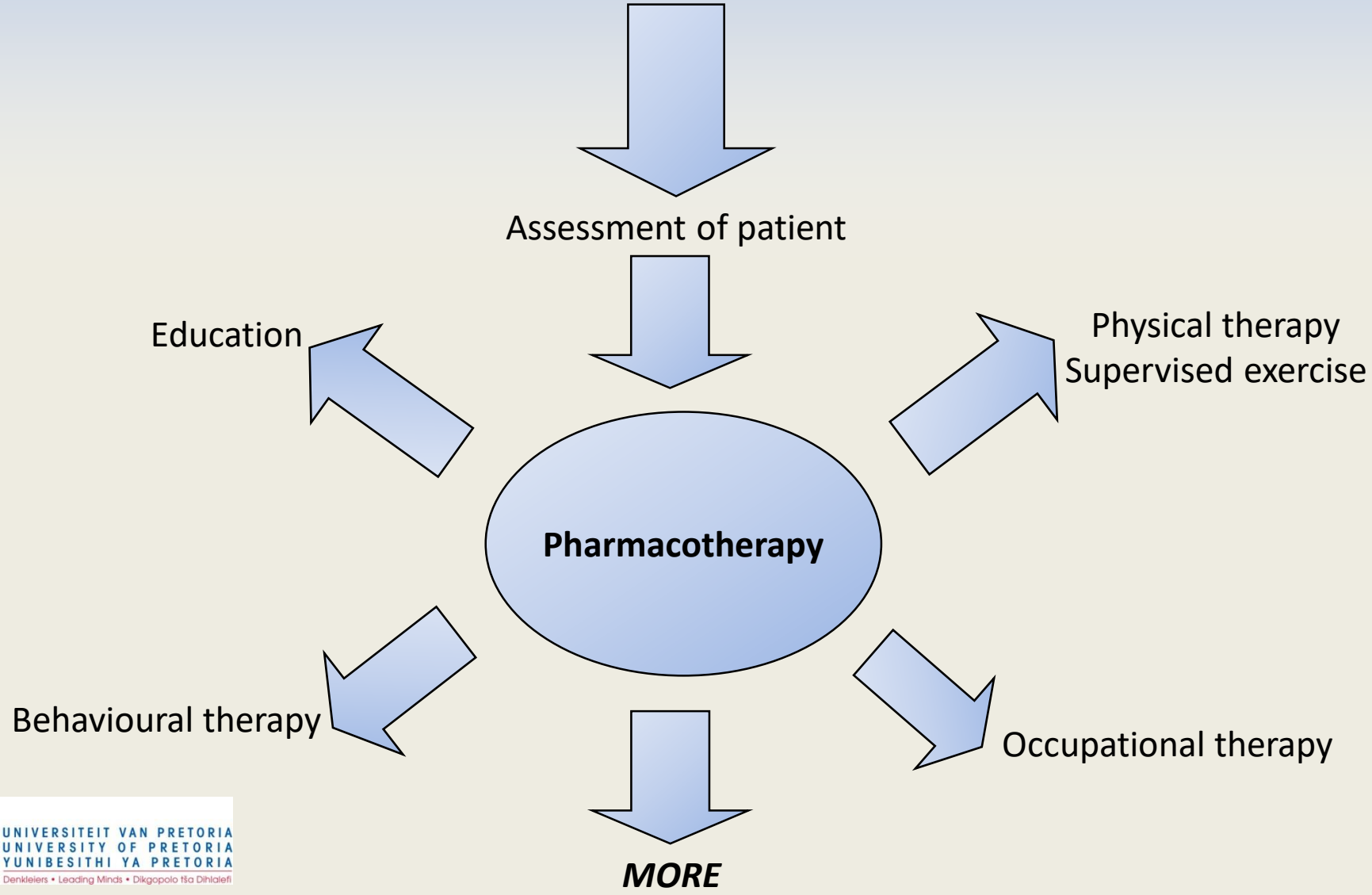
Treatment goals for chronic pain patients

Ashburn in Lancet, 1999
Meyer in SA Fam Pract, 2007

- Reduction of pain *(30% is clinically significant)*
- Improvement in co-morbidities (e.g. mood and sleep)
- Improve patient's functioning

Return to work

Chronic pain – multimodal approach



Pharmacotherapy

Gronow in Anaes and Int Care, 2010

Primary analgesics

- Paracetamol
- NSAID's / COX-2 inhibitors
  - *Ibuprofen*
  - *Diclofenac*
  - *Naproxen*
  - *Celecoxib*
  - *Etoricoxib, etc*
- Opioids
  - Mild
    - *Codeine*
    - *Tramadol*
  - Strong:
    - *Morphine*
    - *Hydromorphone*
    - *Buprenorphine*
    - *Oxycodone*
    - *Fentanyl*
    - *Tapentadol*

Adjuvant analgesics

- Tricyclics
  - *Amitriptyline, Cyclobenzaprine*
- SNRI's
  - *Duloxetine, etc.*
- Anticonvulsants:
  - *Carbamazepine*
  - *Gabapentin*
  - *Pregabalin*

Local anaesthetics

Diverse analgesics

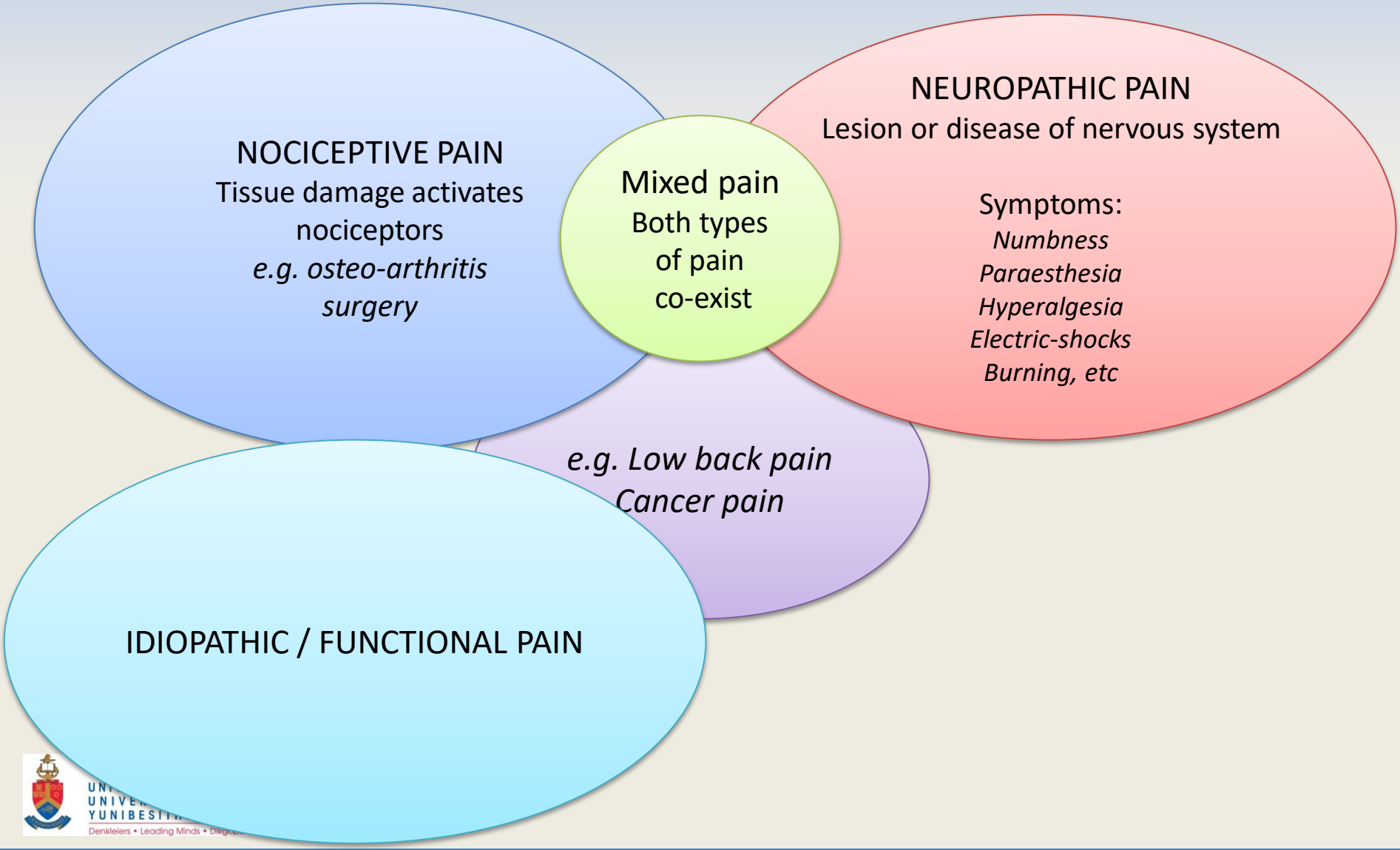
- *Ketamine*
- *Cannabinoids*
- *Muscle relaxants*

Topical analgesics

- *Lidocaine patch*
- *Capsaicin patch*

Mechanism-based pain classification

Woolf in Ann Int Med, 2009



Neuropathic pain

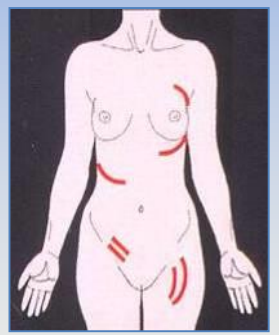
Price in Clin J of Pain, 2004
Management of Pain. Philadelphia, 2006

Disease / lesion of the somato-sensory nervous system

- Diabetic polyneuropathy
- Post herpetic neuralgia
- HIV neuropathy
- Trigeminal neuralgia
- *Low back pain*
- *Chronic post-surgery pain (CPSP)*
- Mechanical compression
- Cancer
- Chemotherapy
- Amputation (“Phantom pain”)

Chronic post-surgery pain (CPSP)

Brown et al in Best Prac Research Clin Anaes, 2003
Kehlet et al in Lancet, 2006



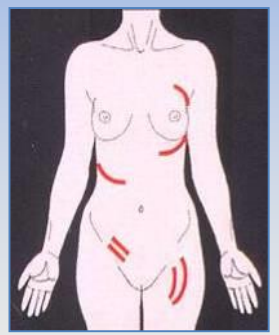
Common causes of chronic pain

- Thoracotomy – up to 20-30%
- Breast surgery – up to 10-15%
- Limb amputation – up to 40%
- Gallbladder surgery – up to 20%
- Failed back surgery syndrome – up to 30%, etc

NB: Analgesia in peri-operative period

Peri-operative pain management

Brown et al in Best Prac Research Clin Anaest, 2003



Systemic analgesics

- Paracetamol
- NSAIDS / COXIBS
- Central diverse analgesics
  - Tramadol
  - Ketamine
- Opioids

Regional techniques

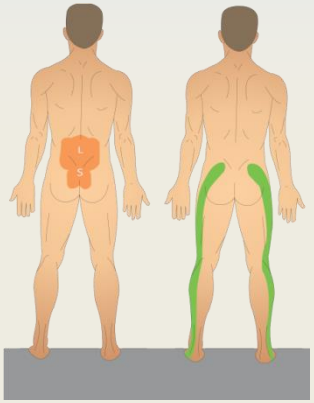
- Epidural analgesia
  - Local anaesthetic
  - Opioids
  - Adjuvants
- Peripheral nerve blocks
- Intra-articular analgesics
- Wound infiltration

MULTIMODAL APPROACH

Low back pain with neuropathic components

Schmidt et al in Eur J Pain, 2009
Beith et al in Pain, 2011
Baron et al in Pain Practice, 2015

- Often overlooked
- 15-59% of LBP patients
- Leg pain
- Higher pain / disability levels



Pharmacotherapy in chronic neuropathic pain

Dworkin et al in Pain, 2007

First line

- **Antidepressants**
  - Tricyclics *(amitriptyline)*
  - SNRI's *(duloxetine)*
- **α2-δ ligands**
  - Pregabalin
  - Gabapentin

Second line

- **Tramadol**
  - Severe pain
  - Acute flare-up

Third line

- **Strong opioids**
  - Very careful patient selection
  - Tapentadol
- **Cannabinoids**

Algorithm for osteoarthritis of knee

Briyere et al in Sem Arthr Rheum, 2014

Step 2: Background treatment

Paracetamol

or

Chronic SYSADOA

(*Symptomatic Slow-acting Drugs for Osteo-arthritis)*

- ➡ *Glucosamine-sulphate*
- ➡ *Chondroitin-sulphate*

↓

Still symptomatic: Add

Topical NSAIDS
Topical capsaicin

Refer to physio for assessment
(e.g. mal-alignment)

Algorithm for osteoarthritis of knee

Briyere et al in Sem Arthr Rheum, 2014

Step 3: Advanced pharmacological management

Oral NSAIDS / COXIBS *(Intermittently)*

Increased GI risk:
- *Avoid non-selective NSAIDs*
- *COX-2 selective NSAIDs (±PPI)*

Increased CV risk:
- *Prefer naproxen*

Increased renal risk:
- *Avoid NSAIDS*

↓

- *Intra-articular hyaluronate*
- *Intra-articular corticosteroid*

Algorithm for osteoarthritis of the knee

Briyere et al in Sem Arthr Rheum, 2014

Short-term tramadol
Duloxetine

End-stage disease

Joint replacement surgery

If contra-indicated

Strong opioid analgesics (NB: guidelines)
"Last resort"

High potency opioids in chronic pain

Evans in Best Practice, 2000
Russell in Pain Medicine, 2002
Niesch et al in Cochrane Rev, 2009
Noble et al in Cochrane Rev, 2010

Short term use for acute pain

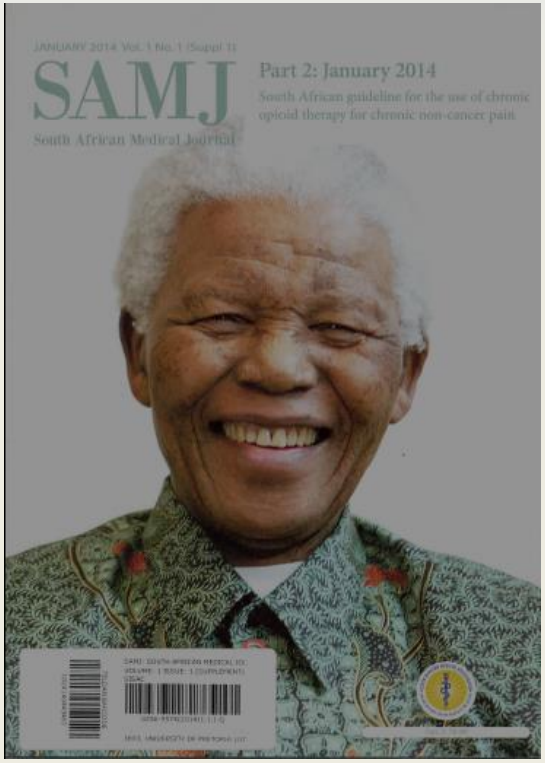
End-of-life pain

Chronic non-cancer pain – controversial

- ***Morphine sulphate***
- ***Fentanyl***
- ***Oxycodone, etc***

SA Guidelines for long term high potency opioid therapy in *chronic non-cancer pain*

Raff et al in SAMJ, 2014 (Suppl)



"… appropriate and very careful patient selection and follow-up is paramount …"

- Opioid risk assessment
- Psycho-social assessment

Opioid-induced hyperalgesia

Chu et al in J Pain, 2006
Edit in Br J Anasth, 2010
Lee et al in Pain Physician, 2011
Velayudhan et al in Cont Educ Anaesth, 2014

Paradoxical increase in pain

- Hyperalgesia
- Mostly more diffuse
- Worsens with ↑ dosage
- May occur within 1 month

NB: Poorly defined pain disorders e.g. low back pain, FMS.

NB: Codeine combination drugs

Chronic widespread pain

Gran in Res Clin Rheum, 2003
Yunus in Best Pract Rheum, 2007

- ±10-12% of general population
- Mostly a spectrum of disorders
  - *Psychiatric disorders*
  - *Rheumatic disorders*
  - *Sleep disorders*
- Fibromyalgia in 30-40% of patients with CWP

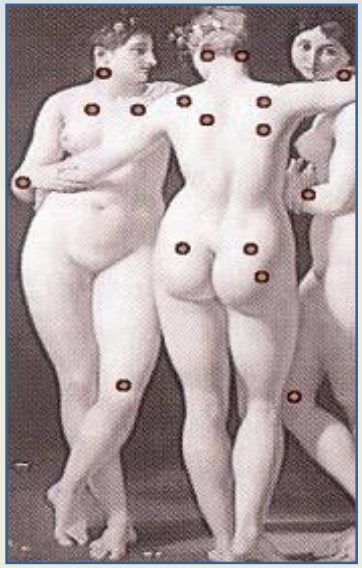
What triggers FMS?

Clauw in Ann Int Med, 2008
Elliot in Spine, 2015

- Psychological stressors
- Early life stressors
- Infections
- Peripheral pain syndromes (eg. RA, SLE)
- Physical trauma (involving the trunk)

1990 ACR classification criteria for FMS

Woolfe et al in Arthr Rheum, 1990

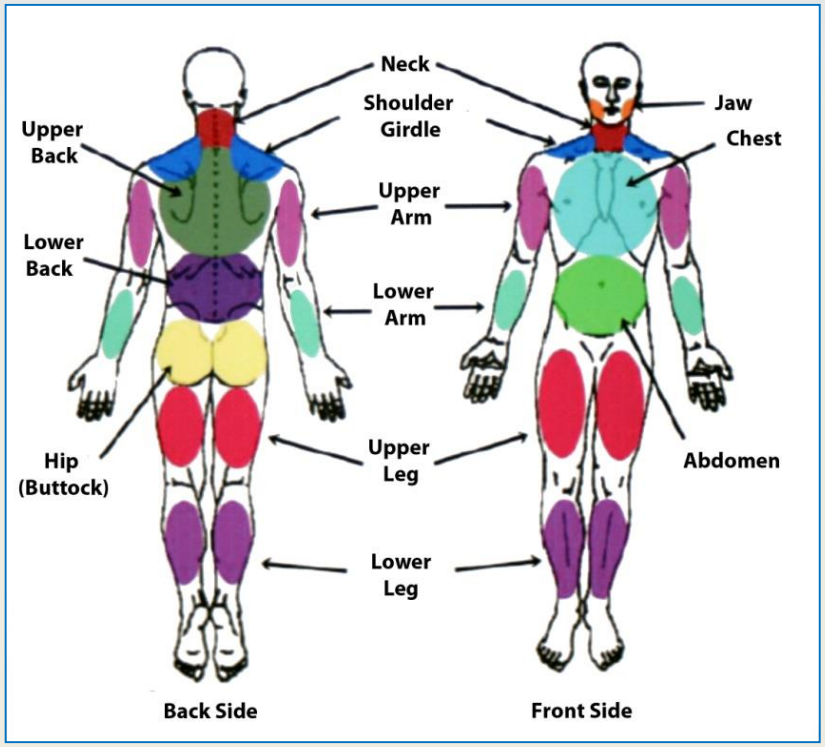


- Widespread musculoskeletal pain > 3 months in all 4 quadrants
- ≥ 11/18 painful tender points with digital pressure of 4kg/cm^2

2010 ACR diagnostic criteria for FMS

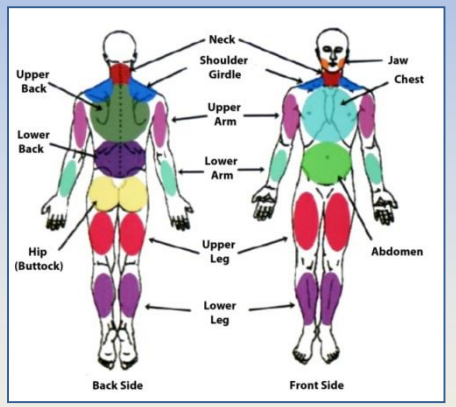
Wolfe et al in Arth Care Res, 2010

- Widespread Pain Index (WPI)
  - *19 body areas*
- Symptom Severity Scale (SS)
  - *Fatigue: 0-3*
  - *Sleep: 0-3*
  - *Cognitive: 0-3*
  - *Somatic symptoms: 0-3*



Canadian guidelines for diagnosis and management of FMS

Canadian Guidelines for FMS in Rheum Arthr, 2013
Fitzcharles et al in Pain Res Manag, 2013



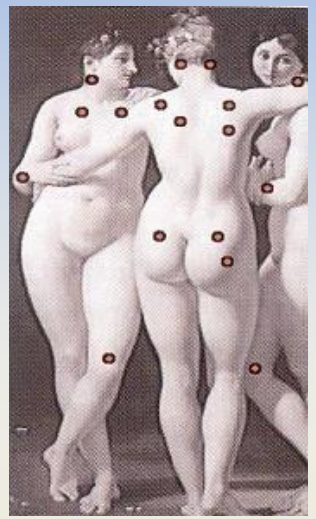
Recognized as a valid pain syndrome based on recent neurophysiological evidence

- ➡ Paradigm shift in diagnosis:
  - ➡ ***Diagnosis and management "concentrated" in primary care***
  - ➡ *Do not "over-investigate" or "over-refer"*
- ➡ Not "all-or-nothing" phenomenon ***("fibromyalgia-ness")***

Emphasis on non-pharmacological strategies

Treatment of FMS

Pooks in Curr Opin Rheum, 2007
Clauw in J of Clin Rheum, 2007



Non-pharmacological

- **Cardiovascular exercise**
- Patient education
- Cognitive behavioral therapy
- Multimodal approach
- Treat peripheral pain generators

Primary Care

Pharmacological

Modest evidence

- Pregabalin
- Duloxetine

} **FDA approved**

- Amitriptyline
- Cyclobenzaprine
- Tramadol ± paracetamol

A new clinical model for the management of low back pain

Gordon Waddell, 1987

"The last 3 decades has seen *a radical shift* in the understanding and *management of chronic LBP*, from the biomedical model of specific organic pathology / structural damage and physical "fixes", to the *comprehensive biopsychosocial model*, with *emphasis* on *restoration of function*."

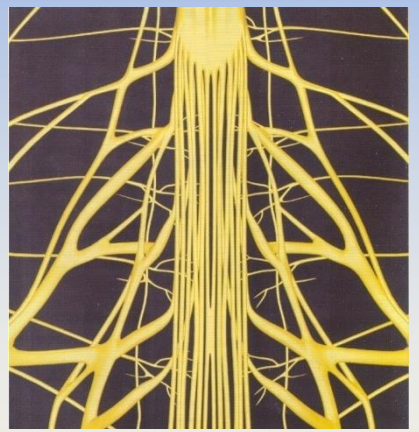
Warning signs of serious causes of back pain

Maher et al in Aus Presciber, 2011

Cancer	History of cancer Unexplained weight loss Failure to improve after 1 month Age >50 years Night pain
Vertebral infection	Fever Intravenous drug use Recent infection Immuno-compromised state Rest pain
Cauda equina syndrome	Urinary retention Faecal incontinence Saddle anaesthesia Lower limb weakness

Cauda equina syndrome

Chou in Ann Int Med, 2007
Garner in MPS Casebook, 2009



- Do you have bilateral leg pain?
- When last did you pass urine / open your bowls?
- Can you feel your bladder when it is full?
- Does you backside / genital area feel normal?
- “Saddle anaesthesia”
- Can you tighten your anus?

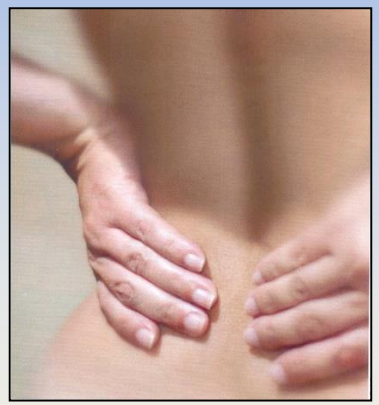
May develop gradually

Most frequent finding: urinary retention

Low back pain assessment

Focused clinical examination

Chou et al in Ann Int Med, 2007
Mackichan in Rheum Dis Clin North Am, 2008
Meyer in SA Fam Pract, 2011



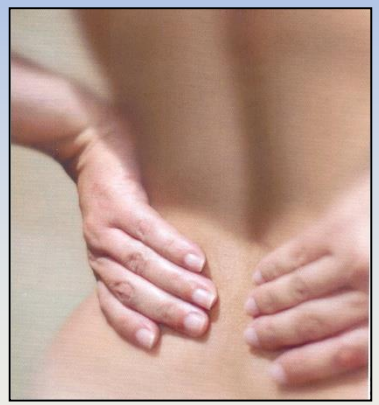
- General observation
- Regional back examination **(tenderness)**
- Ankle and knee reflexes
- Ankle and big toe dorsiflexion strength
- Hop on each leg
- Walk on heels then toes

Remember

- Abdominal / pelvic screening
- Peripheral pulses
- Urine dipstix

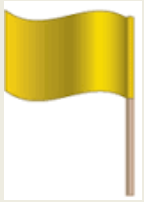
Answer 3 questions

Waddell in Backpain Revolution, 1991
Chou et al in Ann Int Med, 2008
Maher et al in Austr Prescr, 2011

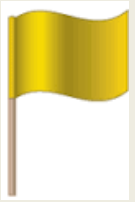


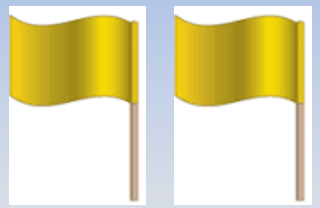
- Serious spinal disease?
- Nerve root involvement?
- Disease elsewhere?
  - Inflammatory e.g. AS
  - Abdominal / Pelvic

If negative: SIMPLE / NON-SPECIFIC BACK PAIN



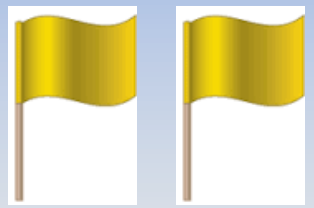
Are there yellow flags?

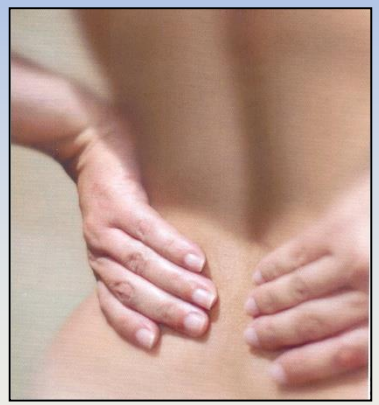




Yellow Flags

Chou et al in Ann Int Med, 2007

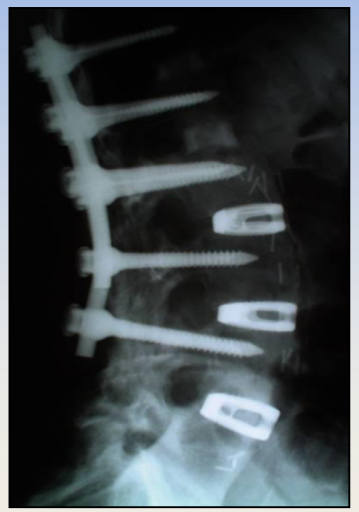




- Belief that LBP is harmful / disabling
- Fear avoidance behaviour / reduced activity
- Reliance on passive treatment versus active participation
- Depressed mood / social withdrawal
- Job dissatisfaction
- Compensation claims
- "*Threatening*" diagnostic labels
- Impaired sleep

Etiology of low back pain

Speed in BMJ,2004
Airaksinen et al in Eur Spine J 2006
Balaque et al in Lancet, 2007
Ann Intern Med, 2007
Savigny P et al in BMJ 2009
Spine, 2009
Ann Intern Med, 2011



Structural

- Facet joint OA
- Prolapsed disc
- Spinal stenosis
- Spondylolisthesis

Infection

- Osteitis
- TB
- Paraspinal abscess

Inflammatory

- Ankylosing spondylitis
- RA
- Spondylo-arthropathies

Metabolic

- Osteoporotic collapse
- Hyperparathyroidism

Neoplasm

- Primary and secondary

Referred pain

- Aorta
- Urogenital
- Hip

Musculoskeletal / Neurological

- Myofascial pain
- Fibromyalgia

International guidelines for acute low back pain

Pain 2002 - An updated review IASP Press, Seattle
Balaque et al in Lancet, 2007

- Exclude red flags
- Reassure patient of good prognosis
  - *90% recover within 4 weeks*
- Patient to stay active
  - *RTW*
- Short course analgesic / NSAID / Coxib / Muscle relaxant
- Consider physical therapy / spinal manipulation
- Be aware of yellow flags

Advice for acute non-specific LBP patient

Maher et al in Austr Prescr, 2011

- Reassure there is no serious disease
- Avoid labelling such as:
  - *“disc trouble”*
  - *“degeneration”*
- Reassure of good natural history
- Encourage staying active
- Use simple safe treatments for symptom control

Management of persistent *non-specific low back pain*: summary of NICE guidelines

Savigny P et al in BMJ, 2009

Persistent LBP (6 – 12 weeks)

- Educational advice
  - *Benign*
- Exercise
  - *Supervised*
- Physical therapy / spinal manipulation *(8-12 sessions over 12 weeks)*
- Needling *(8-10 sessions over 12 weeks)*
- May add:
  - *Amitriptyline*
  - *Pregabalin*
- Combo → Physical / psychological
  - *Cognitive behavioural*

- **Exercise**
- **Manual**
- **Needling**

Guidelines for chronic non-specific LBP

Speed in BMJ,2004
Airaksinen et al in Eur Spine J 2006
Balaque et al in Lancet, 2007
Savigny P et al in BMJ 2009
Chouw in Spine, 2009
www.uptodate.com, 2015

Inter-disciplinary

- Education
- Supervised exercise

- Address psychosocial issues
- Cognitive behavioural therapy
- Short-term pharmacotherapy
  - Paracetamol
  - NSAIDs / COXIBS
  - Muscle relaxants
  - Opioids (intermittently)