Dr John Petrie

Rheumatologist

Lakes Care Medical Centre, Rotorua

Saturday, August 13, 2016 (Room 11)

11:00 - 11:30 Avoiding Iatrogenic Disability in Arthritis Patients

Avoiding Iatrogenic Disability in Arthritis Patients

What you say, matters

John Petrie

South GP CME General Practice Conference & Medical Exhibition

Disclaimer: Commercial support from...

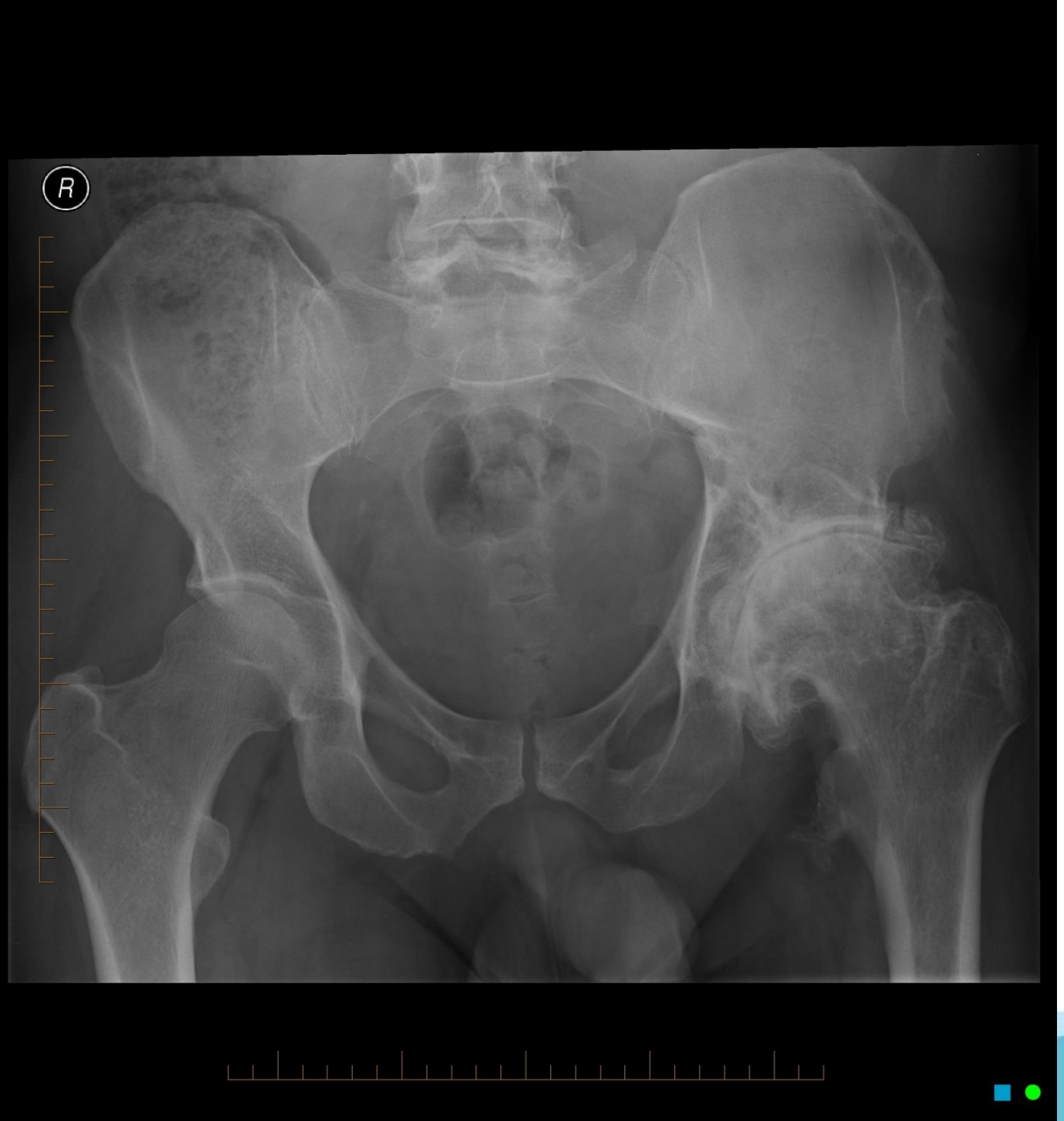
- Ciba-Geigy
- Lilly
- MSD
- Novartis
- Roche
- Pfizer
- Sanofi
- Wyeth
- Abbvie

Message points

- Challenge the use of common words and phrases
- Identify the Nocebo effect, the counterpoint of the Placebo effect
- Facts and figures in regard to side effects of Mobility Enhancing Medicines (MEMs)
- The patient's view on risk and reward

Degeneration

- Dissolving, disintegrating, descent, damaged, dissipation, debasement, decline
- Colloquially “damaged, worn out, stuffed, rooted, collapsing, munted (*cantab*)”
- An invariably negative connotation



South GP

Miscommunication

Dr SAYS:

- Degeneration
- Wear & tear
- No cure
- Learn to live with it
- Take your painkillers only when necessary

Patient HEARS:

- Disintegrating
- Continuing damage
- Nothing can help me
- I'll wind up in a wheelchair
- I must just suffer the pain

Iatrogenic Disability

Pain

Physicians view

- Presenting symptom
- Aid to diagnosis
- Outcome measure
- Frustrating impediment to sense of professional competence

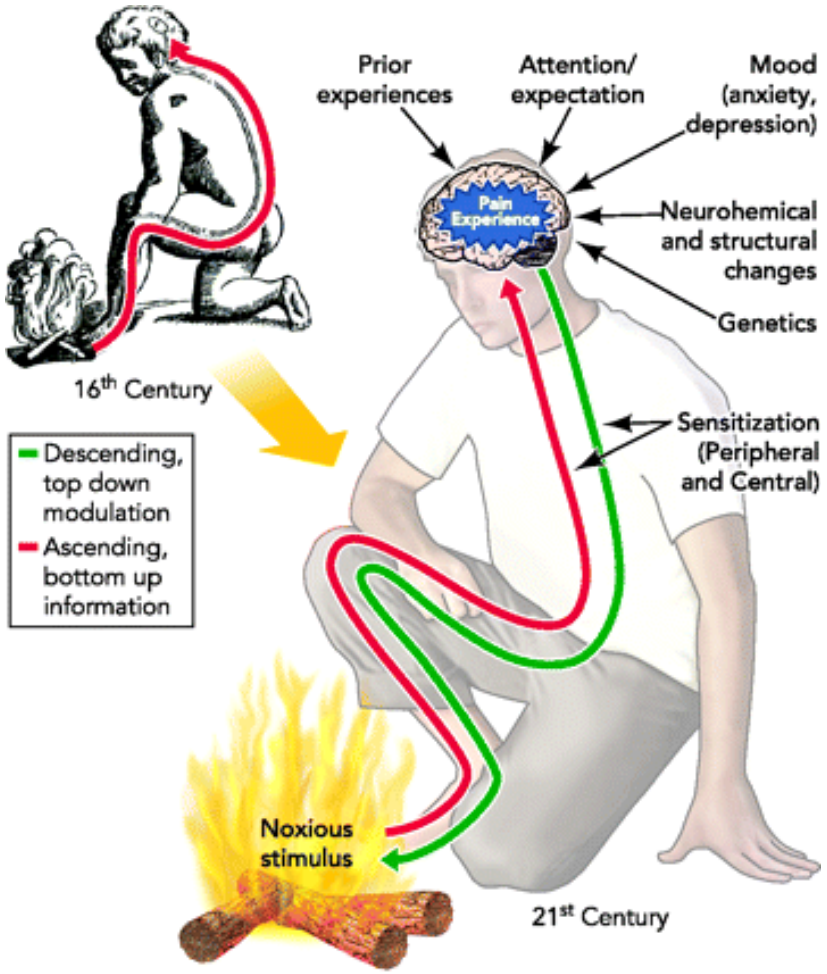
Patients view

- Distressing symptom
- Harbinger of disease
- Threat to independence and freedom of choice
- Major emotional and social stressor

Mechanism of Pain

- Originally it was thought that a sensory input caused a pain "signal" to be sent directly to the brain via a single nerve
- Today’s science reveals a much more complex process, and chain of events

There are many influences on the end pain experience.



Placebo

Nocebo

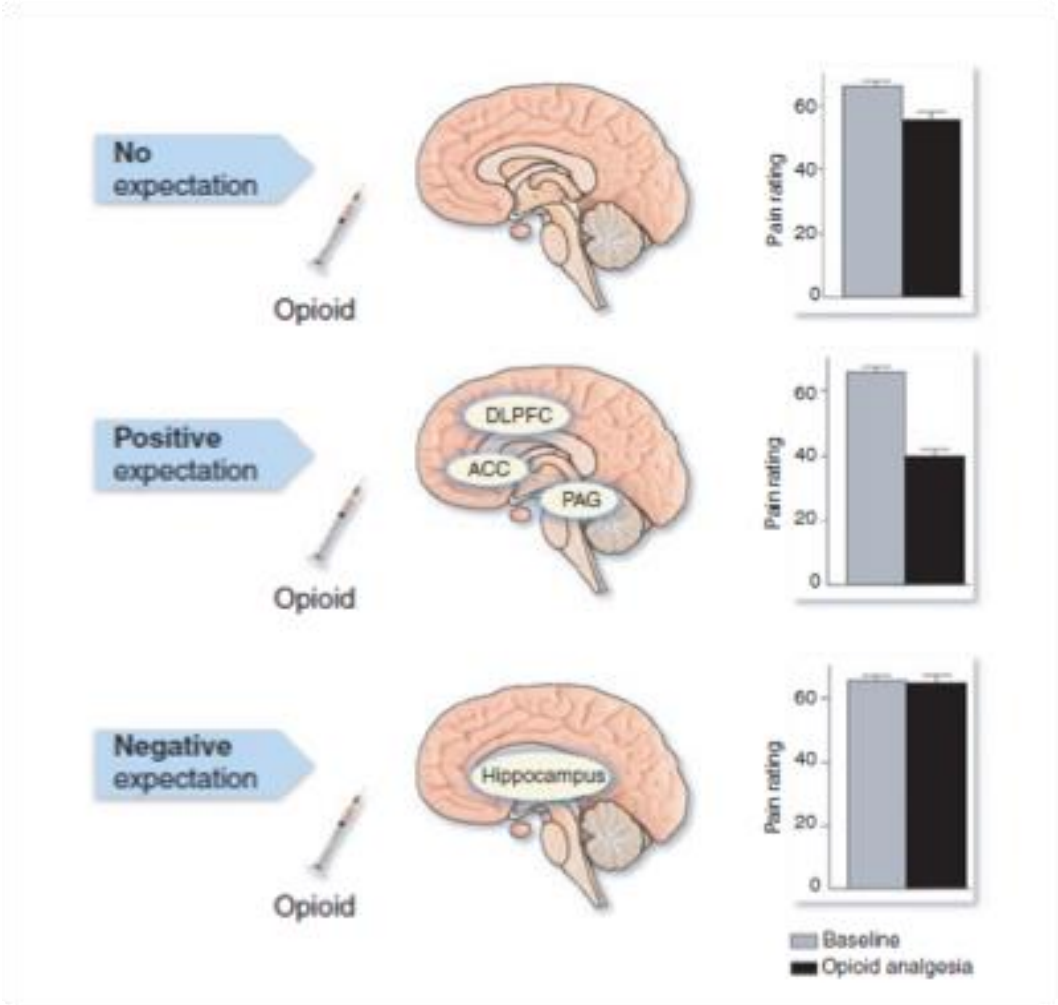
Expectations change the effectiveness of opioids

What is more powerful - opioid or verbal instruction?

"neutral statement"

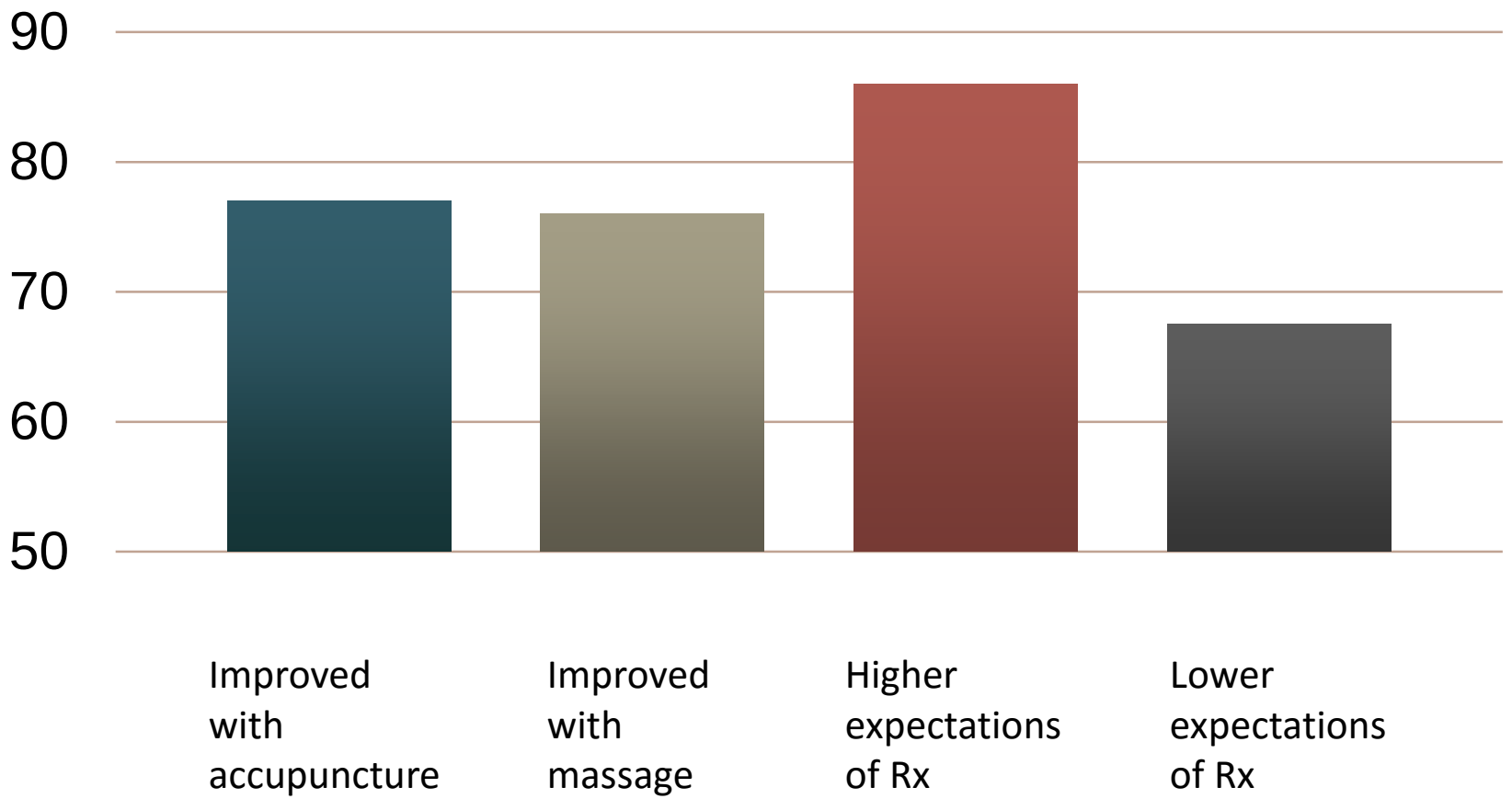
"This will help reduce pain"

"This will make you more sensitive to pain"



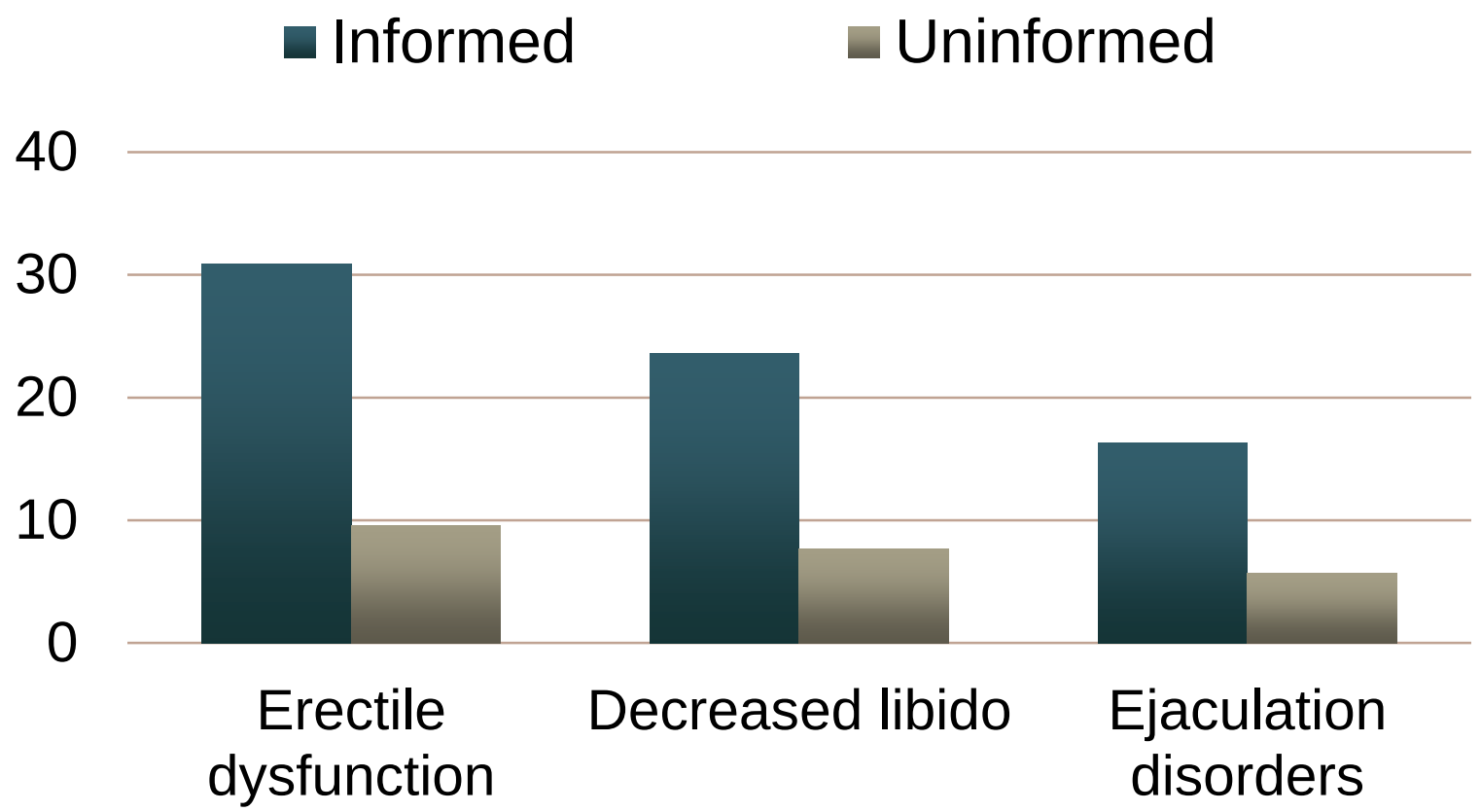
Bingel et al., (2012); Rief et al., (2011)

Back pain expectations and treatment effects



Kalauokalani et al (2001)

Propecia 5 mg and sexual side effects:



(Mondaini et al., 2007)

The words we use…..

- Analgesics = *Pain "killers"*
- NSAIDs = *Non-Steroidal Anti Inflammatory Drugs*
- Arthritis *Drugs*
- "Wear and Tear"

- All with potent Nocebo implications

Challenges of Interpreting Data on NSAIDs

- Many reports published on the risks of using NSAIDs, but they often conflict
- Meta-analyses sometimes concur on the GI and CV risks, but rarely evaluate the benefits vs the harms
- Observational data do not always agree with RCT data
- Most studies present evidence on CV or GI risks for any one agent but don't compare them

Simon LS. *Arthritis Research & Therapy.* 2015;17:130.

Network Meta-Analysis: Evaluated Risks and Efficacy

van Walsem *et al. Arthritis Research & Therapy* (2015) 17:66
DOI 10.1186/s13075-015-0554-0

RESEARCH ARTICLE Open Access

Relative benefit-risk comparing diclofenac to other traditional non-steroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors in patients with osteoarthritis or rheumatoid arthritis: a network meta-analysis

Anneloes van Walsem[1], Shaloo Pandhi[2], Richard M Nixon[2], Patricia Guyot[1], Andreas Karabis[1*] and R Andrew Moore[3]

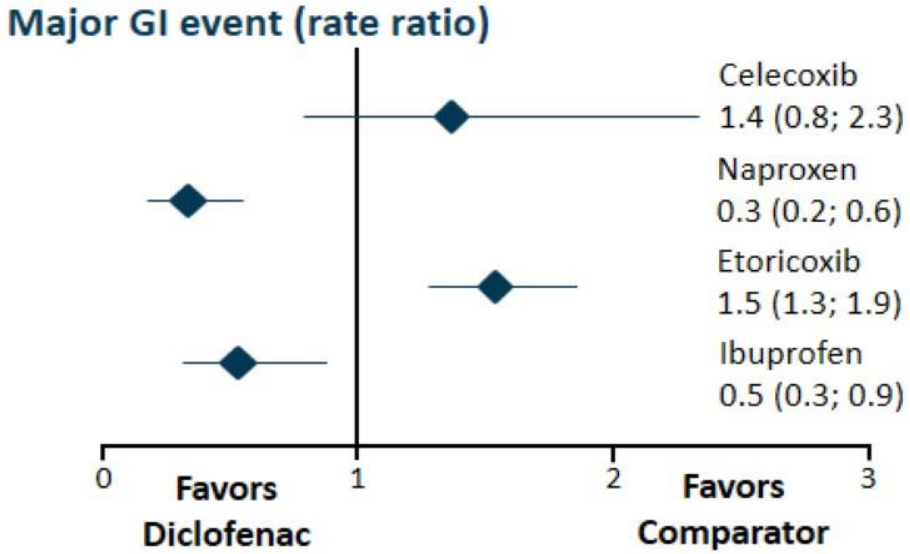
Van Walsem A, et al. *Arthritis Research & Therapy.* 2015;17:66.

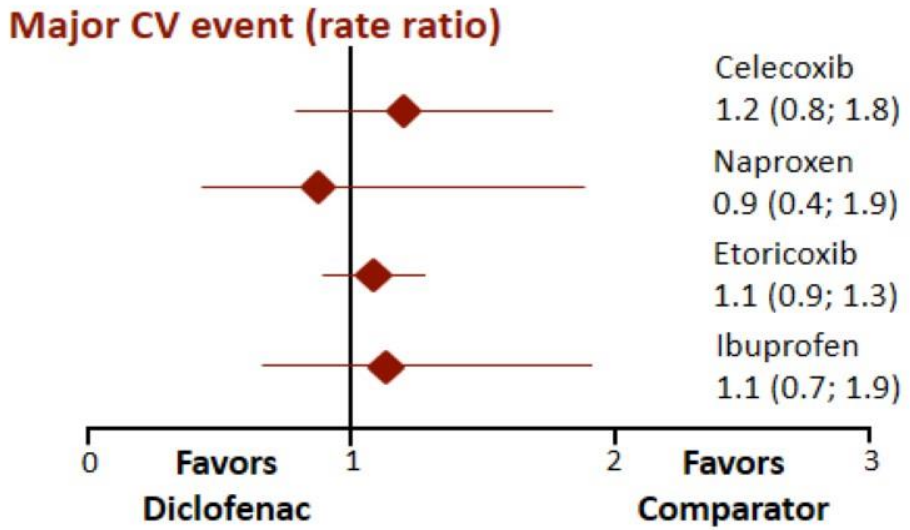
Efficacy Data: Diclofenac vs Other NSAIDs

- Diclofenac at 150 mg/day provided better pain relief than celecoxib (200 mg/day), naproxen (1000 mg/day) and ibuprofen (2400 mg/day), and similar relief to etoricoxib (60 mg/day)
- Diclofenac 100 mg/day was comparable to all other NSAIDs in relieving pain
- Improved physical function with diclofenac (100 mg and 150 mg/day) was mostly similar to all other treatments
- PGA with diclofenac (100 mg and 150 mg/day) was likely to be more effective than or comparable to all other treatments

Van Walsem A, et al. *Arthritis Research & Therapy.* 2015;17:66.

Safety and Tolerability Data: Diclofenac vs Other NSAIDs (cont)





- Risk for major upper GI events with diclofenac was lower than with naproxen and ibuprofen, similar to celecoxib and higher than with etoricoxib
- All agents had a similar incidence of CV outcomes (ATC and major CV events)
- Risk for withdrawal was lower with diclofenac than with ibuprofen, similar to celecoxib and naproxen, and higher than etoricoxib

Adapted from Van Walsem A, et al. *Arthritis Research & Therapy.* 2015;17:66. Published by BioMedCentral.

CNT Collaboration Study of CV and GI Risks With NSAIDs

- Meta-analysis of 280 RCTs NSAIDs vs placebo, and 474 RCTs of one NSAID vs another NSAID
- Focused on risks for major CV events, all-cause mortality, heart failure and upper GI complications
- Risks for major vascular events (adjusted rate ratio vs placebo):

	Adjusted rate ratio vs placebo	95% CI	*P*-value
Coxib	**1.37**	1.14-1.66	.0009
Diclofenac	**1.41**	1.12-1.78	.0036
Ibuprofen	**1.44**	0.89-2.33	.14
Naproxen	**0.93**	0.69-1.27	.66

- High-dose naproxen safer in terms of CV risk but is one of the worst NSAIDs for GI complications (adjusted rate ratio 4.22 vs placebo)
- Helpful analysis but did no data regarding benefits of NSAIDs

CNT Collaboration, et al. *Lancet.* 2013;382:769-779.

Relative Risk

- Taking a NSAID leads to a 30 to 40% increase in heart attacks

P Value significance

- > .01 for diclofenac &coxib

CNT Study authors summary

- We undertook meta-analyses of 280 trials of NSAIDs versus placebo (124 513 participants, 68 342 person-years) and 474 trials of one NSAID versus another NSAID (229 296 participants, 165 456 person-years).

Lancet 2013; 382:769-79

Natural Frequency

- Compared with placebo, of 1000 patients allocated to a coxib or diclofenac for a year, three more had major vascular events, one of which was fatal.

Lancet 2013; 382:769-79

Chance of Injury or Death on NZ Roads

CV Risk With Different NSAIDs

- Several trials and meta-analyses have evaluated the risk for CV events with a range of NSAIDs
- Similar risks found for most NSAIDs: elevated risk across class
- Warnings have been issued for the use of NSAIDs in people with known CVD or a high risk for CVD
- 3 important ongoing or recently completed studies
  - PRECISION trial; SCOT trial; Van Walsem network meta-analysis (2015)

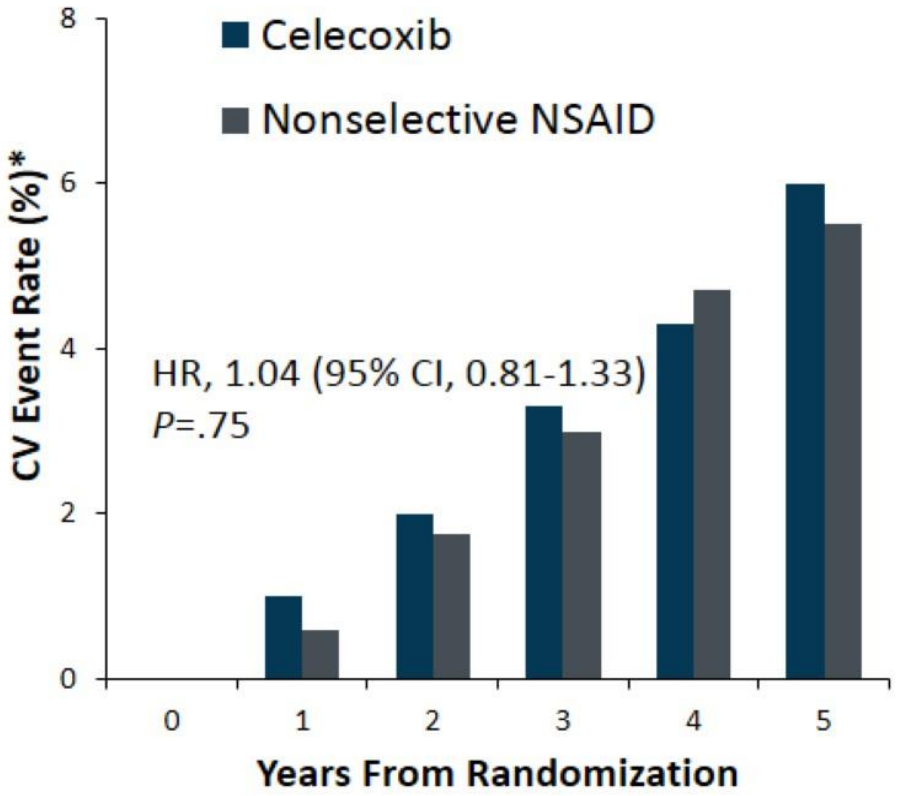
Salvo F, et al. *Clin Pharmacol* Ther. 2011;89:855-866.
www.fda.gov/Drugs/DrugSafety/ucm451800.htm
www.ema.europa.eu/docs/en_GB/document_library/Press_release/2012/10/WC500134090.pdf

PRECISION Trial

- Prospective, long-term, ongoing trial mandated by FDA
- Evaluate the safety of celecoxib vs naproxen or ibuprofen in the treatment of arthritis pain
- Patients with OA or RA who have CVD, or have a high risk for CVD
  - Eligible for chronic, daily therapy with an NSAID
- Primary outcome measure – first occurrence of CV death, nonfatal MI, or nonfatal stroke (ATC composite endpoint)

https://clinicaltrials.gov/ct2/show/NCT00346216

SCOT Trial



* First occurrence of hospitalization or death for the ATC CV endpoint of nonfatal MI, nonfatal stroke, or CV death.

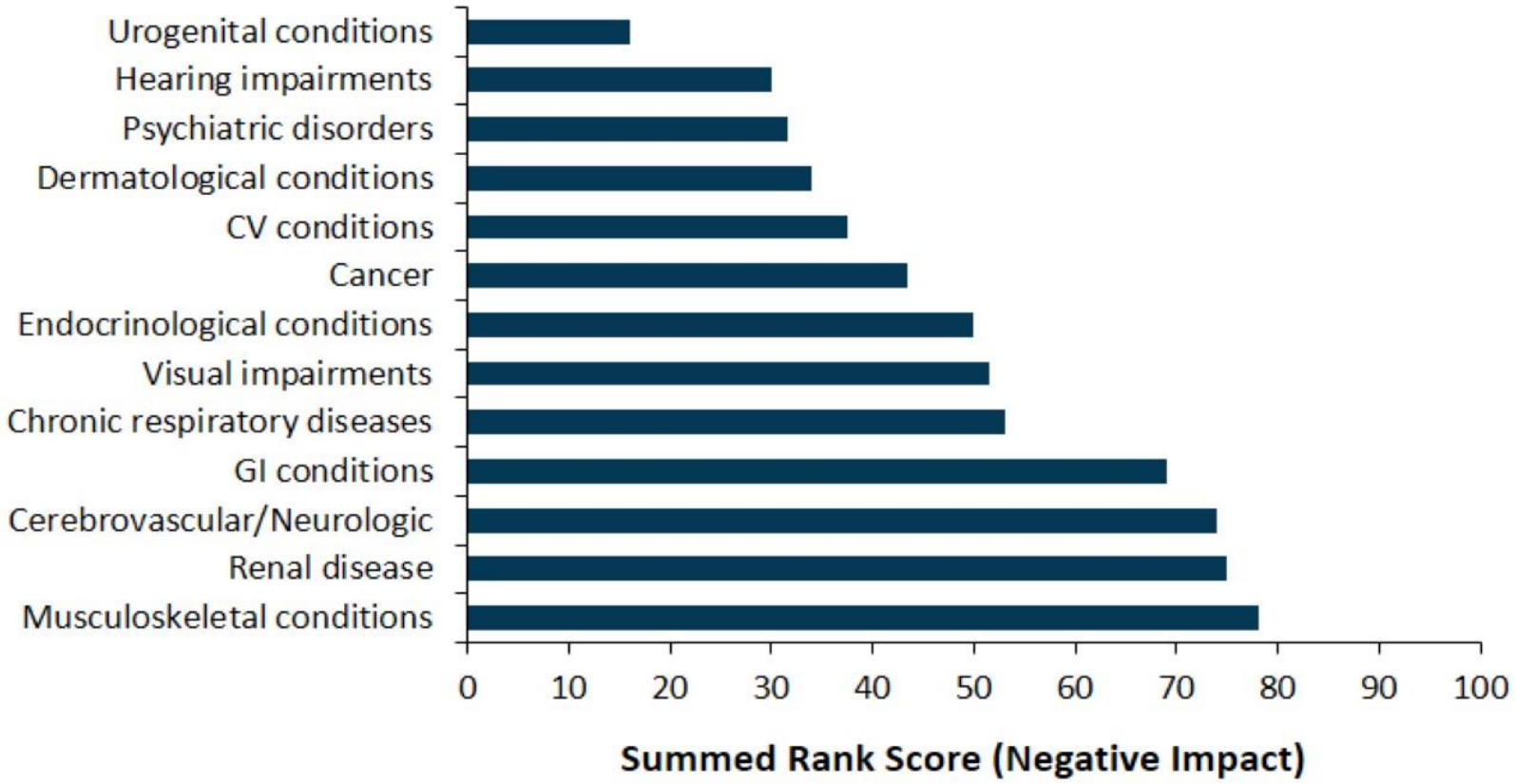
- EMA mandated trial of >7000 patients with OA or RA with CV risk factors, but no known CVD; primary care setting
- Investigated CV and GI safety of continuing NSAID therapy with ibuprofen or diclofenac vs switching to celecoxib
- No difference in CV risk between celecoxib and nonselective NSAIDs
- Rate of serious upper GI complications was low (15 out of 7297 patients)

Mc Donald T, et al. ESC, 2015. Abstract 3156.

Benefits of Pain Control in Arthritis

Hutchings A, et al. *J Rheumatol.* 2007;34:2291-2300.
Majani G, et al. *Health Qual Life Outc.* 2005;3:14.

The Impact of RA and OA on Quality of Life



Musculoskeletal conditions, including RA and OA, have a more negative impact on quality of life than other chronic conditions.

Adapted from Sprangers MAG, et al. *J Clin Epidemiol.* 2000;53:895-907.

Pain Affects the Duration of Life

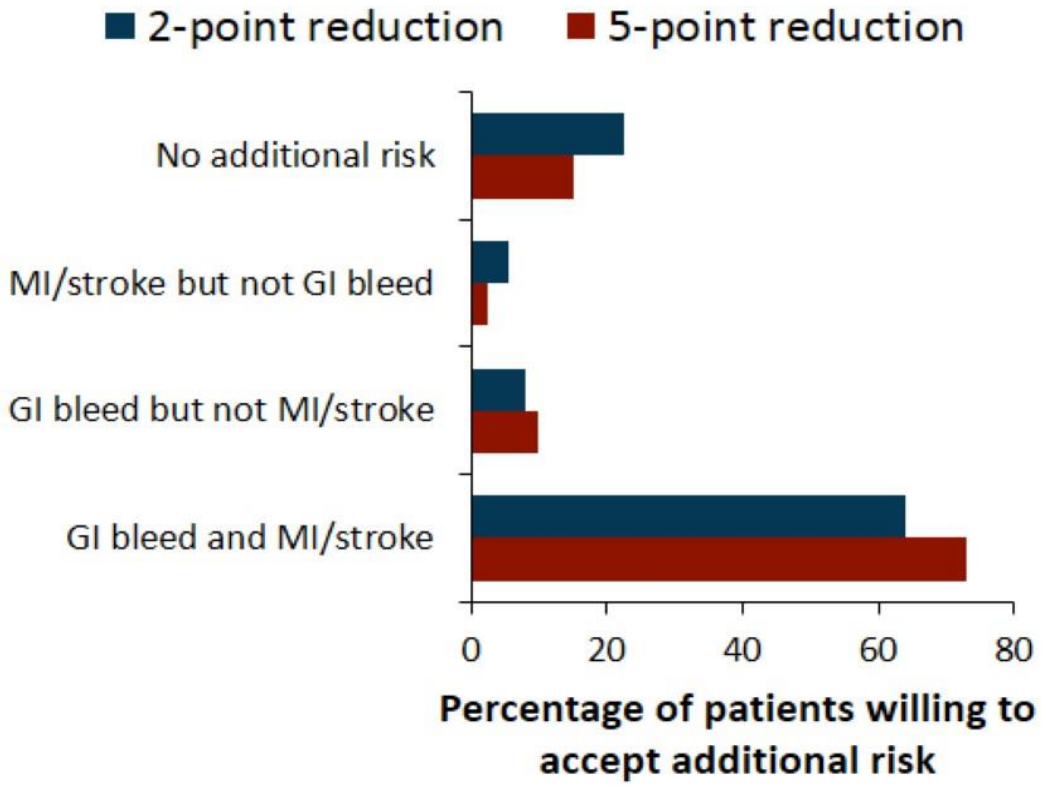
- Cohort record linkage study of >5000 patients for 10 years
- Survival rates among those reporting **severe chronic pain** were significantly lower than among those with mild or no chronic pain:
  - All-cause mortality – **HR* 1.49** (99% CI 1.21-1.84)
  - All circulatory system disease deaths – **HR* 1.68** (99% CI 1.20-2.35)

* Adjusted for age, sex, education, housing, and long-term limiting illness

Torrance N, et al. *Eur J Pain.* 2010;14:380-386.

Balancing Harms Against Benefits

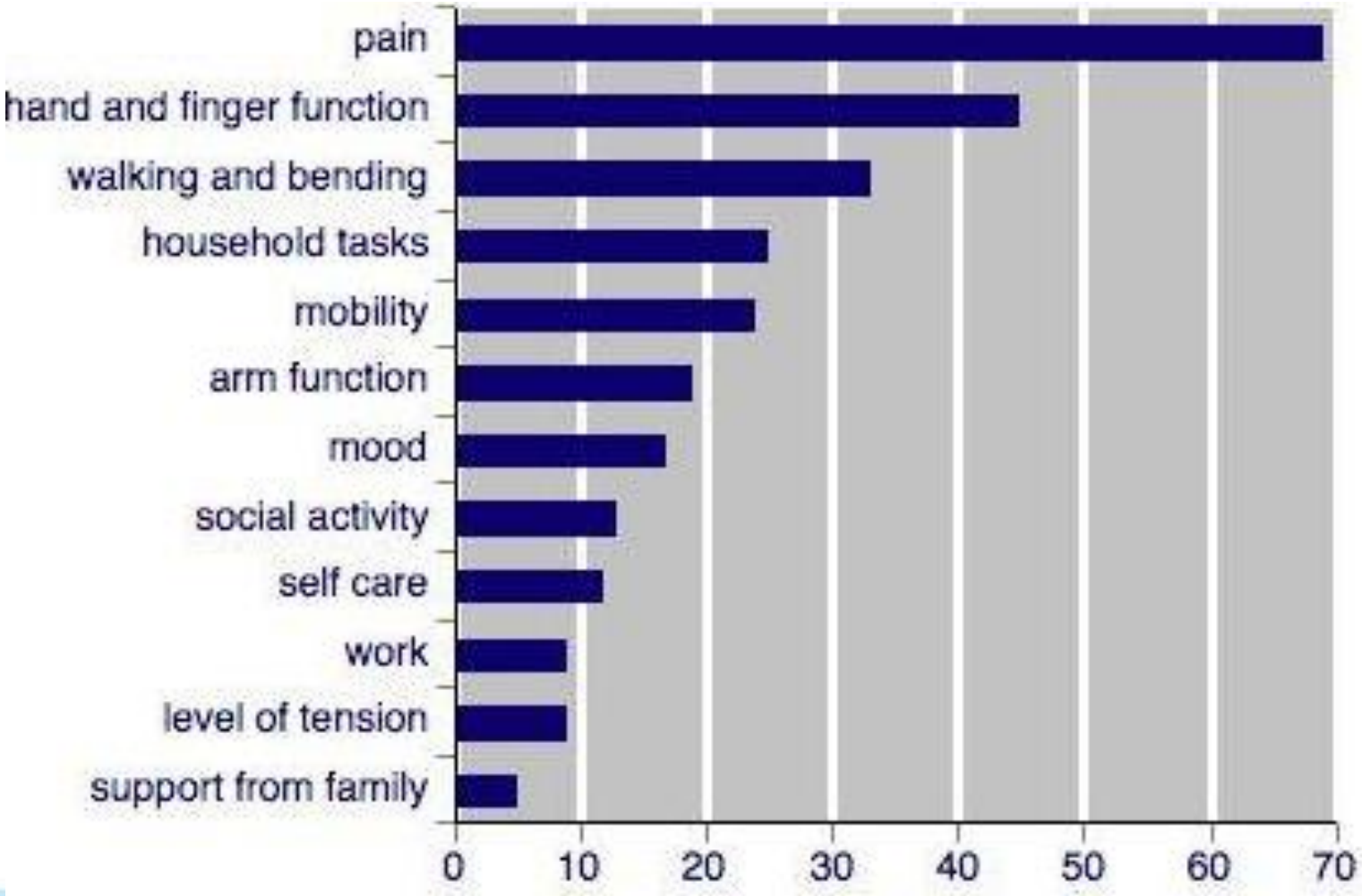
- Important to discuss the benefits and harms with your patient
- Evidence that most patients with OA willing to take some additional risk of GI bleeding/MI to gain pain relief



- Study of 196 patients with hip/knee OA; 45-75 years old; no other cause of pain
- Asked to reveal their maximum acceptable risk levels for GI bleeding and MI/stroke for 2-point and 5-point reductions in pain levels (10-point scale)
- Maximum acceptable increase in risk of death – 1 in 50

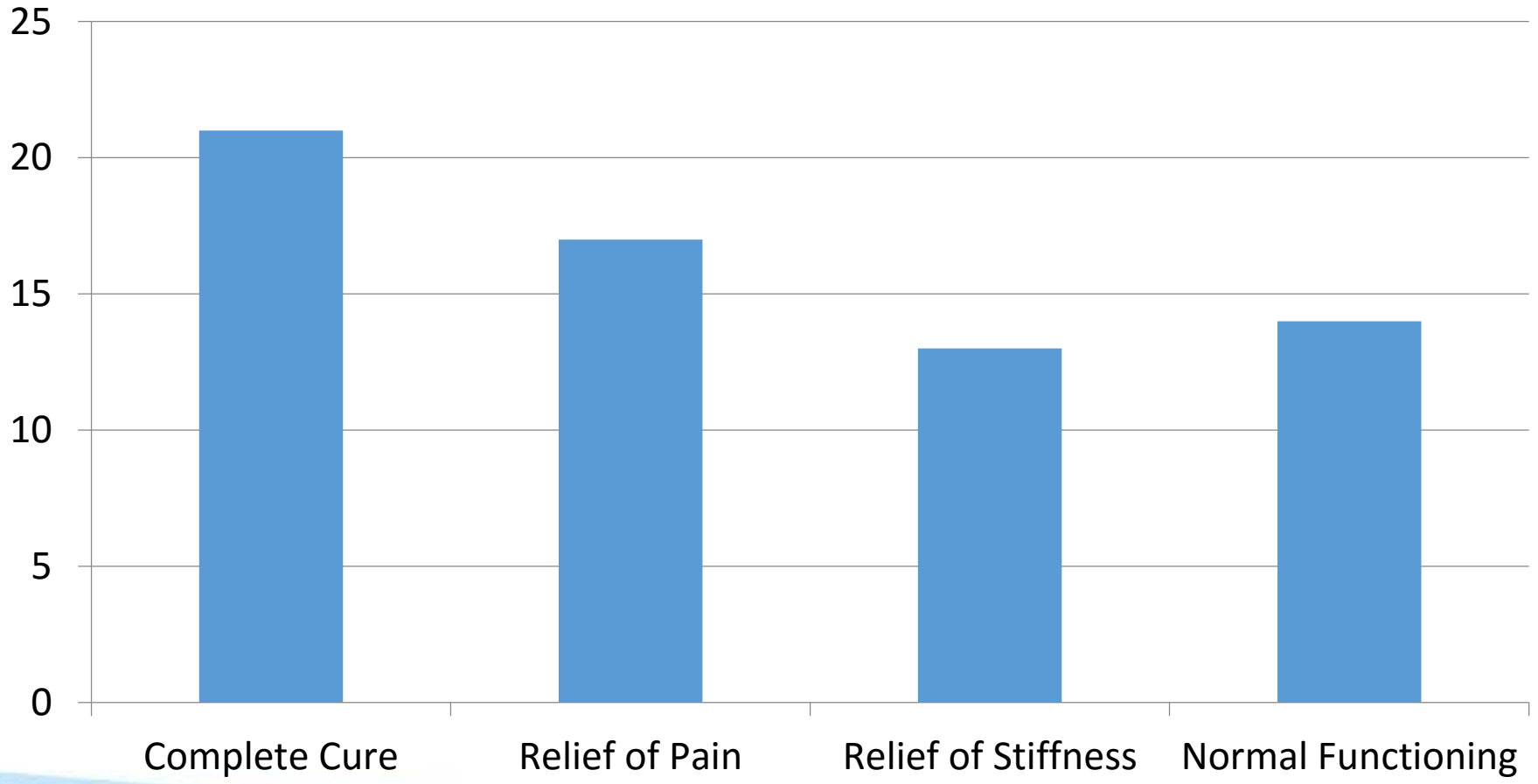
Adapted from Richardson J, et al. *J Rheumatol.* 2007;34:1569-1575.

What rheumatoid arthritis patients want



Arthritis & Rheumatism 2002 47: 391-397

Willingness to accept mortal risk



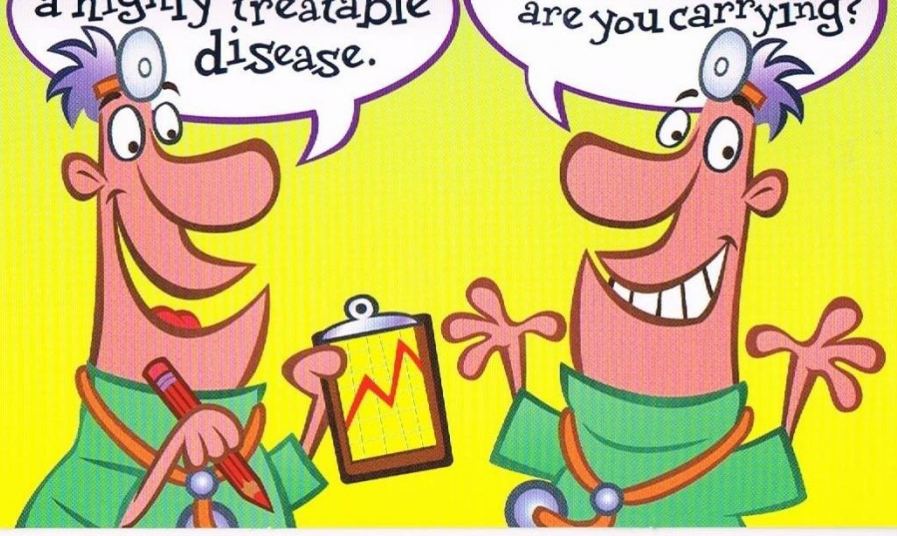
O'Brien, Ellswood, Calin 1990

NewSpeak for Medical Practitioners

- Mobility Enhancing Medicine
  - Identifies the purpose of the medication
  - Uplifting phraseology
  - Benign identification of chemical constituents
  - Positive framing
- Regenerative Bone Changes
  - Identifies bone response to osteoarthritis
  - Often age-appropriate in the absence of disease

The Interpreter's Guide to DOCTORSPEAK

What Your Doctor Says:	What Your Doctor Means:
I'd like to run a few more tests.	I have absolutely no idea what's wrong with you.
I'd like you to see a specialist.	That gets you out of my hair.
Bend over.	Bend over. (Hey, some things are bad enough without some deeper meaning.)
Please make a follow-up appointment.	Don't bother me now - I'm busy.
The nurse will take over from here.	I'm late for my tee-off time.
I have good news and bad news.	I have bad news.
You'll feel some slight discomfort.	This is gonna hurt like hell.
Hmmm... that's interesting...	What the heck is THAT thing?
Any history of medical problems in your family?	Can I blame genetics in case I screw up?
This is a highly treatable disease.	How much insurance are you carrying?




STICKS AND STONES MAY BREAK
MY BONES BUT WORDS ~~WILL NEVER~~
~~HURT ME~~ WILL RIP OUT MY ENTRAILS
AND DANCE ON MY GRAVE
BLOG