

Neuropathic Agents in Cancer Pain: Do They Work?

Chris Kane

Consultant in Palliative Medicine

Sue Ryder Wheatfields Hospice

Leeds Teaching Hospitals NHS Trust

Sue Ryder



surely





Cochrane
Library

Cochrane Database of Systematic Reviews

Opioids for neuropathic pain (Review)

Pharmacotherapy for neuropathic pain in adults: systematic review, meta-analysis and updated NeuPSIG recommendations

Nanna B Finnerup, MD^{*,a}, Nadine Attal, MD^{*,b,c,1}, Simon Haroutounian, PhD^d, Ewan McNicol, MS^e, Ralf Baron, MD^f, Robert H Dworkin, PhD^g, Ian Gilron, MD^h, Maija Haanpaa, MDⁱ, Per Hansson, MD^j, Troels S Jensen, MD^{a,k}, Peter R Kamerman, PhD^l, Karen Lund, MD^a, Andrew Moore, DSc^m, Srinivasa N Raja, MDⁿ, Andrew SC Rice, MD^o, Michael Rowbotham, MD^p, Emily Sena, PhD^q, Philip Siddall, MD^r, Blair H Smith, MD^s, and Mark Wallace, MD^t

- Tramadol NNT 4.7 NNH 12.6
- Opioids NNT 4.3 NNH 11.7

CAUTION

CAUTION

Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Toxicity of Subcutaneous Ketamine in the Management of Cancer Pain

Janet Hardy, Stephen Quinn, Belinda Fazekas, John Plummer, Simon Eckermann, Meera Agar, Odette Spruyt, Debra Rowett, and David C. Currow

- Rapid titration
- Included a secondary analysis of neuropathic v nociceptive
- NNT 25 NNH 6



Cochrane
Library

Cochrane Database of Systematic Reviews

Ketamine as an adjuvant to opioids for cancer pain (Review)

Bell RF, Eccleston C, Kalso EA

Overall conclusion

- Not enough evidence

Oral Ketamine vs Placebo in Patients With Cancer-Related Neuropathic Pain: A Randomized Clinical Trial

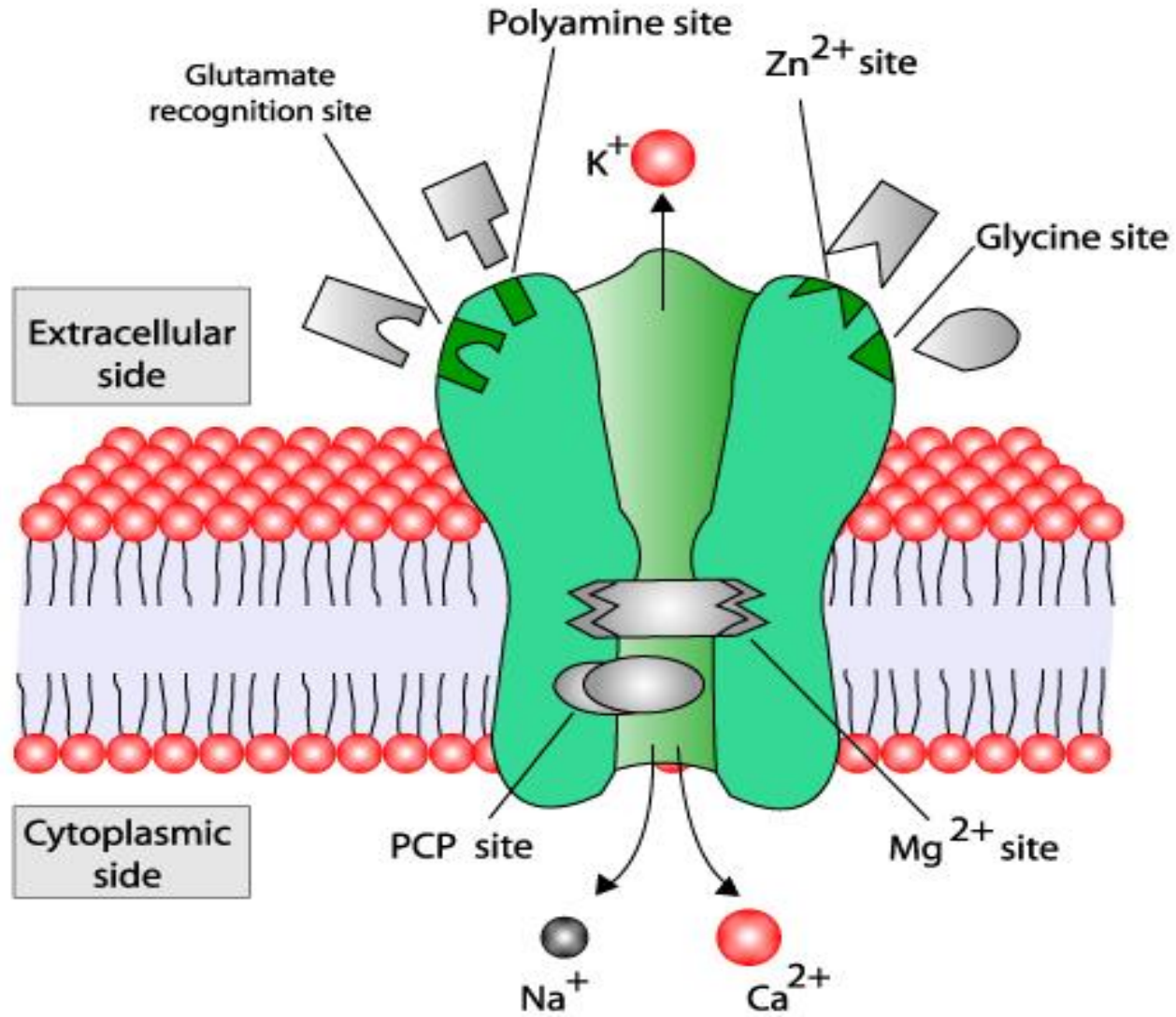
- Multicentre RCT
- Predominately post treatment neuropathic pain
- Previously failed other analgesic treatment
- No benefit and no increase in adverse outcomes

Fallon et al Jama oncology 04/2018

Is that surprising?



Schematic representation of the NMDA (N - Methyl D- Aspartate) receptor complex



Antiepileptic and antidepressant drugs

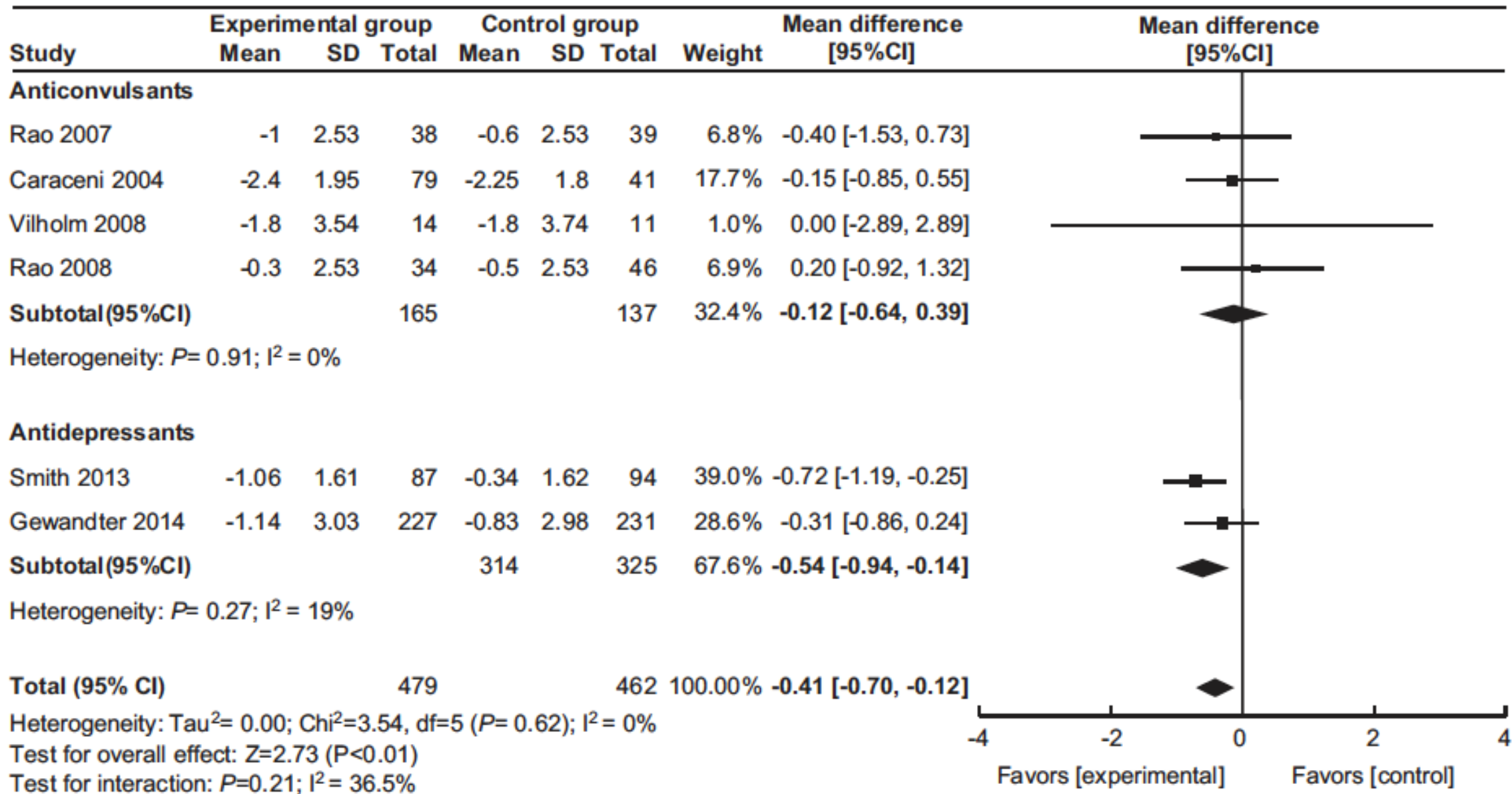
- Pregabalin and Gabapentin
 - Quoted NNT ~ 4.2 -6.4
- SNRIs
 - Quoted 6.4
- Amitriptyline
 - Quoted 3.6

Anticonvulsants or Antidepressants in Combination Pharmacotherapy for Treatment of Neuropathic Pain in Cancer Patients

A Systematic Review and Meta-analysis

Jia Guan, MPH, Shiro Tanaka, PhD, and Koji Kawakami, MD, PhD

- Systematic Review
- Mainly cancer induced peripheral neuropathy







Opioids combined with antidepressants or antiepileptic drugs for cancer pain: Systematic review and meta-analysis

Chris M Kane¹, Matthew R Mulvey¹, Sophie Wright¹, Cheryl Craigs¹, Judy M Wright² and Michael I Bennett¹

Palliative Medicine

1–11

© The Author(s) 2017

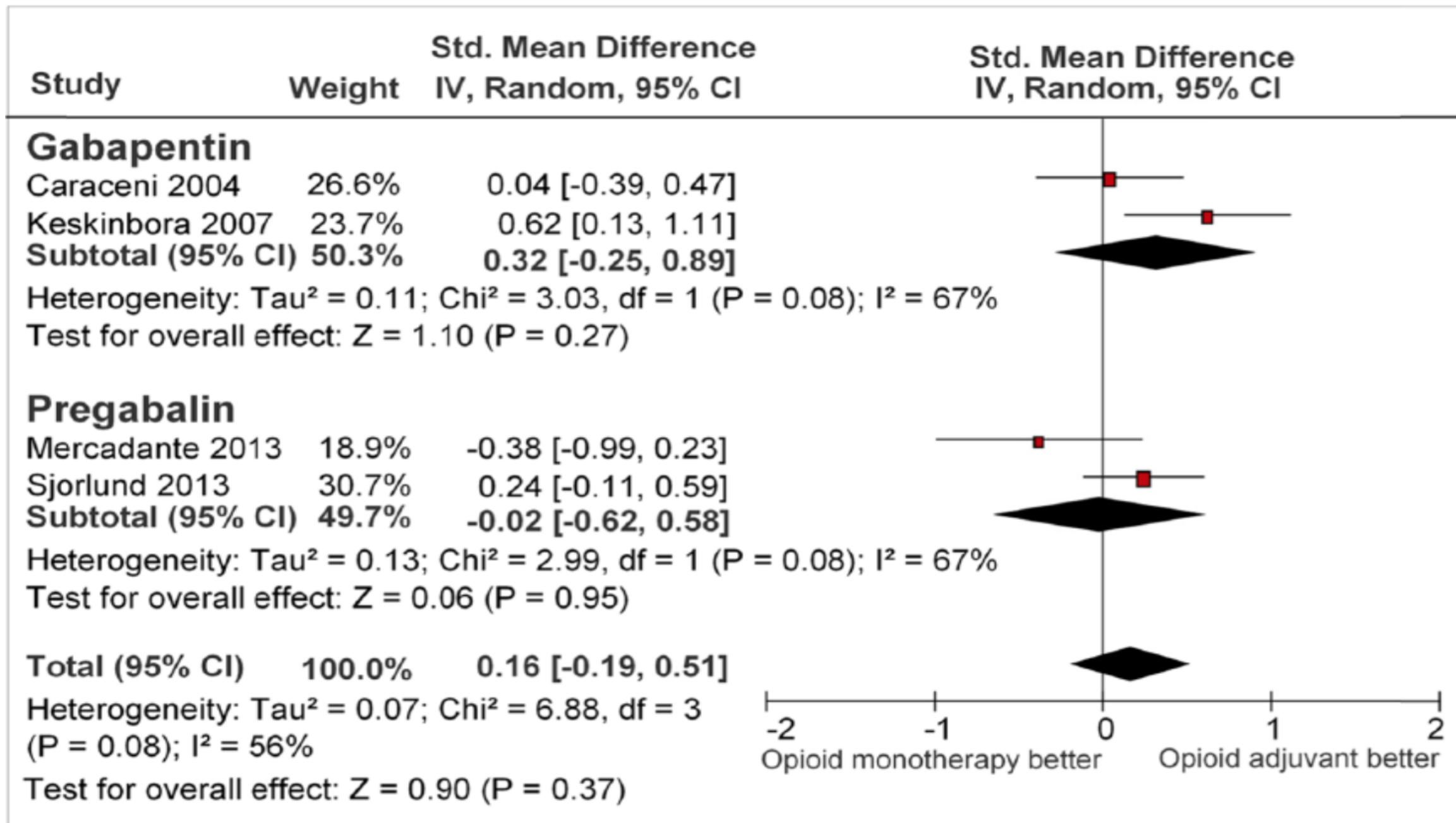
Reprints and permissions:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1177/0269216317711826

journals.sagepub.com/home/pmj





Randomized Trial



Combinations of Low-Dose Antidepressants and Low-Dose Pregabalin as Useful Adjuvants to Opioids for Intractable, Painful Bone Metastases

Makoto Nishihara, MD¹, Young-Chang P Arai, MD¹, Yoshihiro Yamamoto, PhD¹,
Kikuyo Nishida, PhD¹, Maki Arawawa, MD, Takahiro Ushida, MD¹, and Masahiko Ikeuchi, PhD²

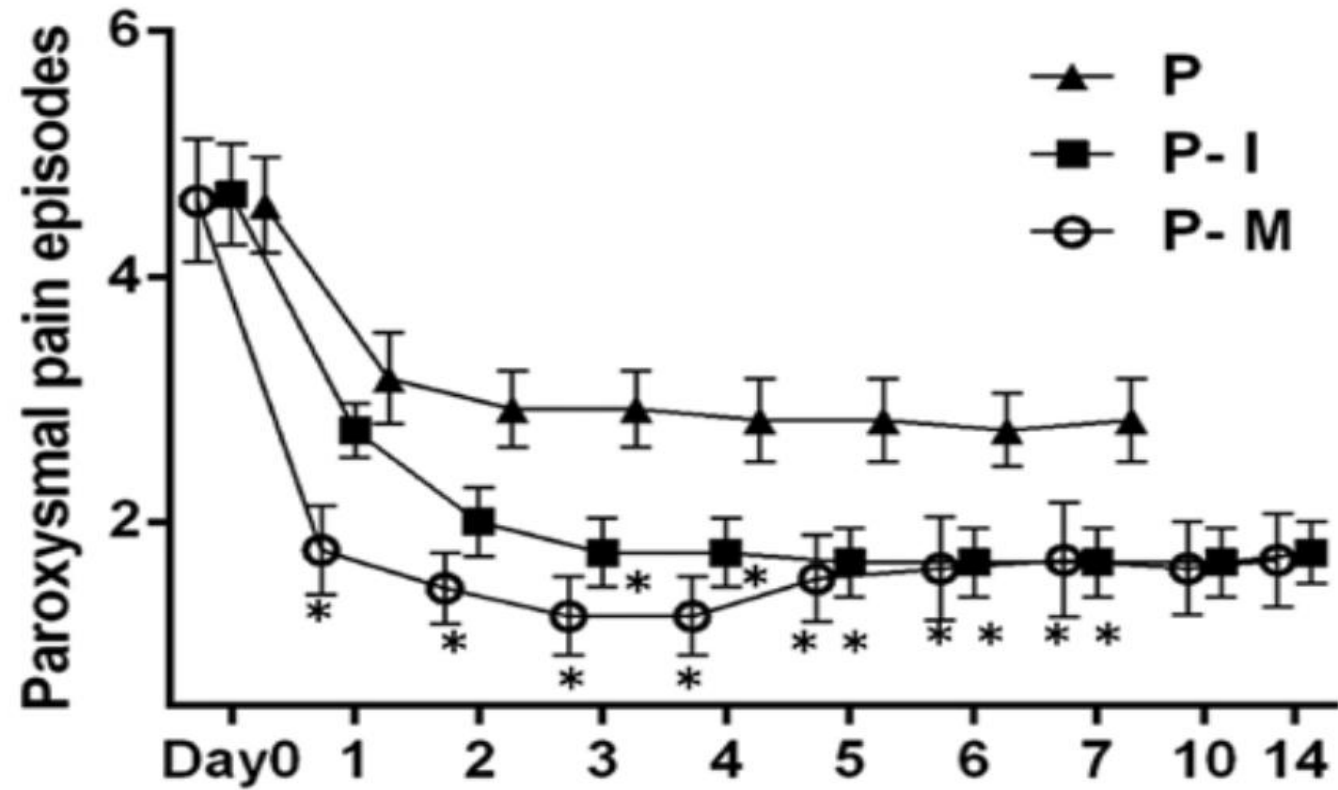


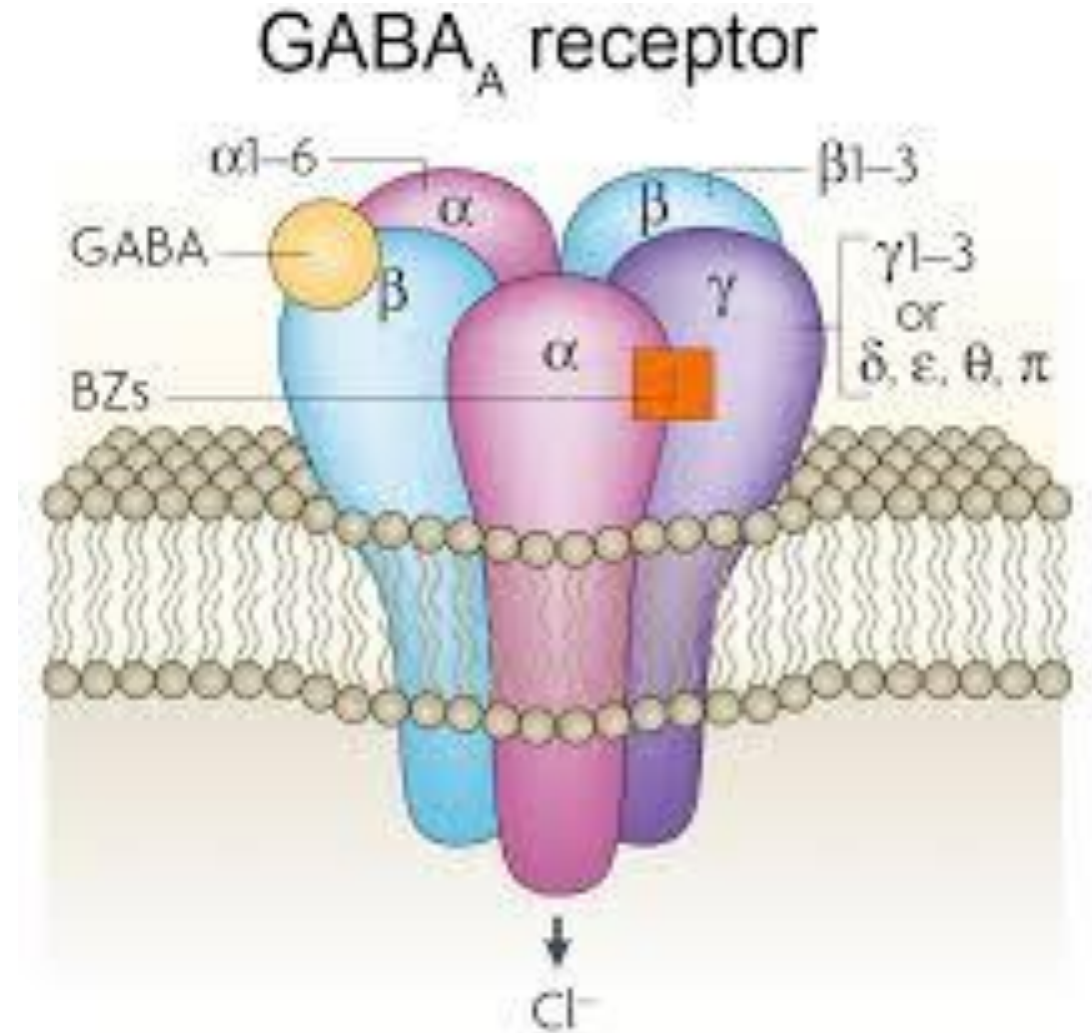
Fig. 2. Changes of the daily paroxysmal pain episodes. P, pregabalin. P-I, pregabalin- imipramine. P-M, pregabalin- mirtazapine. Error bar represents standard error of the mean (SEM). * $P < 0.05$ vs pregabalin.

Overall conclusion

- No evidence currently of benefit in cancer tumour pain
- Likely benefit in treatment associated pain
- Need more studies
- May be appropriate to try BUT review regularly

Benzodiazepines

- GABA_A receptor modulators
- Muscle relaxation
- Anxiolysis
- Clonazepam





Cochrane
Library

Cochrane Database of Systematic Reviews

Methadone for neuropathic pain in adults (Review)

McNicol ED, Ferguson MC, Schumann R



Cochrane
Library

Cochrane Database of Systematic Reviews

Methadone for cancer pain (Review)

Nicholson AB, Watson GR, Derry S, Wiffen PJ

'For Pain relief there did not seem to be much difference between methadone and morphine'

Methadone



Sativex oromucosal spray as adjunctive therapy in advanced cancer patients with chronic pain unalleviated by optimized opioid therapy: two double-blind, randomized, placebo-controlled phase 3 studies

**Marie T Fallon^{1,2}, Eberhard Albert Lux^{3,4}, Robert McQuade⁵,
Sandro Rossetti⁵, Raymond Sanchez⁵, Wei Sun⁵, Stephen Wright⁶,
Aron H Lichtman⁷ and Elena Kornyeveva⁵**

British Journal of Pain

2017, Vol 11(3) 119–133

© The British Pain Society 2017

Reprints and permissions:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1177/2049463717710042

journals.sagepub.com/home/bjp







Evidence

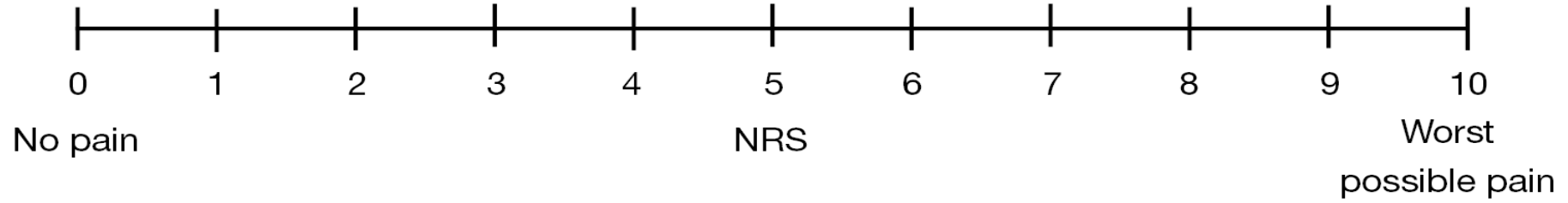
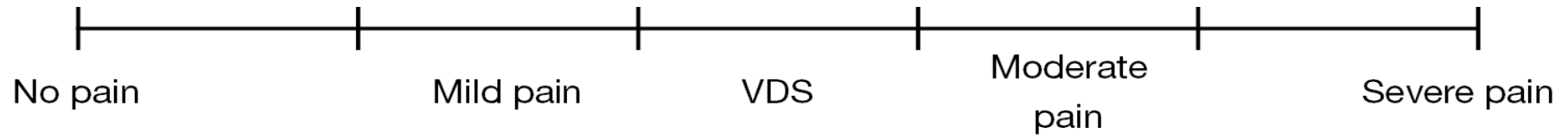
- Consistently low quality
- Very difficult to draw strong conclusions
- Patient selection

The Pain Paradox

Despite rating their pain as high patients continue to rate their satisfaction of their pain management as high

Measurement





Original Article

What Patients with Cancer Want to Know About Pain: A Qualitative Study

Jacqueline L. Bender, BSc, MSc, Joanne Hohenadel, BHSc, Jennifer Wong, BSc,
Joel Katz, PhD, Lorraine E. Ferris, PhD, LLM, Cindy Shobbrook, RN, MN, ACNP,
David Warr, MD, and Alejandro R. Jadad, MD, DPhil, FRCPC

Table 2 **Themes**

-
1. Understanding cancer pain
 2. Knowing what to expect
 3. Options for pain control
 4. Coping with cancer pain
 5. Talking with others with cancer pain
 6. Finding help managing cancer pain
 7. Describing pain
-

Factors Associated with High Satisfaction

- Physician stating importance of pain control
- Receiving instructions to manage pain at home
- Managing side effects
- Allaying fears about addiction

Dawson R, Spross JA, Jablonski ES, Hoyer DR, Sellers DE, Solomon MZ. Probing the paradox of patients' satisfaction with inadequate pain management. *J Pain Symptom Manage.* 2002 Mar;23(3):211-20

Reid CM, Gooberman-Hill R, Hanks GW. Opioid analgesics for cancer pain: symptom control for the living or comfort for the dying? A qualitative study to investigate the factors influencing the decision to accept morphine for pain caused by cancer. *Ann Oncol* 2008;19(1):44-8.

What Happens in Real life?

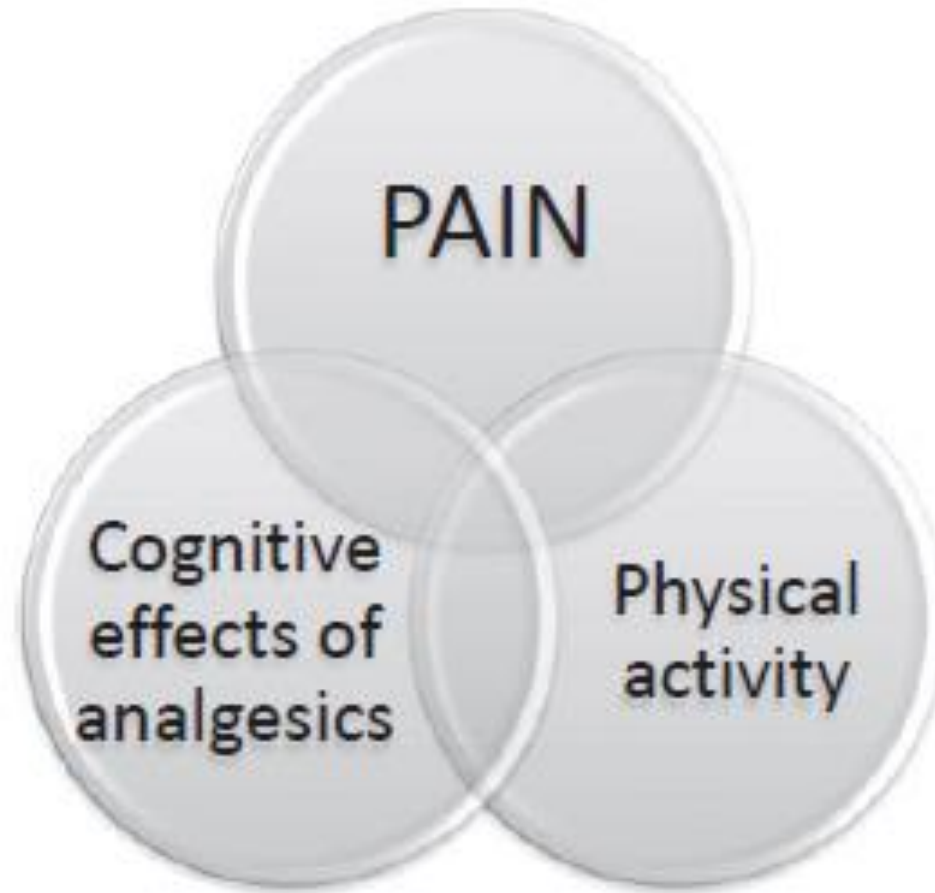


Figure 2 Triad of elements balanced in cancer pain.

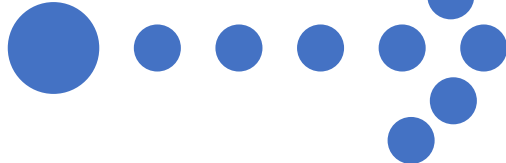
Nociception



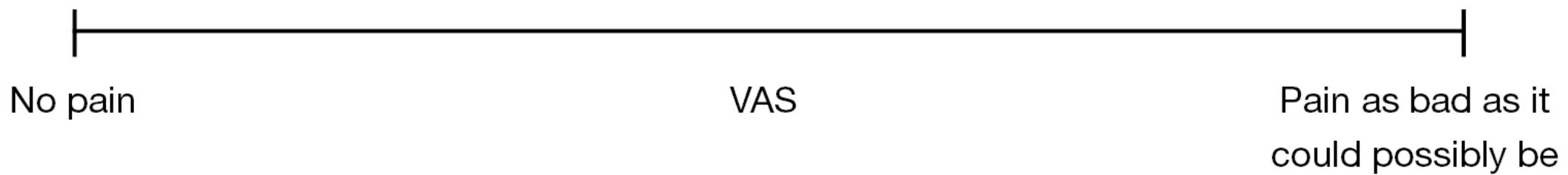
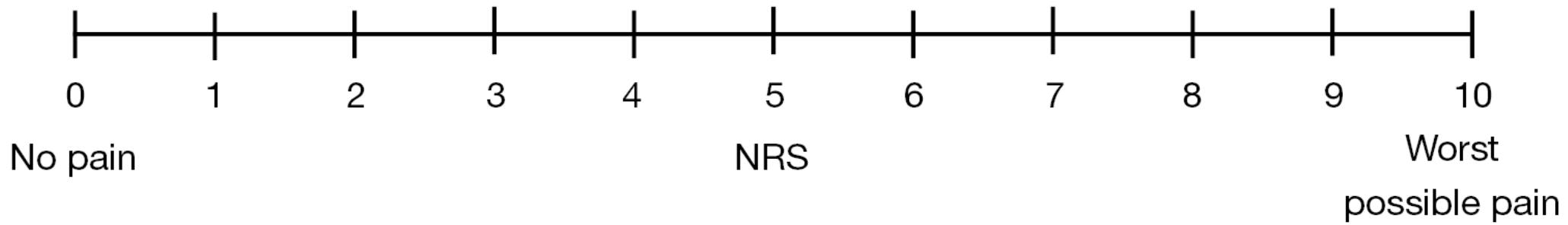
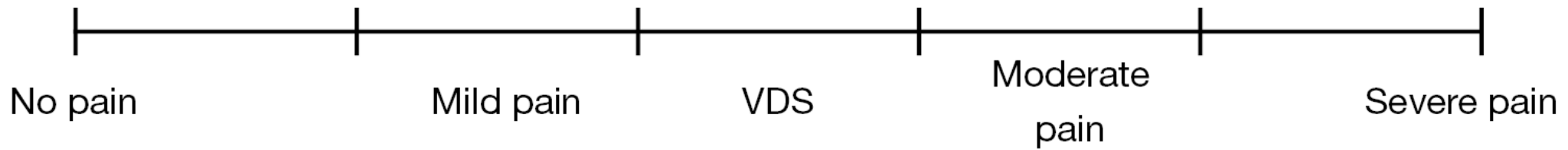
Lack of knowledge
and understanding



Poor coping and low
expectations



**Experience
of pain
'intensity'**



Conclusions

Clinically

- Think
- Review

Research

- Time to think again about how we measure 'Pain'

Thank You

