

Managing fatigue during cancer therapy

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Overview

- NCCN guidelines
- Psycho-social interventions
- Exercise
- Drug treatment
- Conclusions

Prevalence

- Fatigue affects 39% - 90% of patients undergoing...
 - Surgery
 - Chemotherapy
 - Radiotherapy
 - Hormone therapy
 - Biological therapies

NCCN recommendations

- Screen using NRS (>3)
- Assess for treatable contributing factors
 - Pain, emotional distress, anaemia, insomnia, nutritional assessment, activity level, medication side-effects, co-morbidities
- Patient /family education, general strategies
- Activity enhancement and/or psychological interventions
- Drug treatment

Psycho-social interventions

- At least three systematic reviews
 - Jacobsen 2007, Kangas 2008, Goedendorp 2009

Systematic reviews

- Goedendorp MM et al. Psychosocial interventions for reducing fatigue during cancer treatment in adults. Cochrane database of systematic reviews 2009; Issue 1

Goedendorp MM et al.

- RCTs
- Patients on treatment
- Types of interventions
 - Psychotherapy, psycho-education, cognitive restructuring, coping strategies, behavioural therapies, self-help, support groups, relaxation, energy conservation, stress management...
- Outcomes
 - Fatigue

Results

- On-going studies (n = 8)
 - Yoga, group education and support, self-help for insomnia, mindfulness relaxation, music relaxation, CBT and nursing intervention
- Included 29 publications (27 studies)
- Participants
 - Mostly breast cancer, mostly on-treatment
- Format of intervention
 - Extremely heterogeneous
 - Only 5 studies specifically focused on fatigue

Results

- Seven studies reported a significant effect of the intervention
 - Effect sizes varied between 0.17 to 1.07
- 20 studies reported no significant effect on fatigue
- Interventions specific for fatigue
 - 4/5 (80%) positive
- Interventions not specific for fatigue
 - 3/22 (14%) positive

Nature of fatigue specific interventions

- Brief
 - Three individual sessions (10-60 mins)
- Content
 - Education about fatigue
 - Taught self-care or coping techniques
 - Taught activity management
 - (emotional support)
- Administered
 - Trained oncology nurses

Exercise treatment

- At least 10 systematic reviews and meta-analyses!
 - Stevinson 2004, Schmitz 2005, Knols 2005, Conn 2006, McNeeley 2006, Markes 2006, Luctkar-Flude 2007, Jacobsen 2007, Cramp 2008, Kangas 2008
- New primary studies occurring all the time
 - Segal et al JCO 2009; 27:344 – 351
 - Prostate cancer, RT \pm anti-androgen therapy
 - Usual care, resistance, aerobic exercise
 - Both forms of exercise beneficial

Exercise is effective

- Cramp F and Daniel J *Cochrane Database of Systematic Reviews* 2008, Issue 2
 - Patients on treatment, after treatment or receiving palliative care
 - Randomised controlled trials only (usual care, no treatment, alternative treatment)
- Outcomes
 - Fatigue
 - Exercise maintenance and attrition
 - Time spent exercising
 - Aerobic capacity
 - Quality of life
 - Anxiety and depression
 - Self-efficacy

Comparison 1. Fatigue: All data

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Exercise versus no exercise control. Post test means.	30	1662	Std. Mean Difference (IV, Fixed, 95% CI)	-0.23 [-0.33, -0.13]
2 Exercise versus no exercise control. Change data.	11	853	Std. Mean Difference (IV, Fixed, 95% CI)	-0.23 [-0.36, -0.09]

Comparison 2. Fatigue: Breast cancer

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Exercise versus No intervention control. Post test means.	18	977	Std. Mean Difference (IV, Fixed, 95% CI)	-0.36 [-0.49, -0.23]

Comparison 3. Fatigue: During anti-cancer therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Exercise versus no exercise control. Post test means	15	929	Std. Mean Difference (IV, Fixed, 95% CI)	-0.18 [-0.32, -0.05]

Exercise is effective, but...

- More research is needed to identify...
 - Optimal type
 - Intensity
 - Timing
- More work needed...
 - To assess multi-modal approaches
- Improved methodology needed, including better...
 - Participant selection criteria
 - Concealment of allocation and blinding of assessors
 - Outcome endpoints
 - Inclusion of longer term follow-up assessments

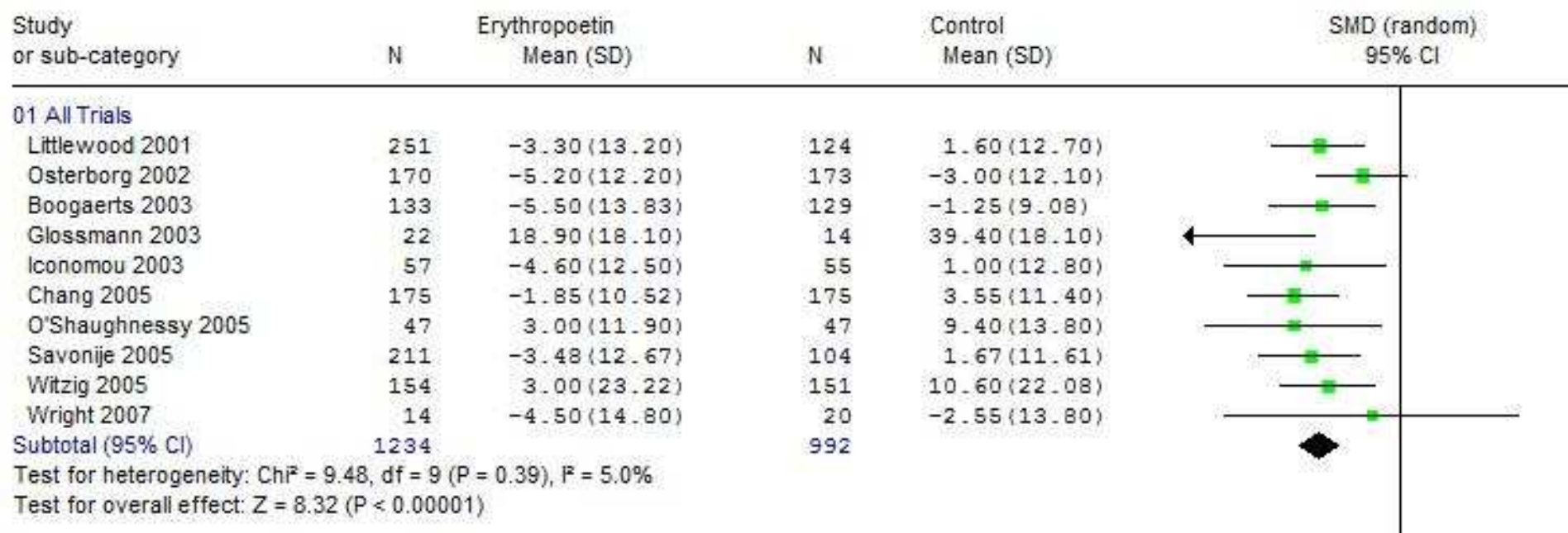
Drug treatment

- Minton et al J Natl Cancer Inst 2008; 100: 1155 - 1166

Minton et al 2008

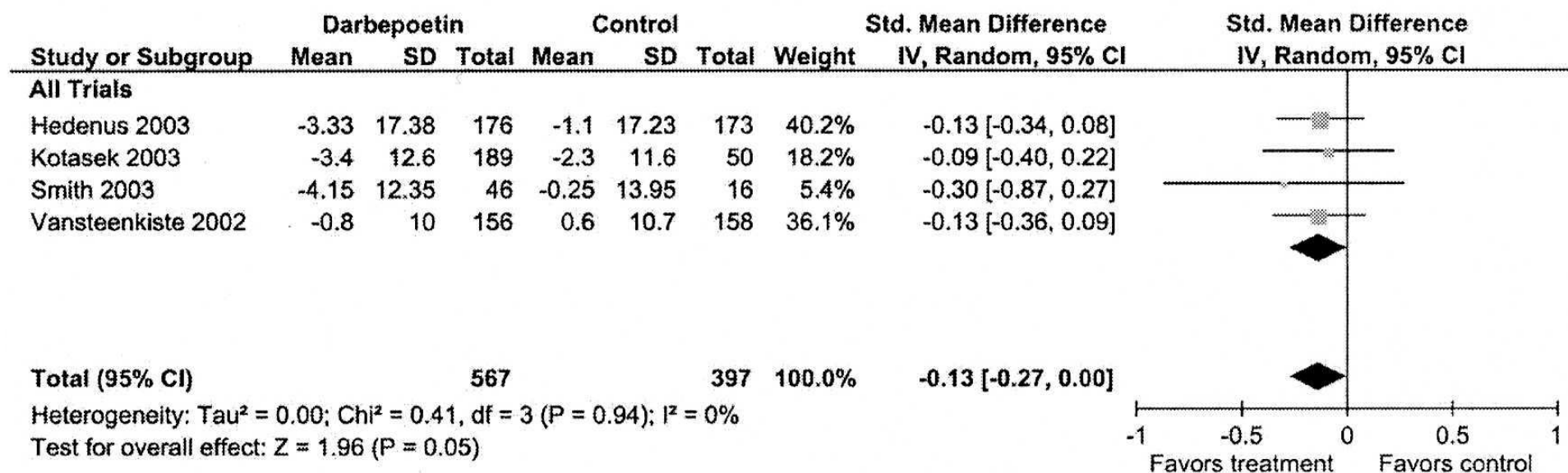
Erythropoietin (SMD = -0.3)

Review: Drug therapy for the management of cancer related fatigue
 Comparison: 01 Erythropoietin versus no intervention (subanalysis versus placebo)
 Outcome: 01 Difference in fatigue score



Minton et al 2008

Darbepoetin (SMD = -0.13)

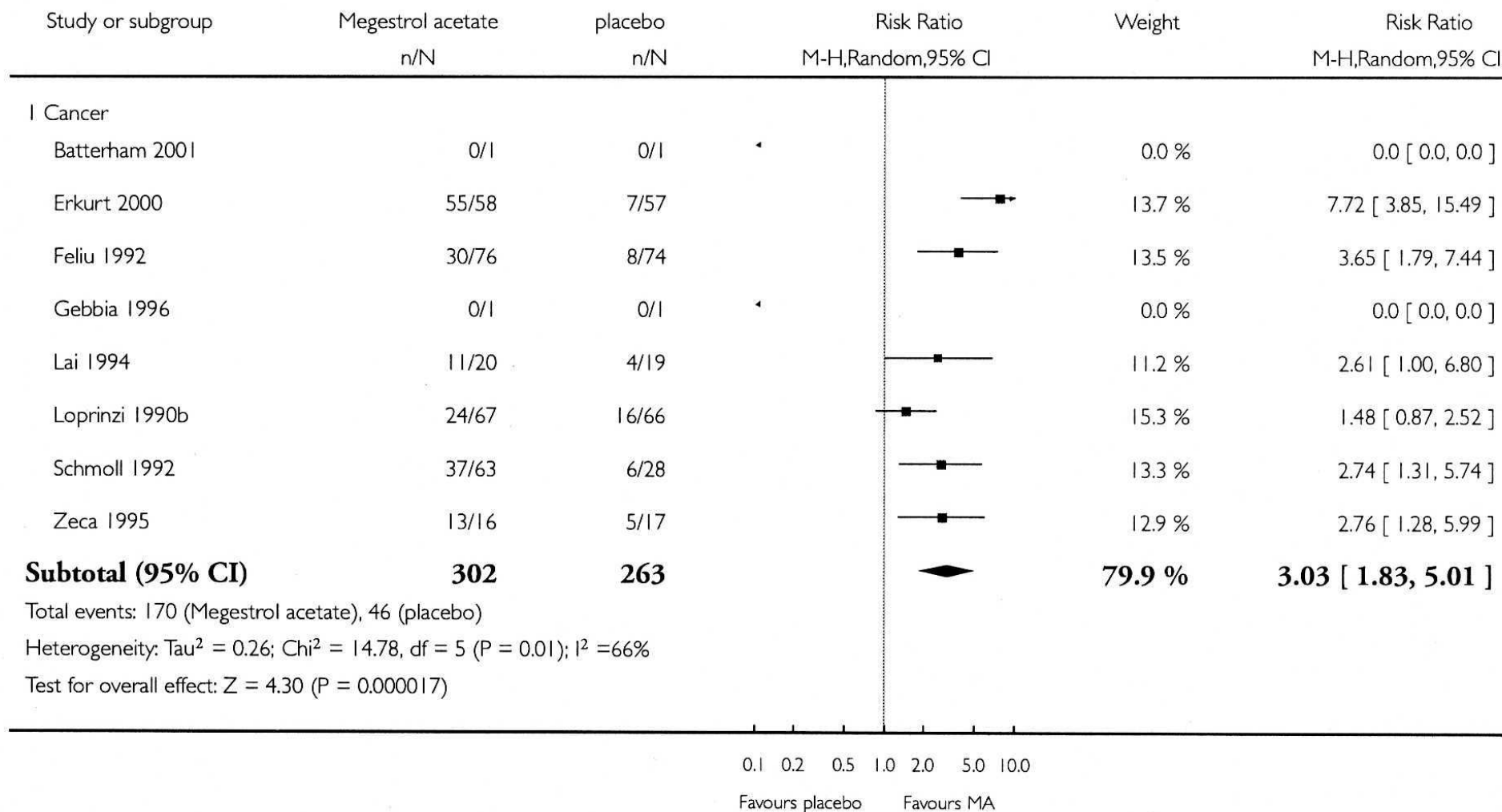


Berenstein 2009

Review: Megestrol acetate for treatment of anorexia-cachexia syndrome

Comparison: 1 Megestrol acetate vs placebo (ITT)

Outcome: 1 Appetite improvement

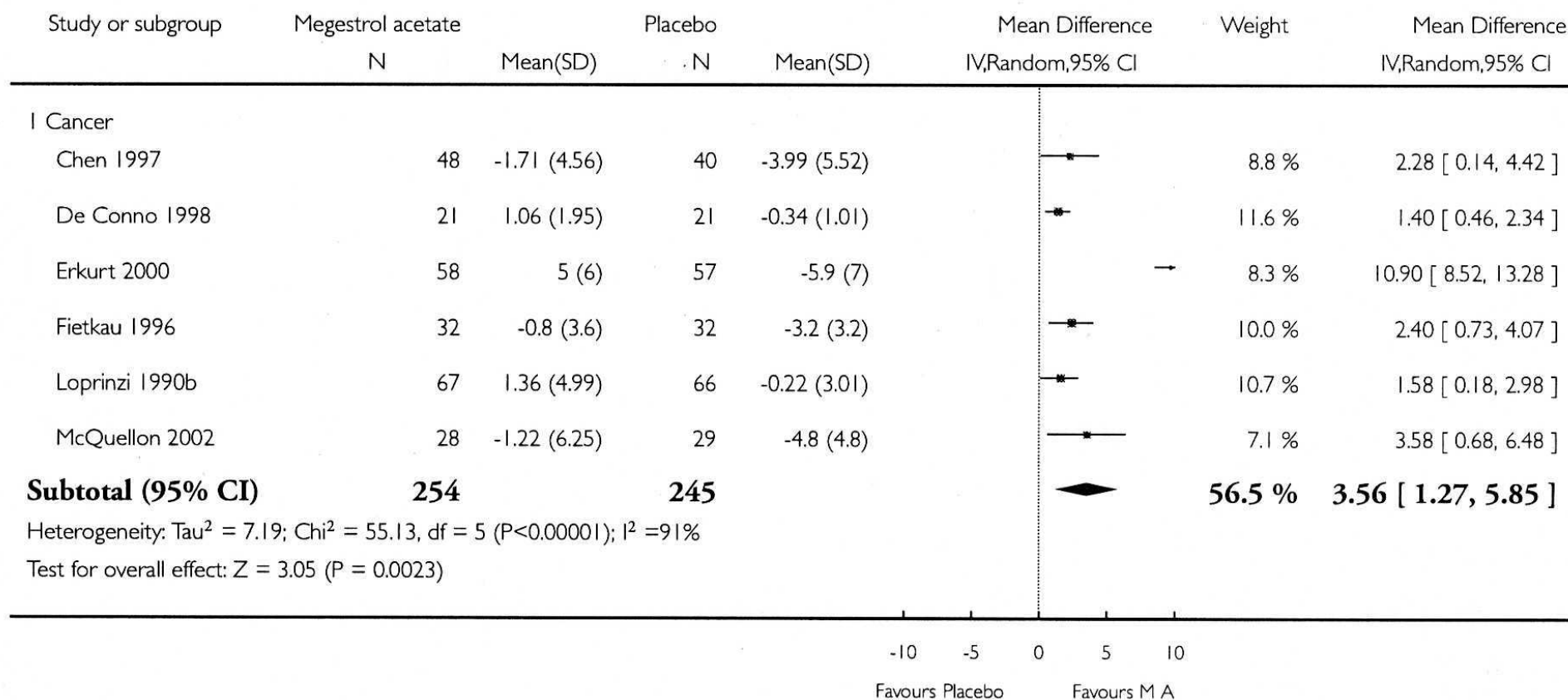


Berenstein 2009

Review: Megestrol acetate for treatment of anorexia-cachexia syndrome

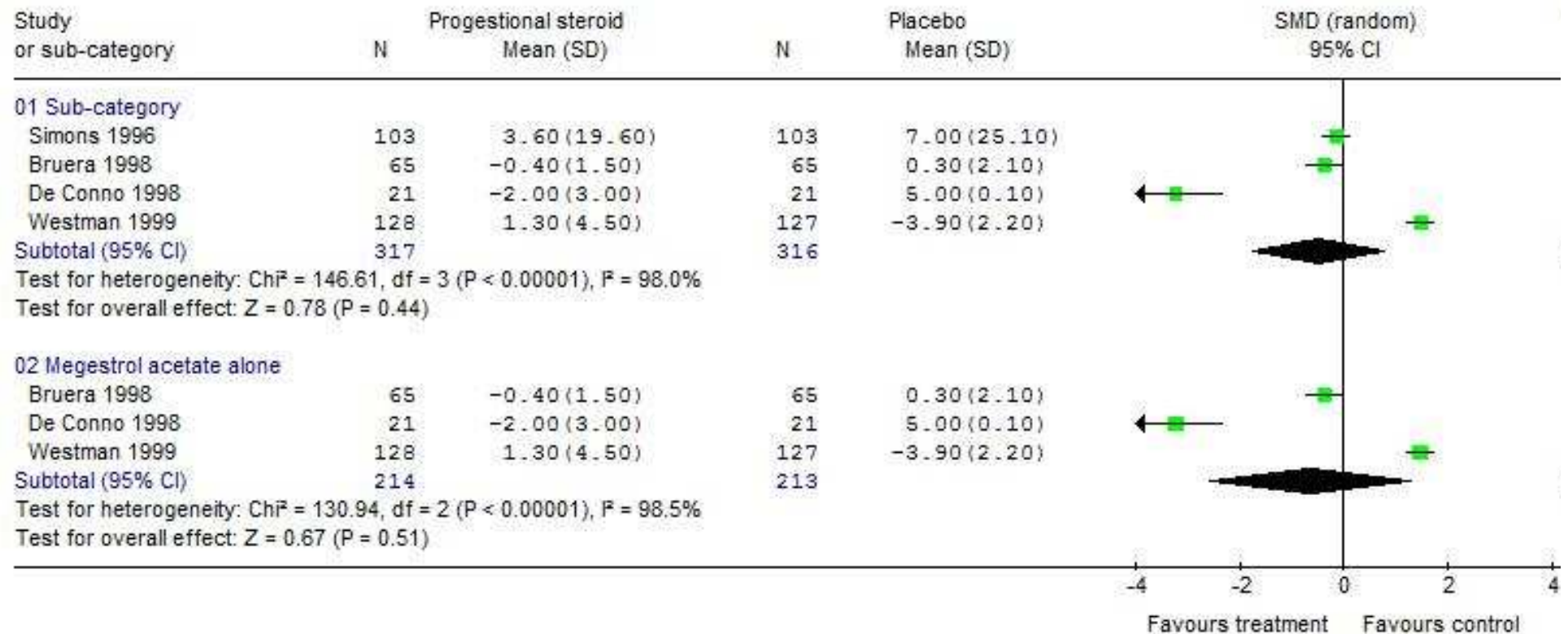
Comparison: 1 Megestrol acetate vs placebo (ITT)

Outcome: 2 Weight gain



Minton et al 2008

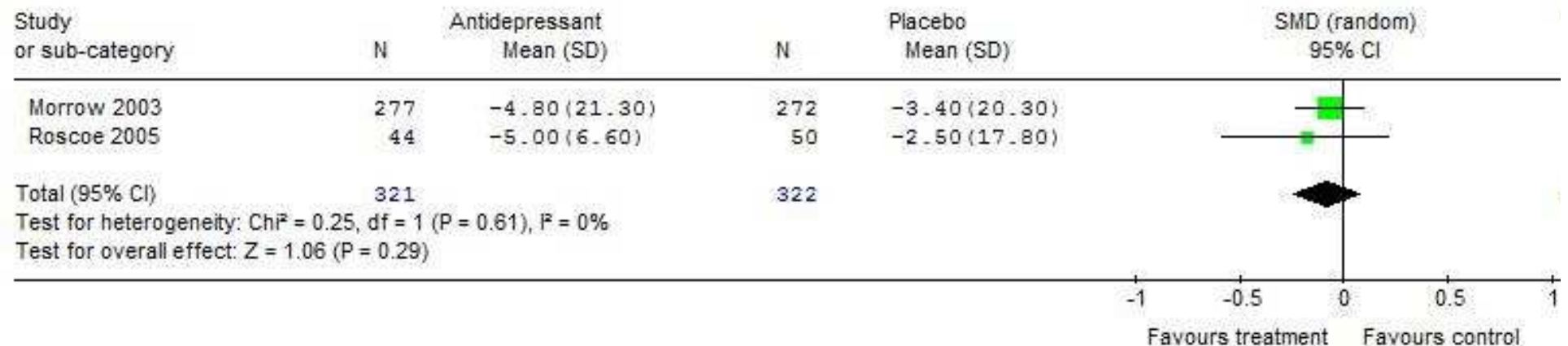
Progestational steroids



Minton et al 2008

Anti-depressants

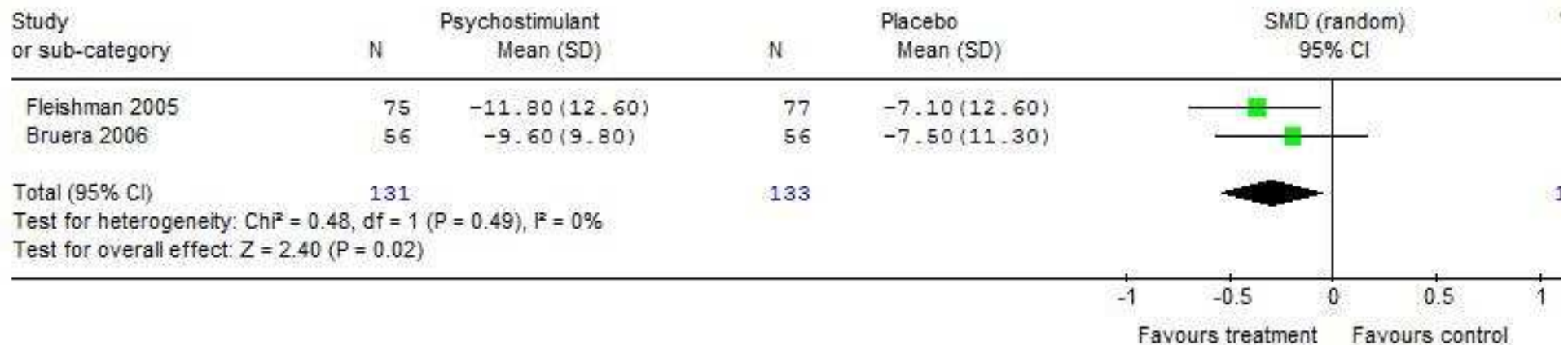
Review: Drug therapy for the management of cancer related fatigue
Comparison: 04 Antidepressants versus placebo
Outcome: 01 Fatigue score change



Minton et al 2008

Psychostimulants (SMD = -0.3)

Review: Drug therapy for the management of cancer related fatigue
Comparison: 05 Psychostimulants versus placebo
Outcome: 01 Fatigue score change



Drug treatment

- Minton et al 2008
 - Ibandronate
 - Etanercept
- New studies
 - Donepezil (Bruera et al JCO 2007; 25: 3475 – 3481)
 - N = 142, 1 week, RCT, no effect
- On-going studies
 - Modafanil

Conclusions

- Fatigue is a major problem for cancer patients from diagnosis through to long-term survivorship
- Exercise, psychological interventions and drugs have all been shown to be effective
- The specific effects of nutritional interventions on fatigue have not been adequately researched
- More work is required to assess effectiveness of individual interventions and to assess the role of multi-modal therapy