

Neurokinin-1 Receptor Antagonists for Prevention of Chemotherapy-related Nausea and Vomiting in Adults: Preliminary Results of a Cochrane Systematic Review

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Background

- Chemotherapy-induced nausea and vomiting (CINV) are the top 2 fears of patients when initiating cancer treatment.
- A systematic review of serotonin receptor antagonists (5HT-3RA) suggest efficacy in acute and delayed phases of CINV.
- NK-1 receptor antagonists (NK-1RA) are thought to provide further benefit in preventing delayed CINV.
- There are no published systematic reviews of NK-1RA for CINV.

Objective

To conduct a systematic review of randomized-controlled trials on NK-1RA + standard therapy versus placebo + standard therapy in adult cancer patients receiving highly emetogenic chemotherapy (HEC).

Methods

- Methodology based on the Cochrane Handbook for Systematic Reviews of Interventions.

Types of studies:

- Randomized, double-blind, placebo-controlled trials.

Types of patients:

- Adult cancer patients undergoing HEC.

Types of interventions:

- NK-1RAs + standard therapy (5HT-3RA ± corticosteroid ± rescue therapy) versus placebo + standard therapy.

Types of outcomes:

Primary Outcomes	Secondary Outcomes
• Quality of life	• Total mortality
• Complete response	• Serious adverse events
• Emesis control	• Adverse events
• Nausea control	• Need for rescue therapy

Electronic searches:

- Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE up to February 2012.

Data analysis:

- Review Manager. Version 5.1 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2011).

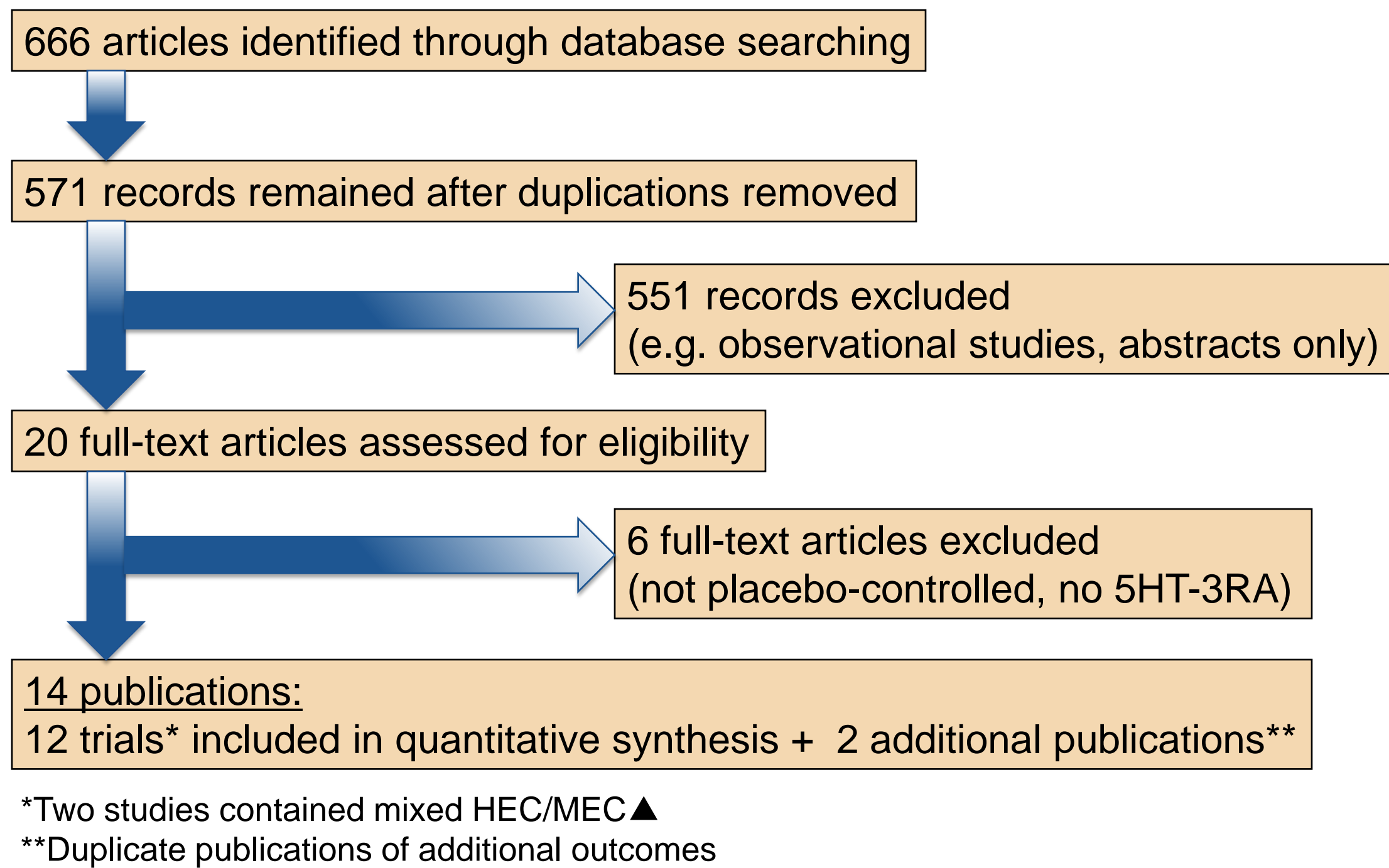


Figure 1: Trial Flow Diagram

Results

No. of patients: NK-1RA	2769
No. of patients: Placebo	1831
NK-1RA identified in trials	aprepitant, casopitant, fosaprepitant [†] , ezlopitant [‡]

Primary Outcomes	ABI [£] [95% CI] ^{\$}
Complete Response (no emesis and no rescue therapy)	
• Overall (0-120hr)	18% [15-20%]
• Acute (0-24hr)	8% [6-10%]
• Delayed (24-120hr)	19% [17-22%]
No Impact on Daily Life (5-day recall)	
• FLIE [€] score >108	12% [8-15%]

Secondary Outcomes	ARI [¥] [95% CI]
Serious Adverse Events (SAE)	3% [1-5%]
Other Adverse Events	
• Fatigue, asthenia, weakness	3% [1-5%]
• Hiccups	3% [1-6%]

Footnotes

- ▲ MEC = moderately emetogenic chemotherapy
- £ ABI = absolute benefit increase
- \$ CI = confidence interval
- ¥ ARI = absolute risk increase
- € FLIE = Functional Living Index – Emesis
- † Excluded due to lack of placebo comparator
- ‡ Not included in preliminary results

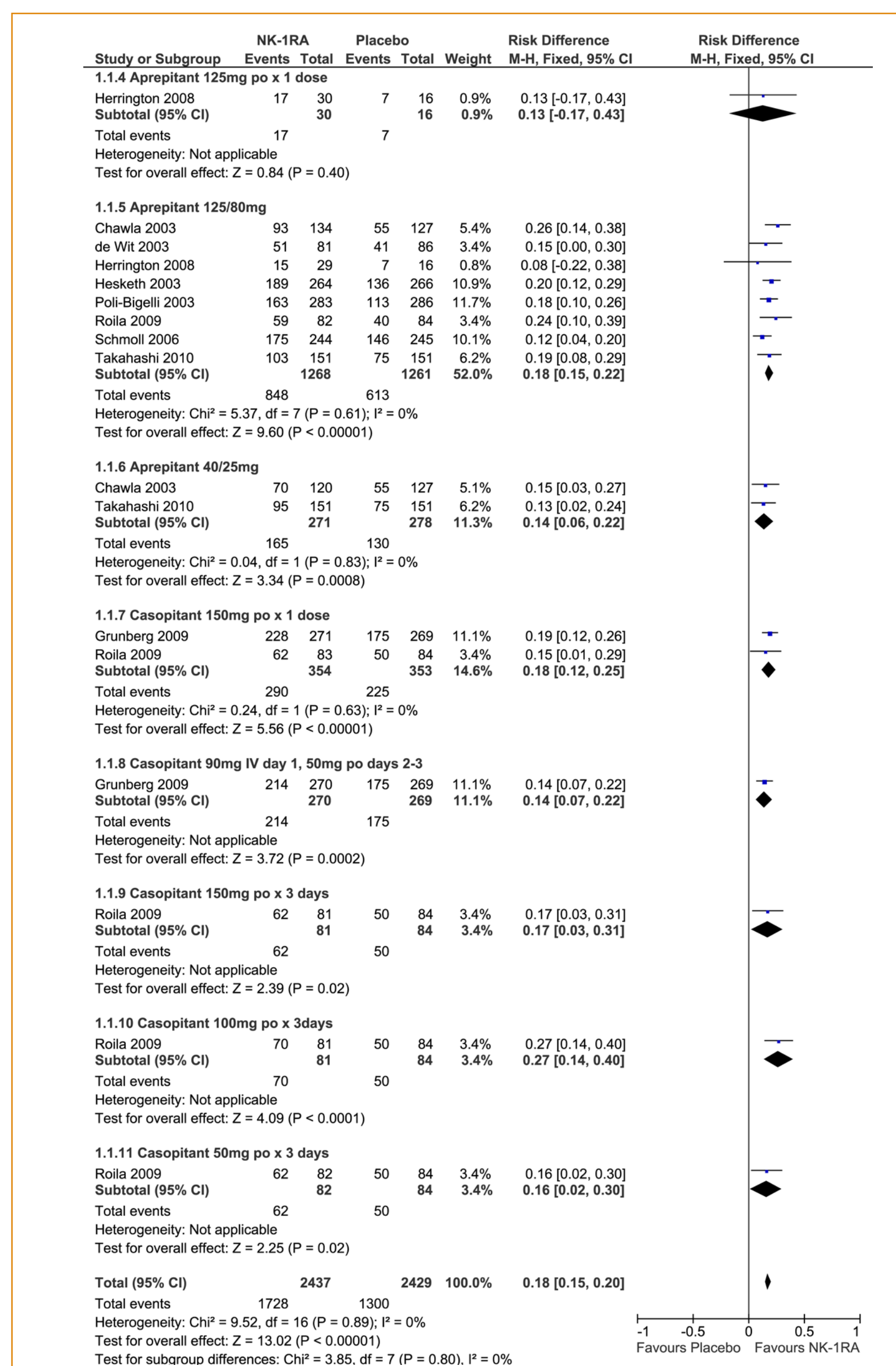


Figure 2: Complete Response (Overall)

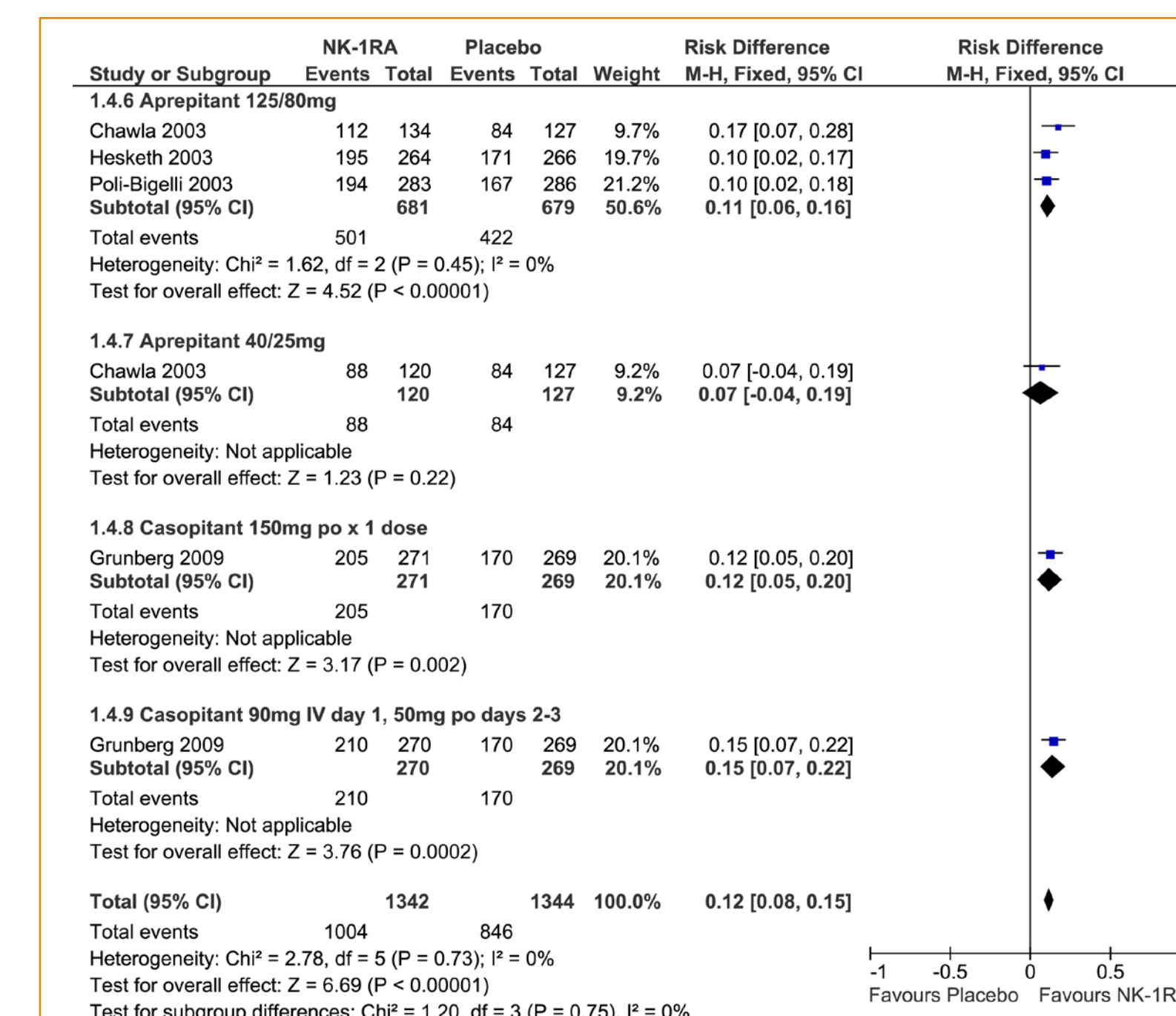


Figure 3: No Impact on Daily Life

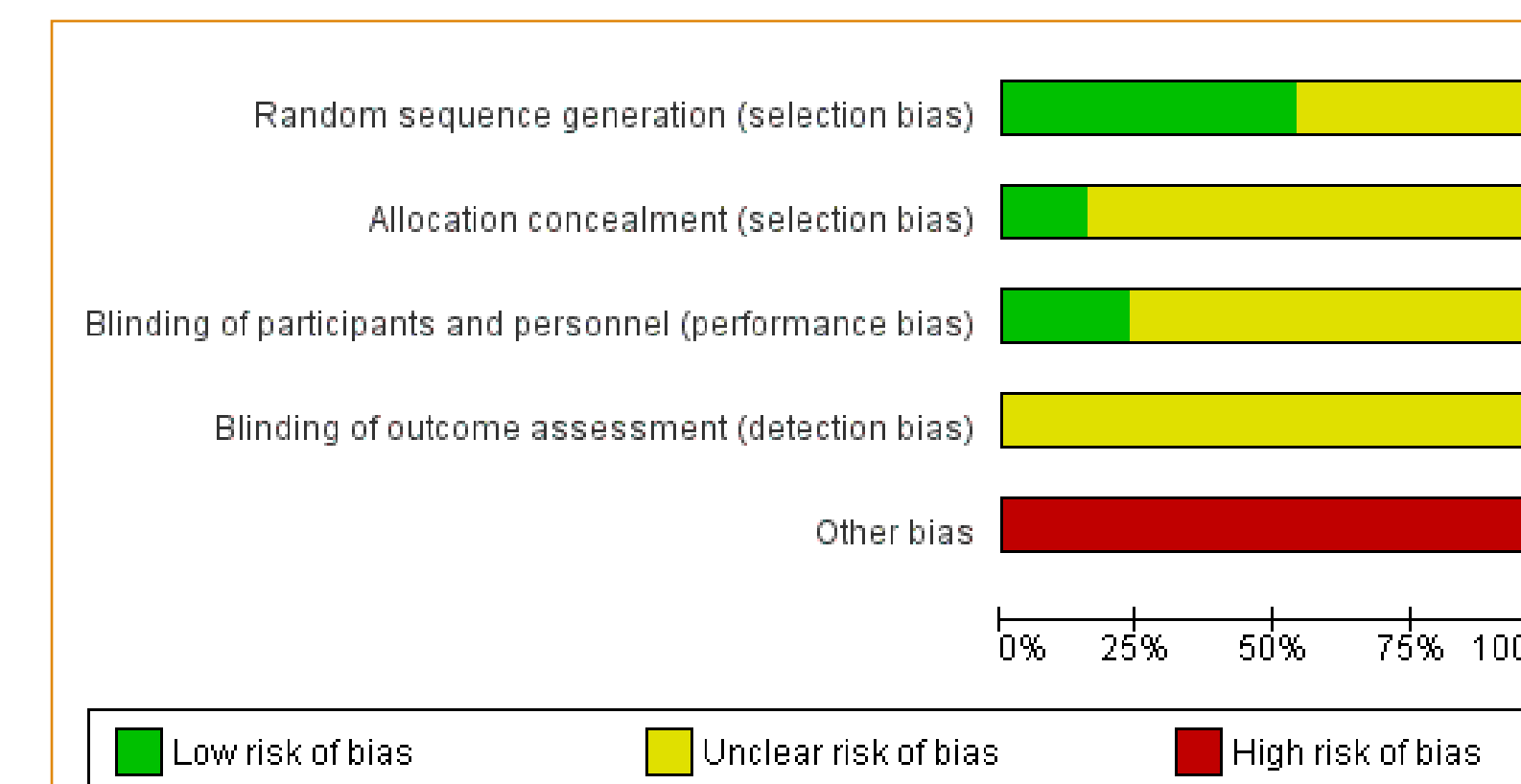


Figure 4: Risk of Bias Table

Discussion

No dose response?

- Analysis suggests that aprepitant 40/25mg may be as effective as aprepitant 125/80mg for complete response.

Implications of Risk of Bias (see Figure 4)

- High risk of “Other bias” due to industry funding of all included trials.
 - Potential over-estimation of treatment effects.
 - Need for independently-funded trials in this area.

Duplicate publication bias

- Two cases of inappropriate reporting of similar or same trial data in multiple journals.

Conclusions

Preliminary data suggests that NK-1RAs versus placebo significantly:

- Increase # of patients that said CINV had “No impact on daily life” (NNT = 8).
- Increase # of patients with complete response (overall, NNT = 5).
- Increase risk of a patient from experiencing at least 1 SAE (NNH = 33).

Resources

- Protocol citation: Wong H, Tejani AM. Neurokinin-1 receptor antagonists for prevention of chemotherapy-related nausea and vomiting in adults. *Cochrane Database of Systematic Reviews* 2012, Issue 4. Art. No.: CD006844. DOI: 10.1002/14651858.CD006844.pub2.
- References available upon request
- Contact email: HerbertC.Wong@fraserhealth.ca

