Analysis report (Supporting information)

Effect of oral nutritional supplements with or without nutritional counselling on mortality, treatment tolerance, and quality of life in head and neck cancer patients receiving (chemo)radiotherapy: a systematic review and meta-analysis

Mello et al. (2020)

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1 Abbreviations

CCRT: concurrent chemo-radiotherapy

CI: confidence interval

CT: chemotherapy

MD: mean difference

MID: minimal important difference

NC: nutritional counselling

ONS: oral nutritional supplements

RR: risk ratio

RT: radiotherapy

SD: standard deviation

seTE: standard error

SMD: standardized mean difference

TE: estimated treatment effect

2 Packages

```
library(meta)
```

```
## Loading 'meta' package (version 4.9-7).
## Type 'help(meta)' for a brief overview.
```

```
library(readr)
library(rmeta)
library(devtools)
```

```
## Loading required package: usethis
```

```r
library(robvis)
library(patchwork)
library(ggplot2)
library(tidyr)
```

3 Standard configurations for the meta-analyses

```r
settings.meta(hakn = TRUE) # Hartung-Knapp adjustment
```

```
Parsed with column specification:
cols(
  .default = col_double(),
  outclab = col_character(),
  D1 = col_character(),
  D2 = col_character(),
  D3 = col_character(),
  D4 = col_character(),
  D5 = col_character(),
  Overall = col_character(),
  bias = col_character(),
  site = col_character(),
  studlab = col_character(),
  X23 = col_logical()
)

See spec(...) for full column specifications.
```

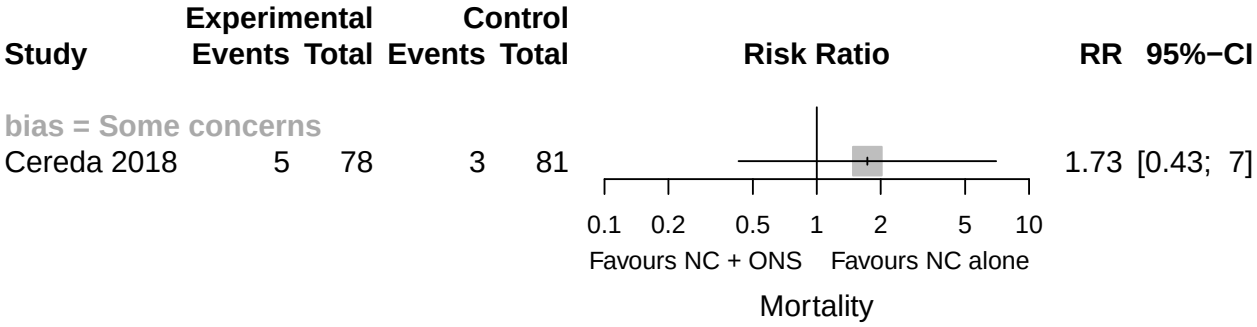
4 Comparison 1

4.1 Mortality

4.1.1 Main analysis

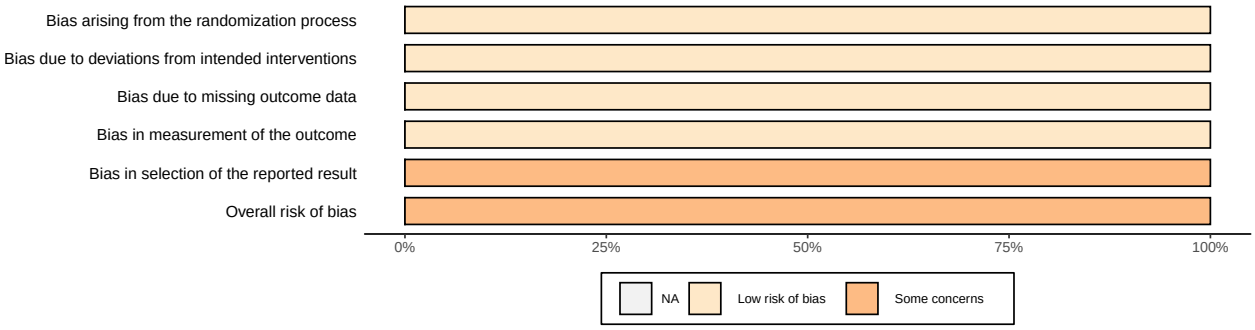
Including only results at most at some concerns of bias.

4.1.1.1 Forest plot



4.1.1.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



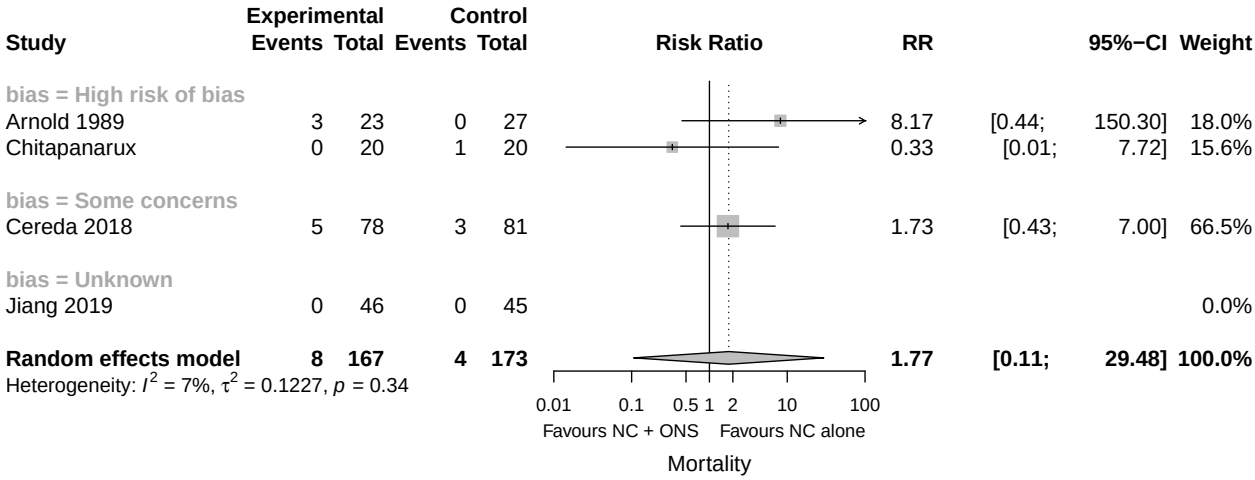
4.1.2 Sensitivity analysis

Including all available results.

4.1.2.1 Forest plot

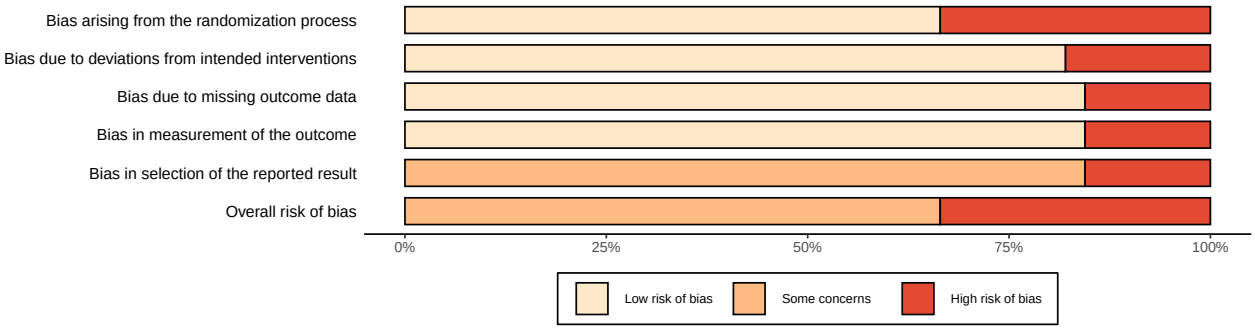
```
## Warning in qt(1 - alpha/2, df = df): NaNs produzidos

## Warning in qt(1 - alpha/2, df = df): NaNs produzidos
```

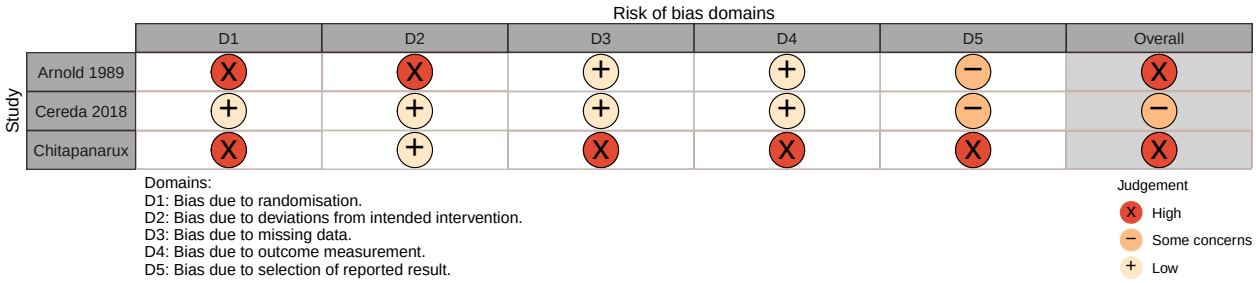


4.1.2.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



4.1.2.3 Risk of bias assessments by study

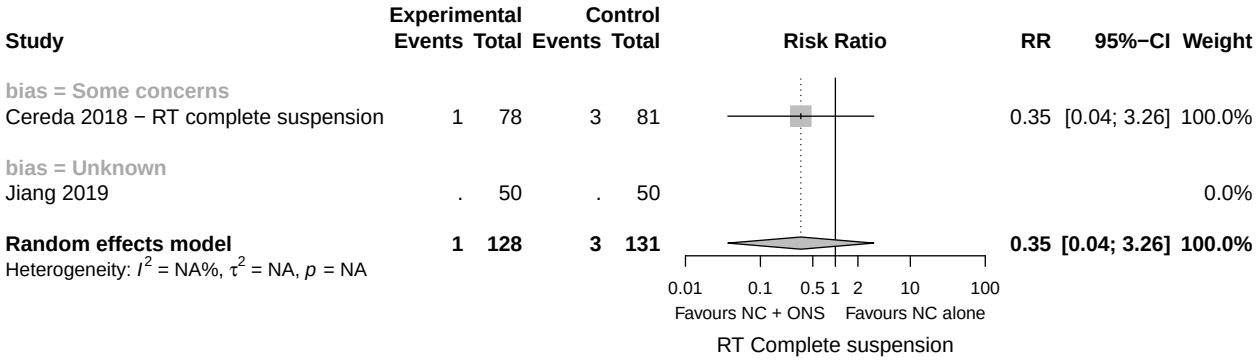


4.2 Treatment tolerance

4.2.1 RT Complete suspension

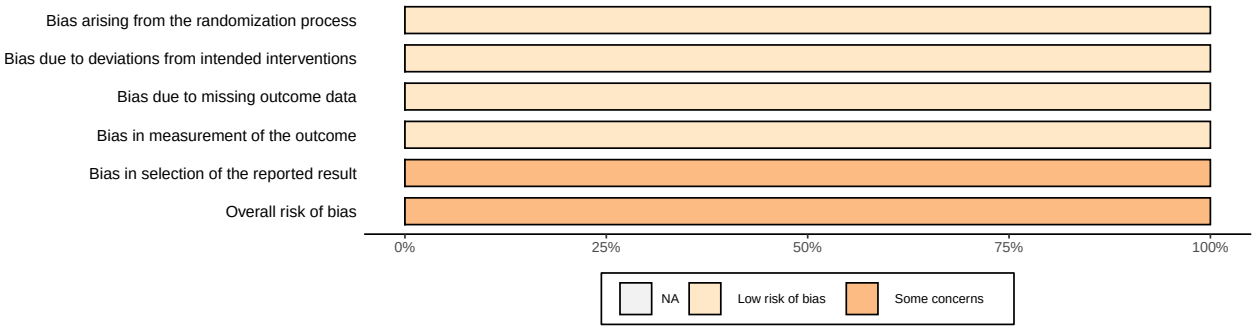
4.2.1.1 Forest plot

```
## Warning: For a single study, inverse variance method used instead of Mantel-
## Haenszel method.
```

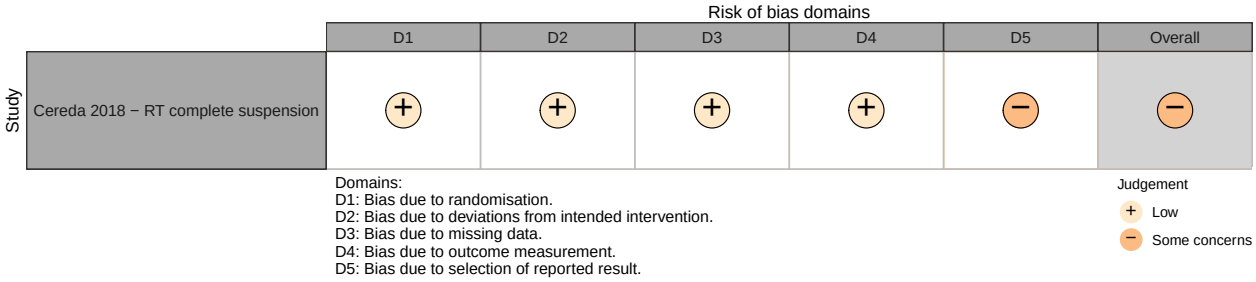


4.2.1.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

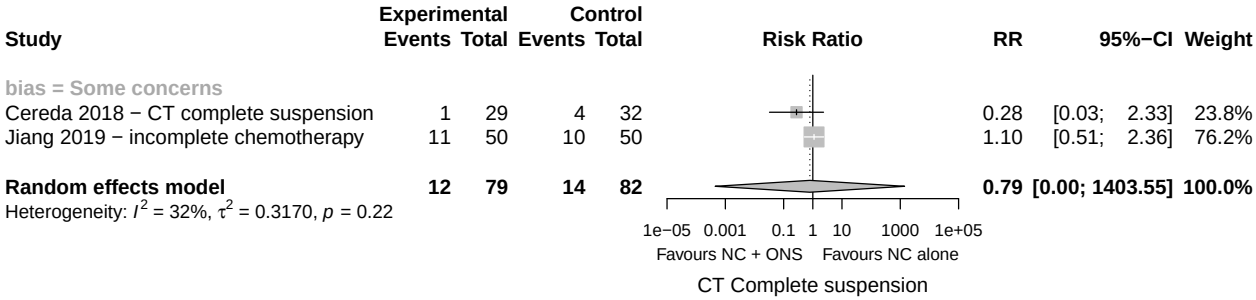


4.2.1.3 Risk of bias assessments by study



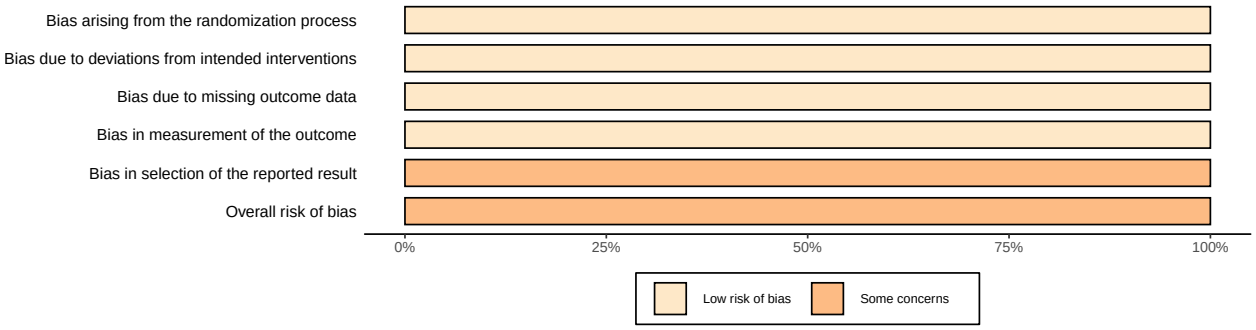
4.2.2 CT Complete suspension

4.2.2.1 Forest plot

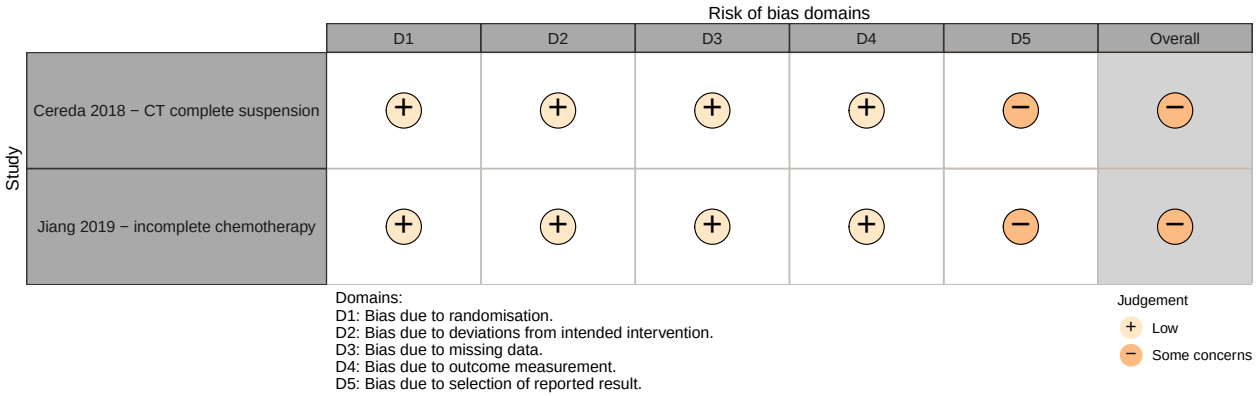


4.2.2.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

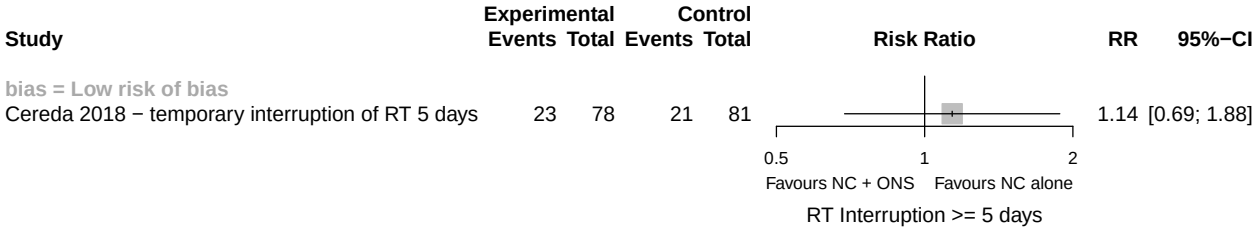


4.2.2.3 Risk of bias assessments by study



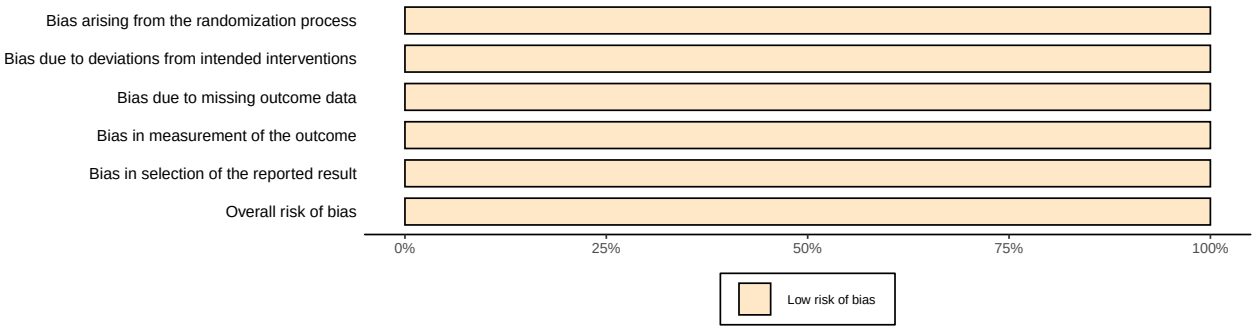
4.2.3 RT interruption >= 5 days

4.2.3.1 Forest plot

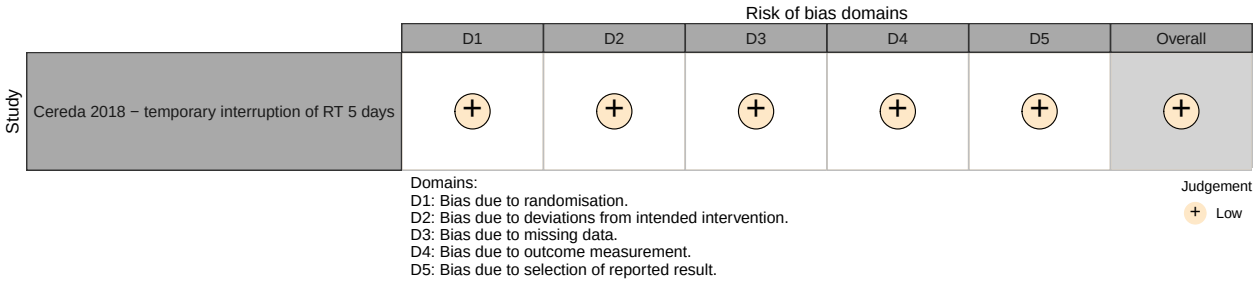


4.2.3.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

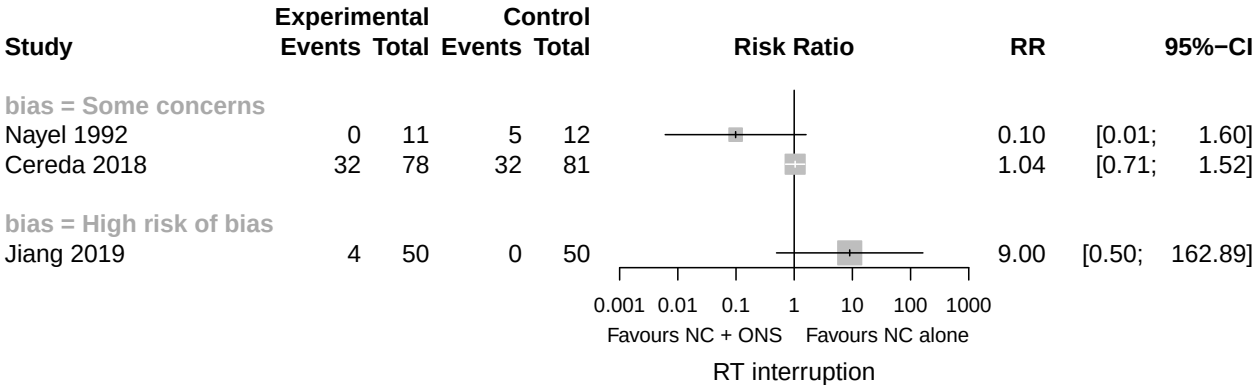


4.2.3.3 Risk of bias assessments by study



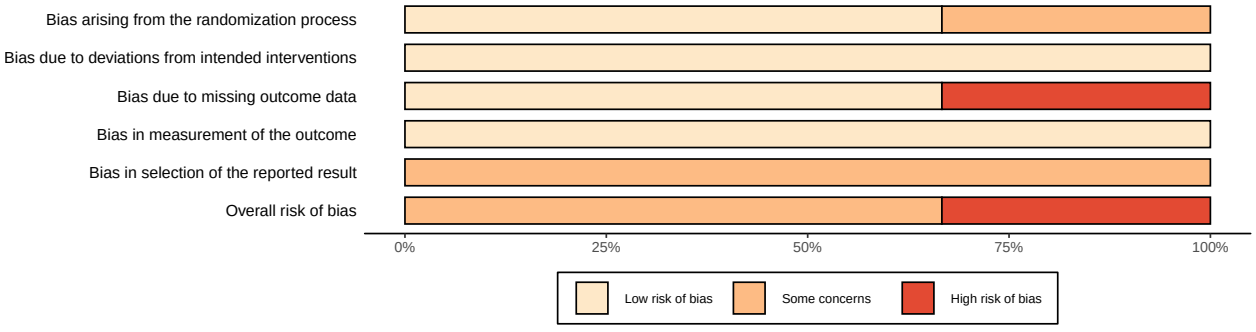
4.2.4 RT interruption

4.2.4.1 Forest plot

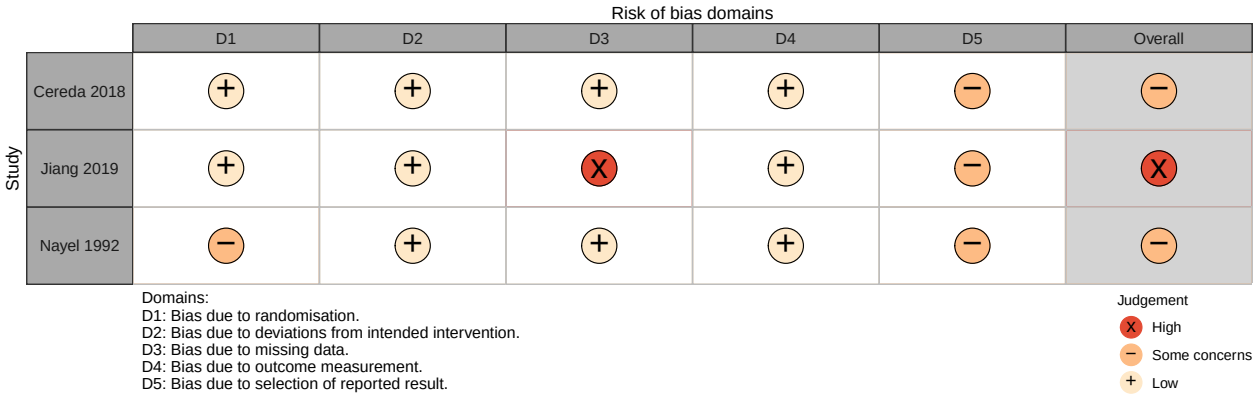


4.2.4.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

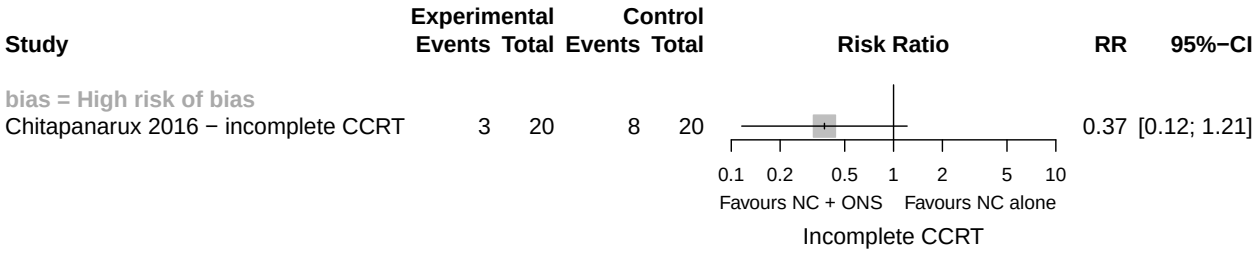


4.2.4.3 Risk of bias assessments by study



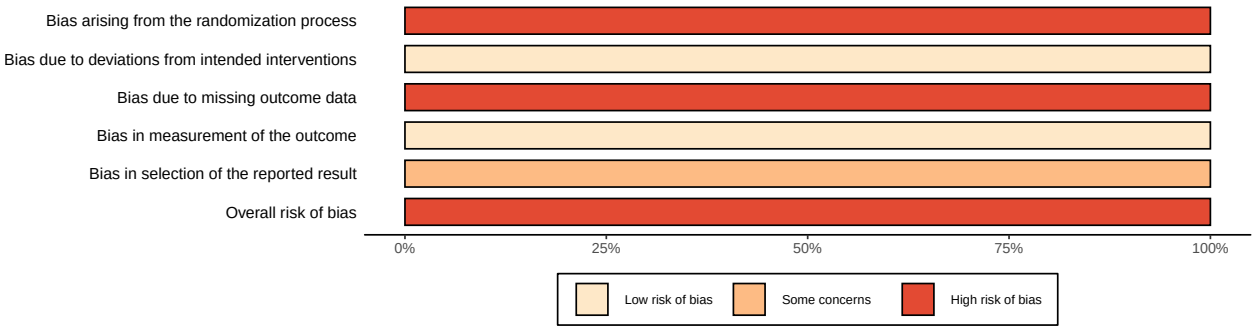
4.2.5 Incomplete CCRT

4.2.5.1 Forest plot

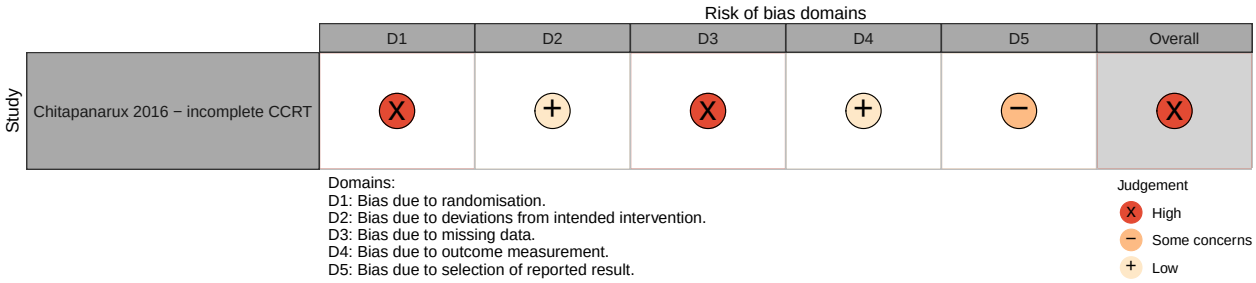


4.2.5.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

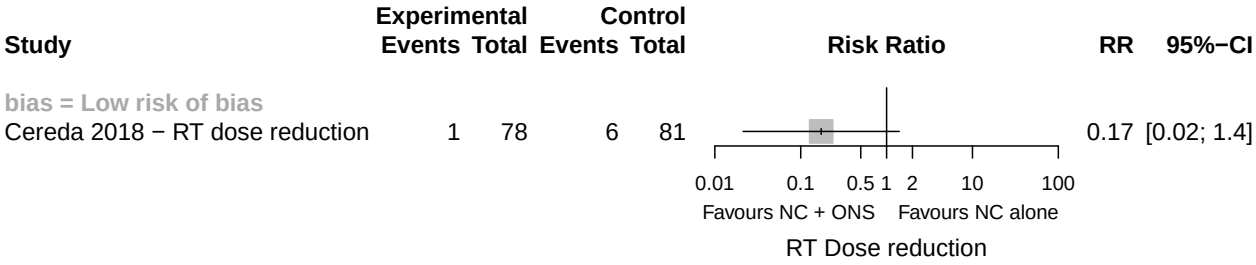


4.2.5.3 Risk of bias assessments by study



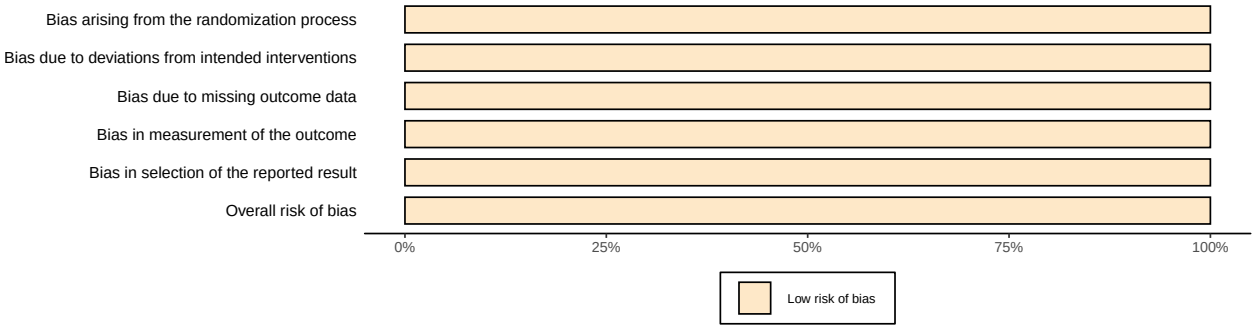
4.2.6 RT Dose reduction

4.2.6.1 Forest plot

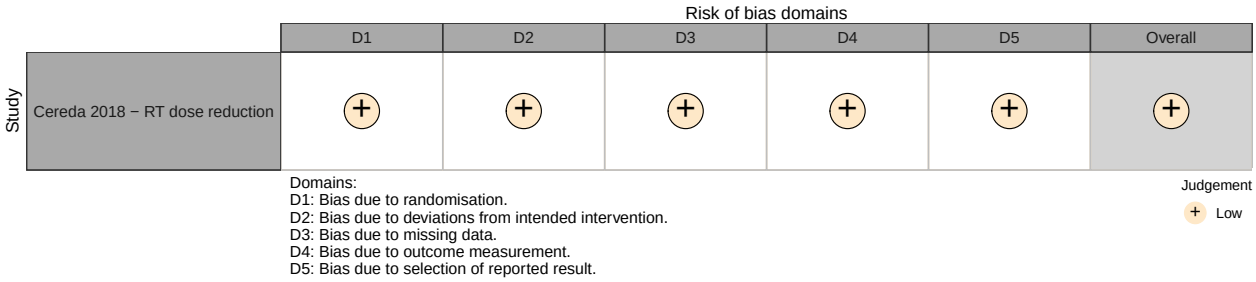


4.2.6.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

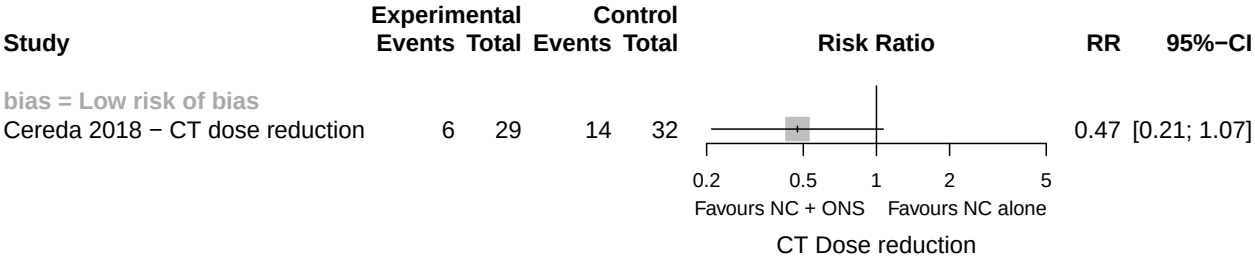


4.2.6.3 Risk of bias assessments by study



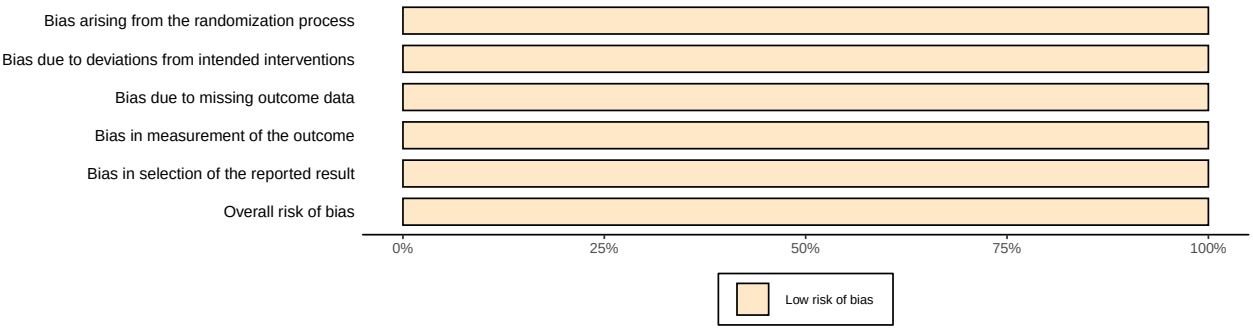
4.2.7 CT Dose reduction

4.2.7.1 Forest plot

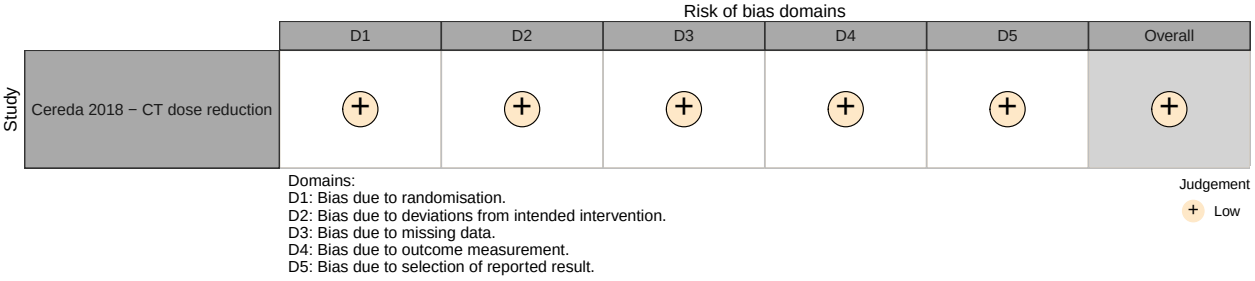


4.2.7.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

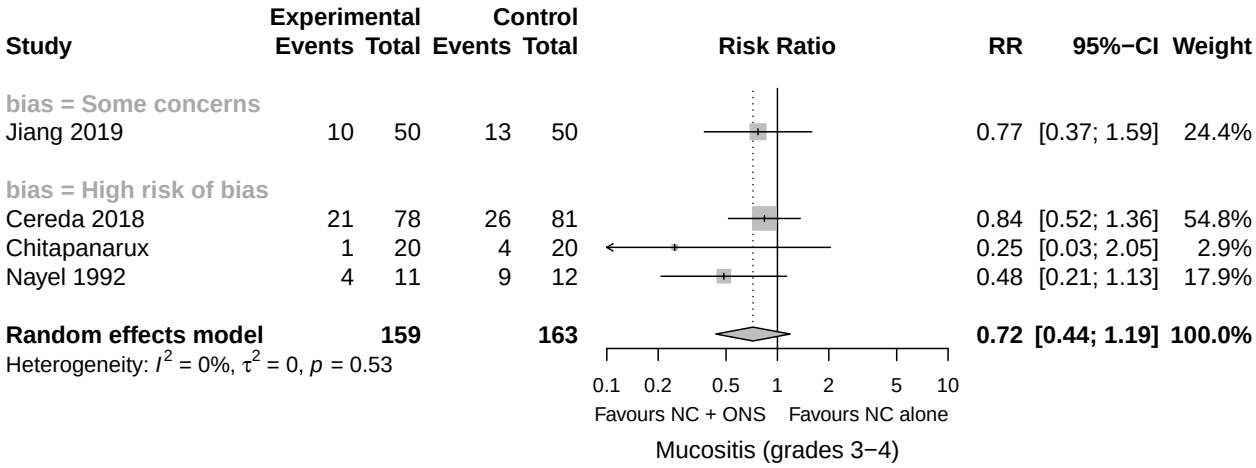


4.2.7.3 Risk of bias assessments by study



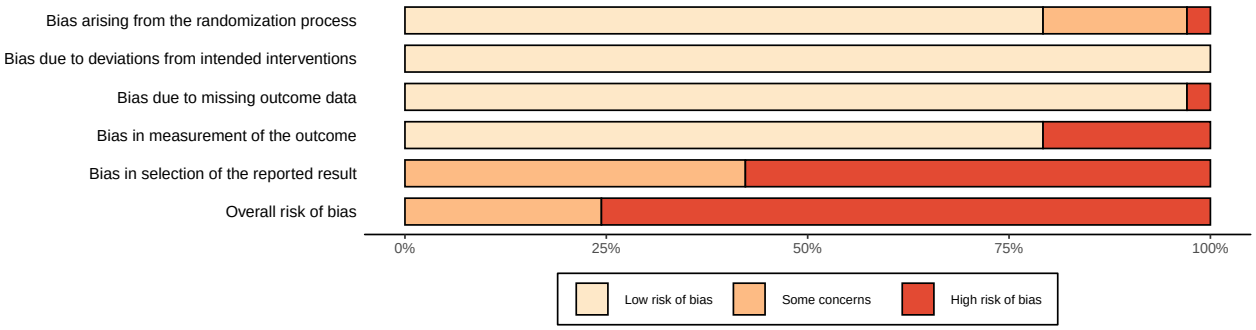
4.2.8 Mucositis (severe)

4.2.8.1 Forest plot

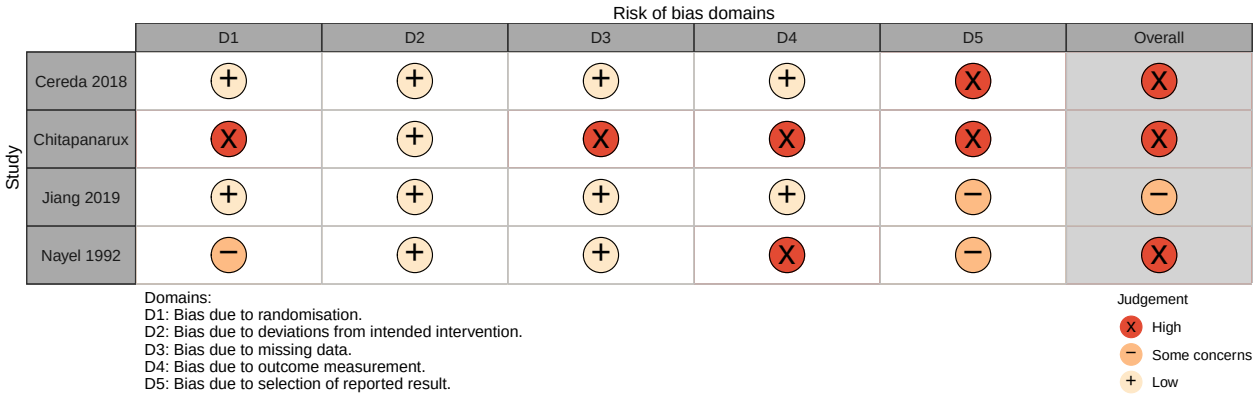


4.2.8.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

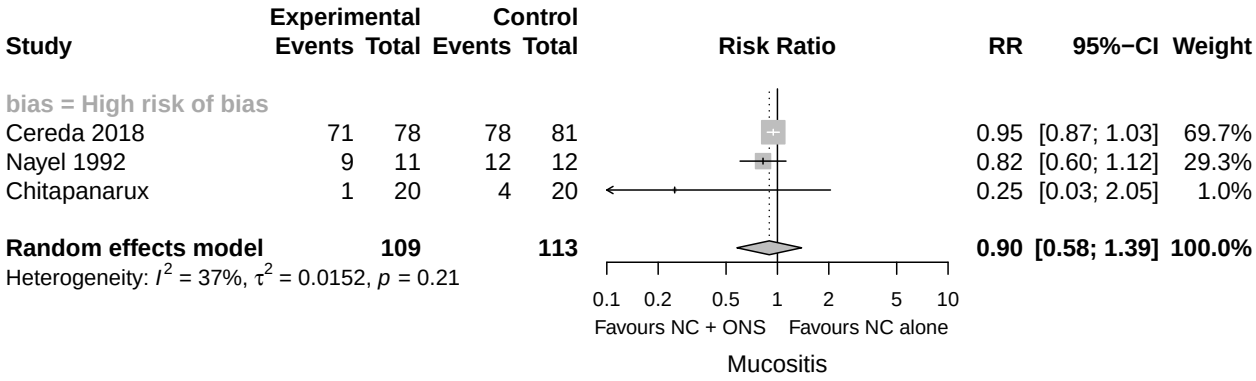


4.2.8.3 Risk of bias assessments by study



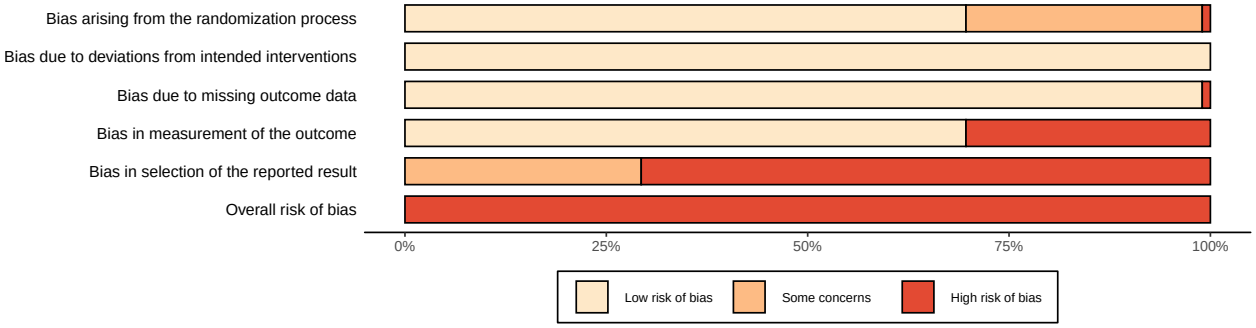
4.2.9 Mucositis (overall)

4.2.9.1 Forest plot

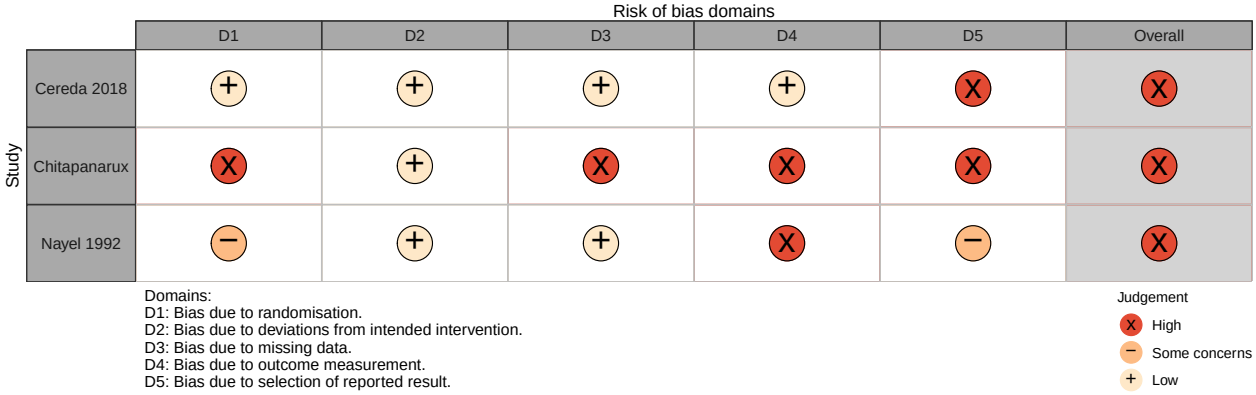


4.2.9.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

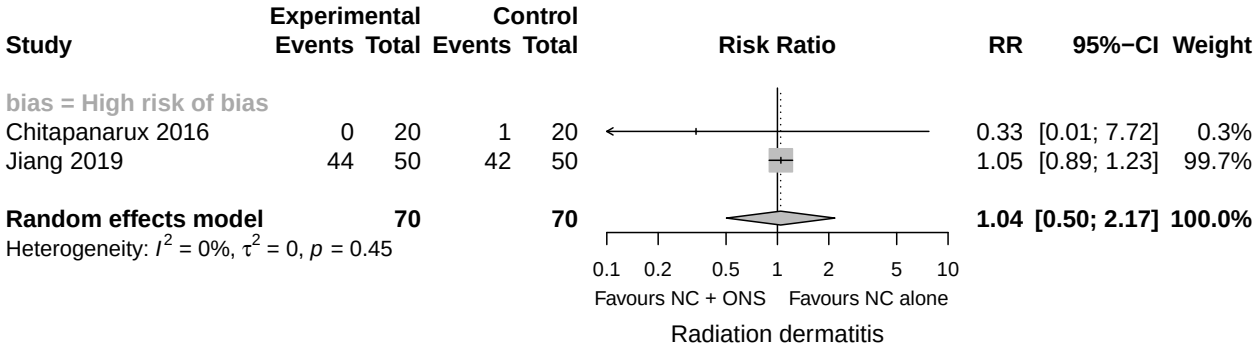


4.2.9.3 Risk of bias assessments by study



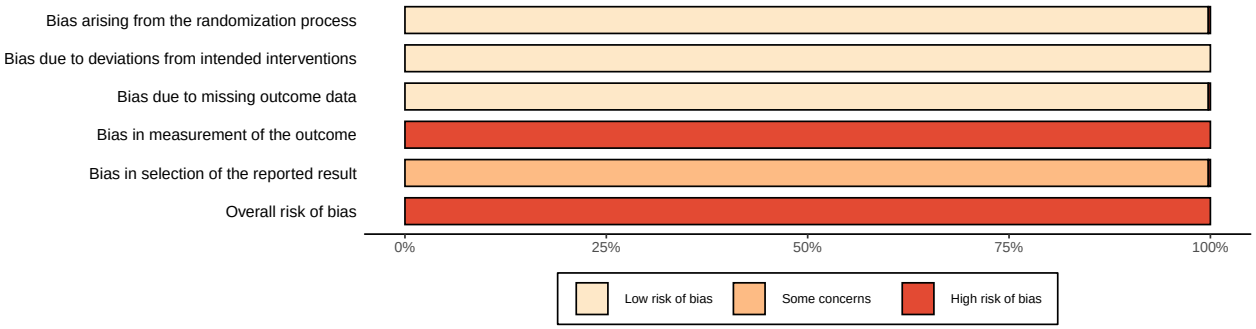
4.2.10 Radiation dermatitis

4.2.10.1 Forest plot

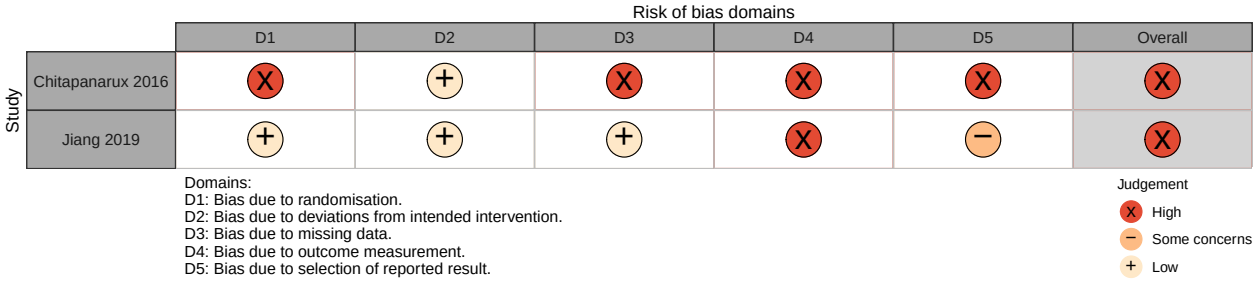


4.2.10.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

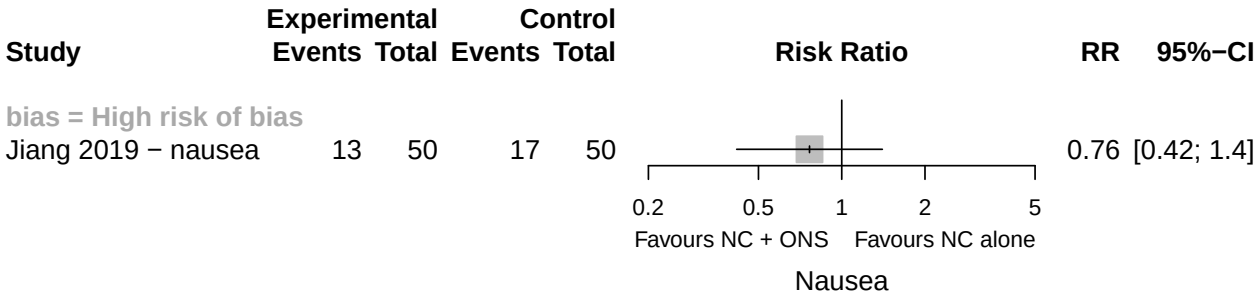


4.2.10.3 Risk of bias assessments by study



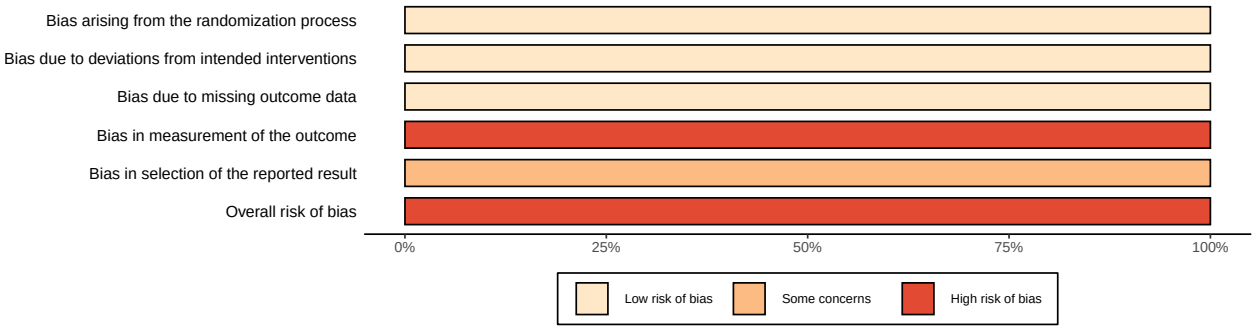
4.2.11 Nausea

4.2.11.1 Forest plot

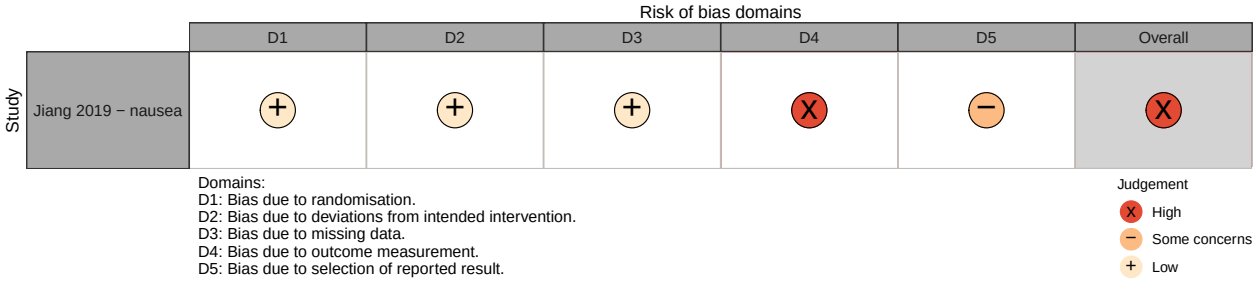


4.2.11.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

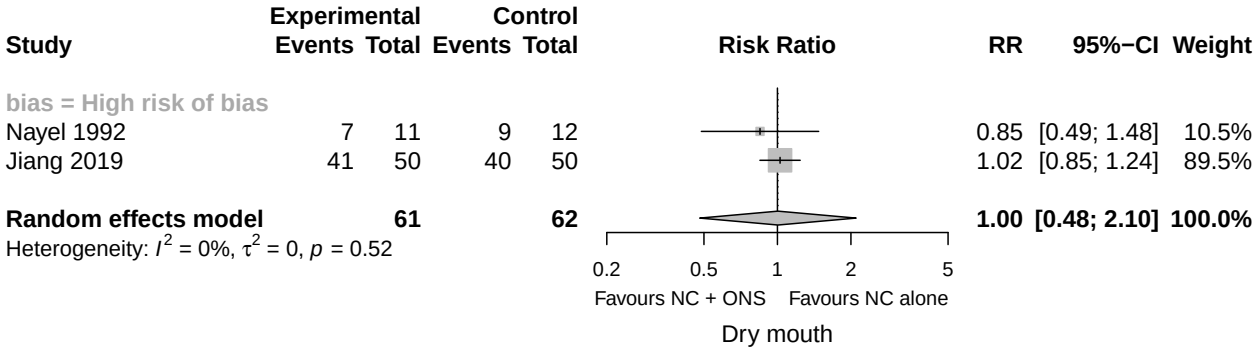


4.2.11.3 Risk of bias assessments by study



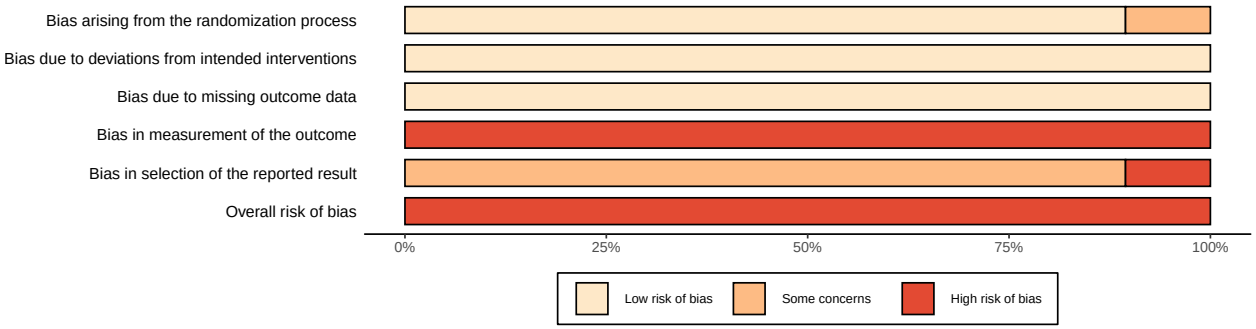
4.2.12 Dry mouth

4.2.12.1 Forest plot

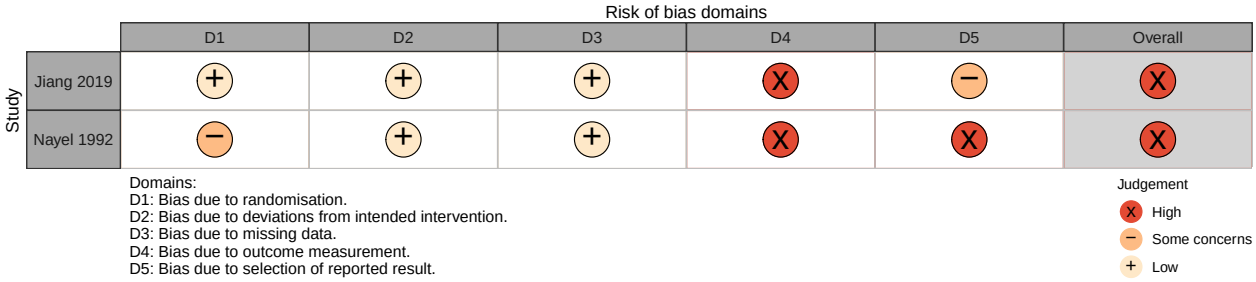


4.2.12.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

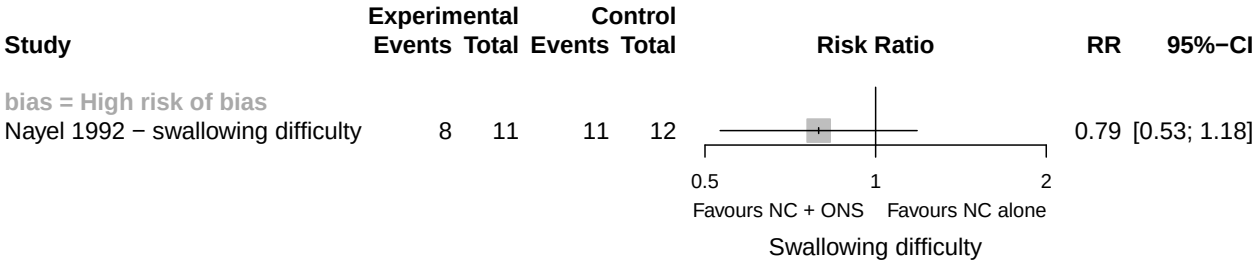


4.2.12.3 Risk of bias assessments by study



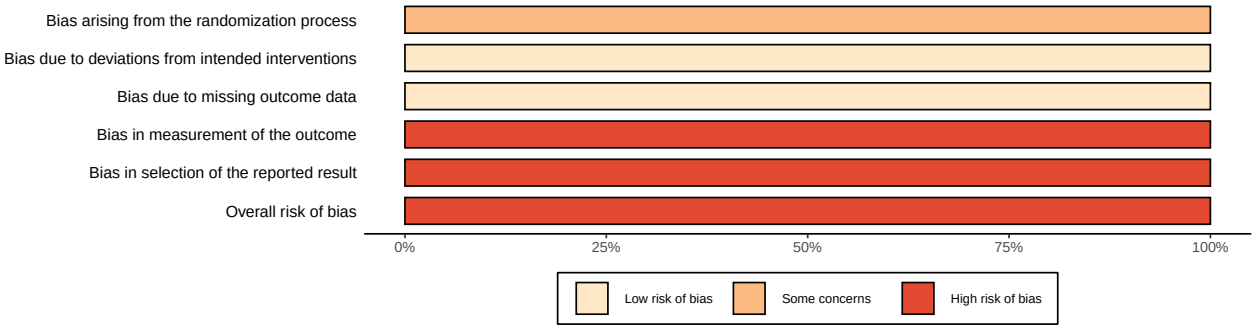
4.2.13 Swallowing difficulty

4.2.13.1 Forest plot

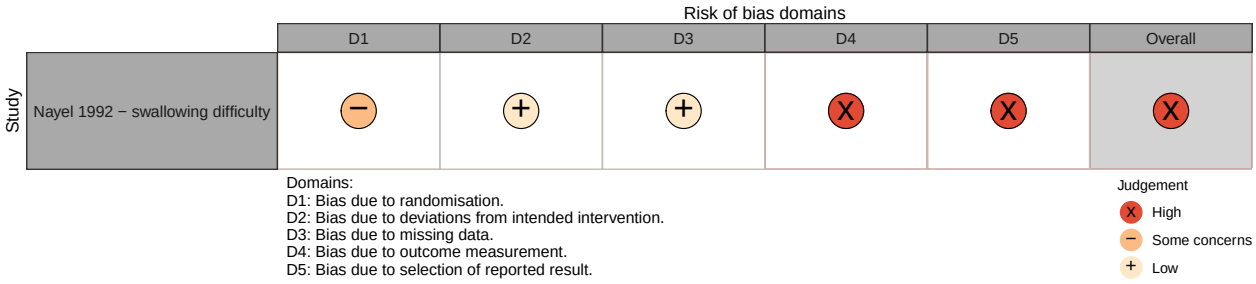


4.2.13.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

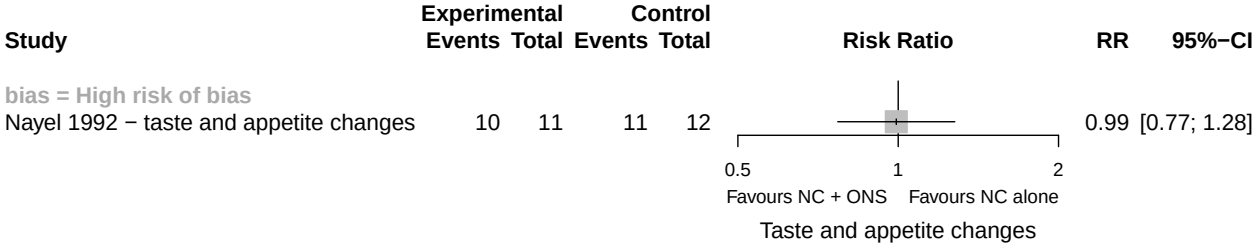


4.2.13.3 Risk of bias assessments by study



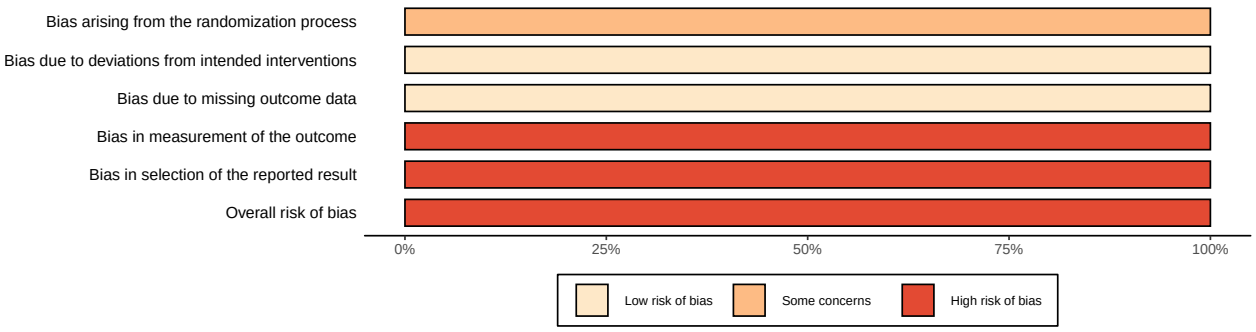
4.2.14 Taste and appetite changes

4.2.14.1 Forest plot

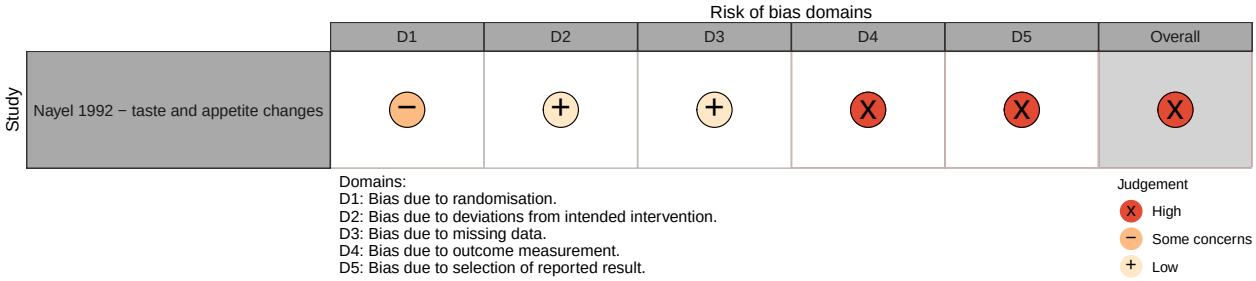


4.2.14.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

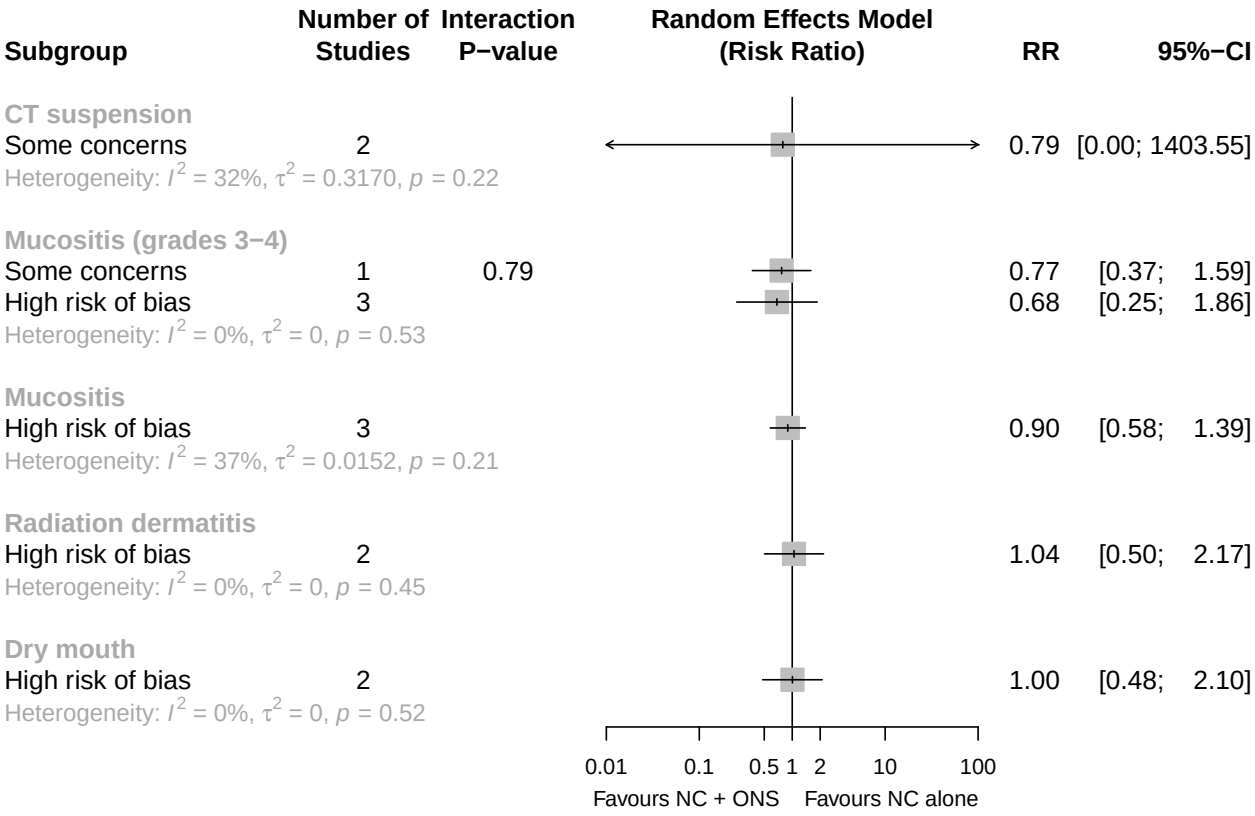


4.2.14.3 Risk of bias assessments by study

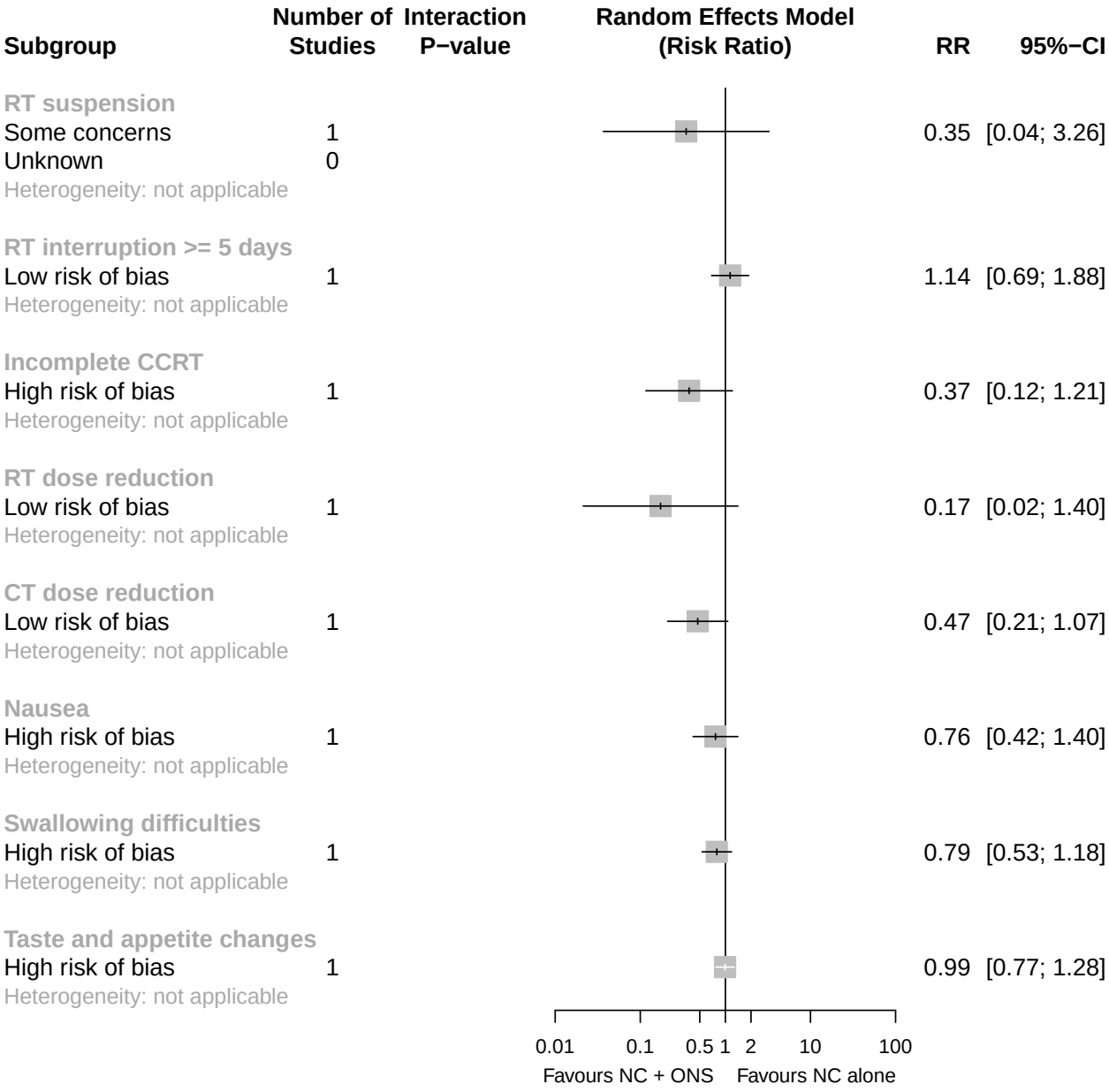


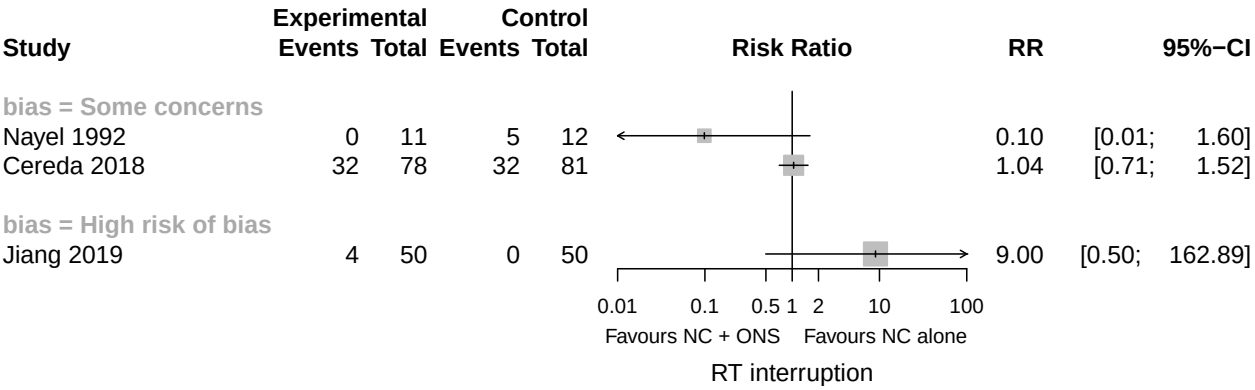
4.2.15 Summary of treatment tolerance outcomes

4.2.15.1 Results of meta-analysis



4.2.15.2 Results of structured reporting (no meta-analysis)

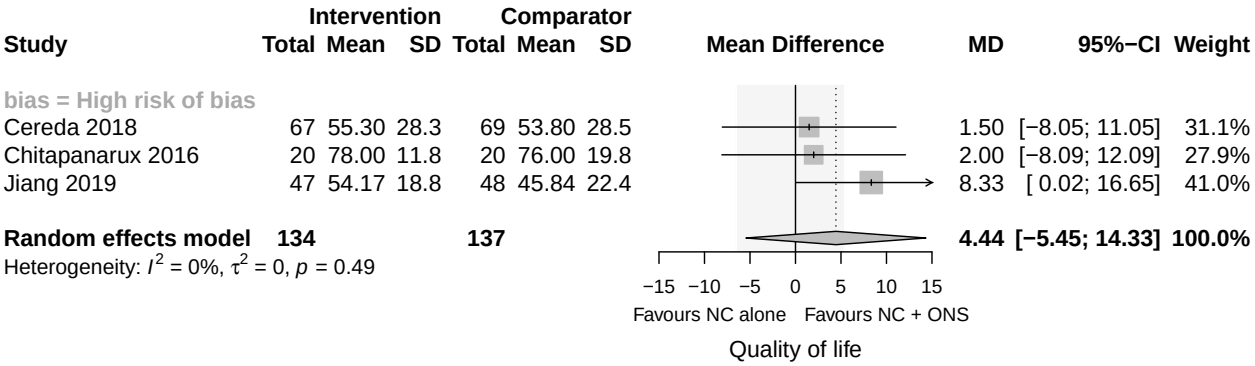

Subgroup
Number of Studies
Interaction P−value
Random Effects Model (Risk Ratio)
RR
95%−CI
RT suspension
Some concerns 1 0.35 [0.04; 3.26]
Unknown 0
Heterogeneity: not applicable
RT interruption >= 5 days
Low risk of bias 1 1.14 [0.69; 1.88]
Heterogeneity: not applicable
Incomplete CCRT
High risk of bias 1 0.37 [0.12; 1.21]
Heterogeneity: not applicable
RT dose reduction
Low risk of bias 1 0.17 [0.02; 1.40]
Heterogeneity: not applicable
CT dose reduction
Low risk of bias 1 0.47 [0.21; 1.07]
Heterogeneity: not applicable
Nausea
High risk of bias 1 0.76 [0.42; 1.40]
Heterogeneity: not applicable
Swallowing difficulties
High risk of bias 1 0.79 [0.53; 1.18]
Heterogeneity: not applicable
Taste and appetite changes
High risk of bias 1 0.99 [0.77; 1.28]
Heterogeneity: not applicable
0.01 0.1 0.5 1 2 10 100
Favours NC + ONS
Favours NC alone


Study
Experimental Events Total
Control Events Total
Risk Ratio
RR
95%−CI
bias = Some concerns
Nayel 1992 0 11 5 12 0.10 [0.01; 1.60]
Cereda 2018 32 78 32 81 1.04 [0.71; 1.52]
bias = High risk of bias
Jiang 2019 4 50 0 50 9.00 [0.50; 162.89]
0.01 0.1 0.5 1 2 10 100
Favours NC + ONS
Favours NC alone
RT interruption

4.3 Quality of life (end of treatment)

4.3.1 Global quality of life

4.3.1.1 Forest plot

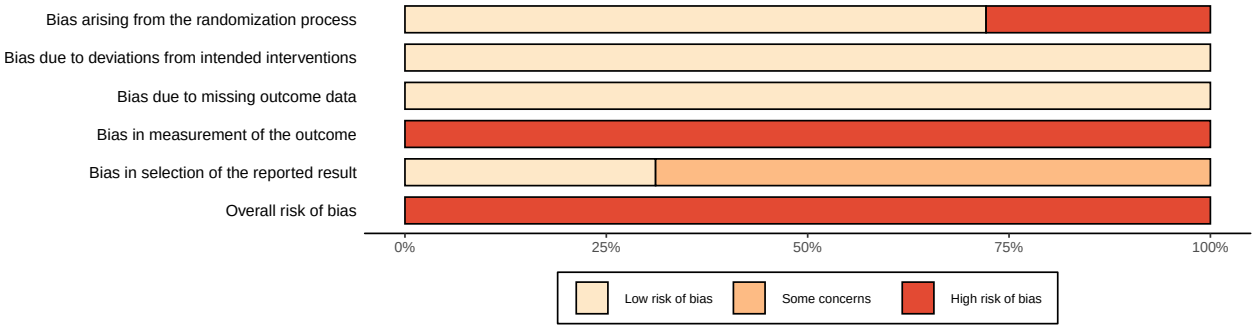


MIDs for the global health status (QL) scale for improvement (deterioration) were QL: 5.4 (- 6.5) and SF: 4.9 (- 7.7) in head and neck cancer patients (shaded area)

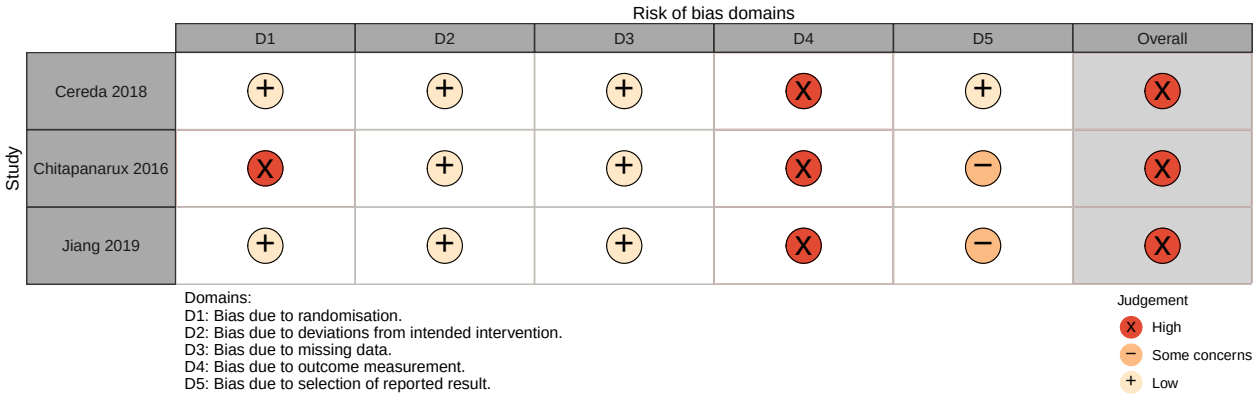
Musoro J, Coens C, Fiteni F, et al. Evidence-based approach to determine meaningful change in scores of the EORTC QLQ-C30 in breast and head and neck cancer: on behalf of the EORTC Breast, Head and Neck and Quality of Life Groups. 25th annual conference of the international society for quality of life research, Dublin, Ireland. Qual Life Res 2018;27 (Suppl 1): ab101.4, 18. https://doi.org/10.1007/s11136-018-1946-9

4.3.1.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



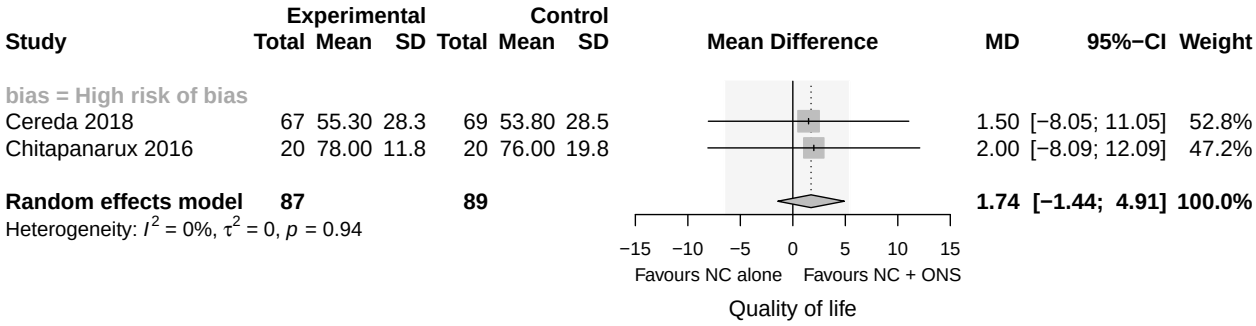
4.3.1.3 Risk of bias assessments by study



4.3.2 Sensitivity analysis

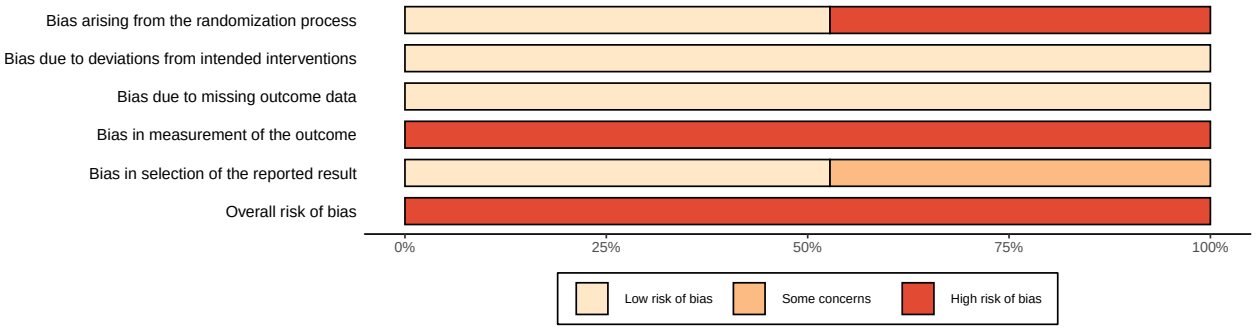
Excluding Jiang 2019, because mean and standard deviation for this study were inputted (as described in the methods section of the primary report).

4.3.2.1 Forest plot

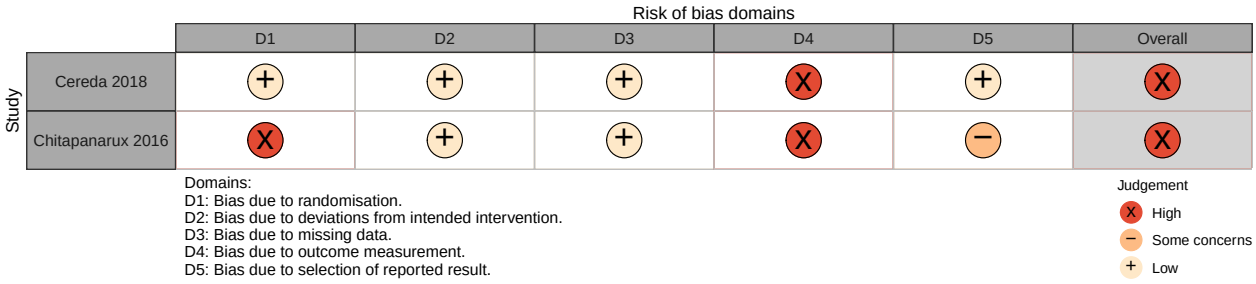


4.3.2.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

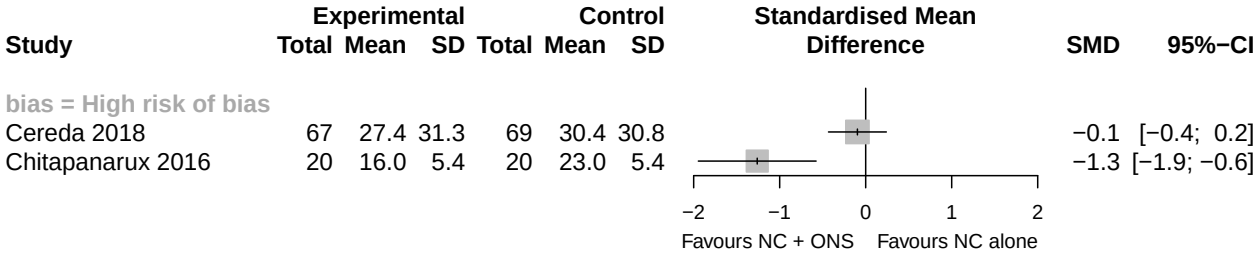


4.3.2.3 Risk of bias assessments by study

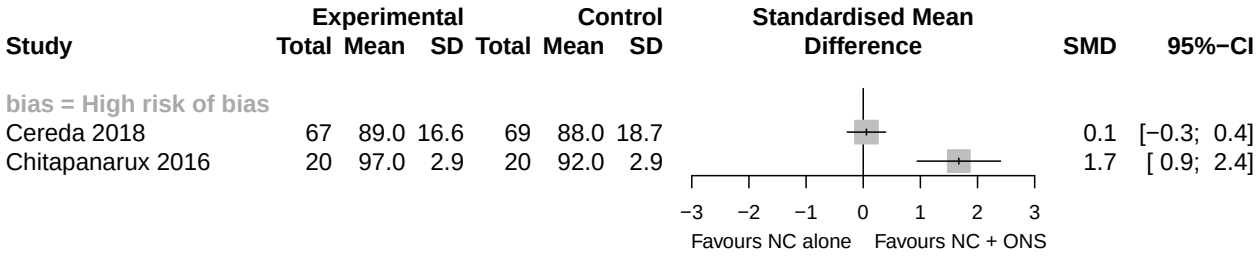


4.3.3 Quality of life subscales

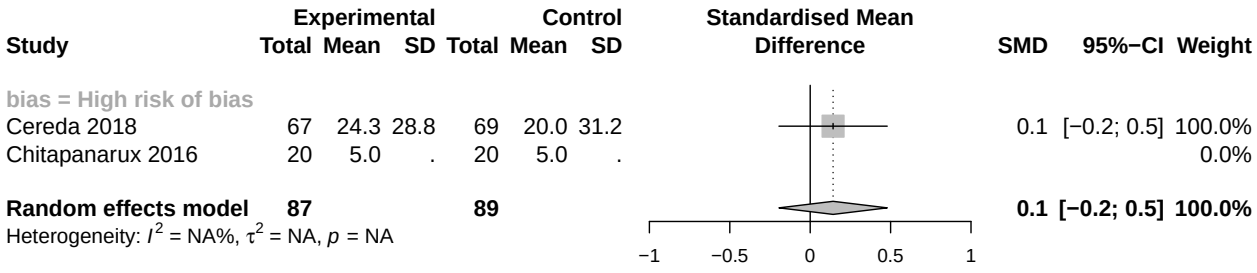
4.3.3.1 Appetite loss



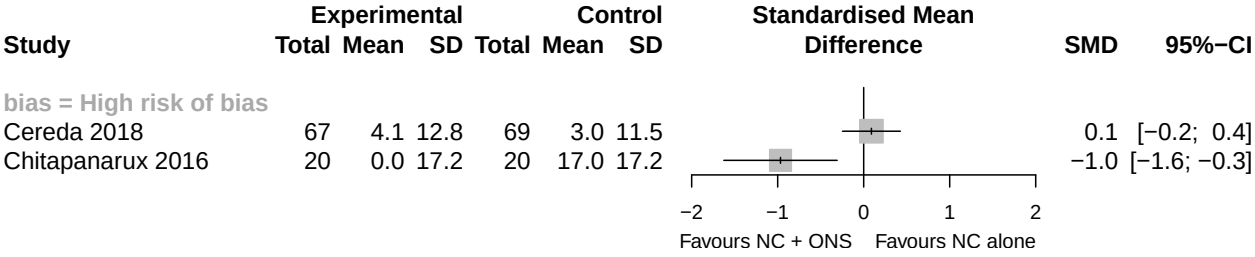
4.3.3.2 Cognitive



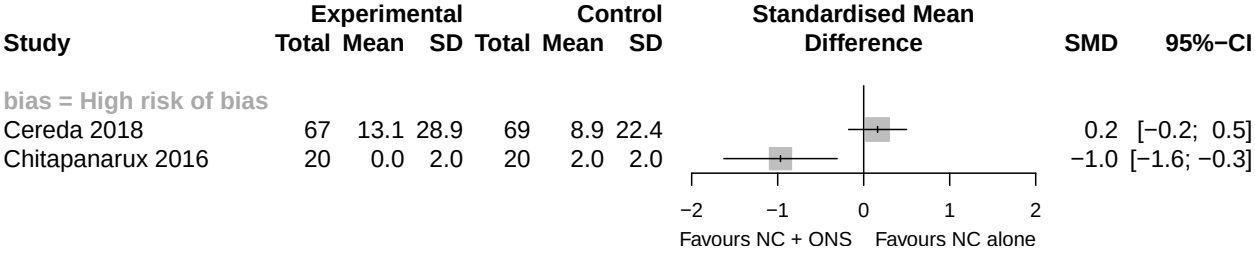
4.3.3.3 Constipation



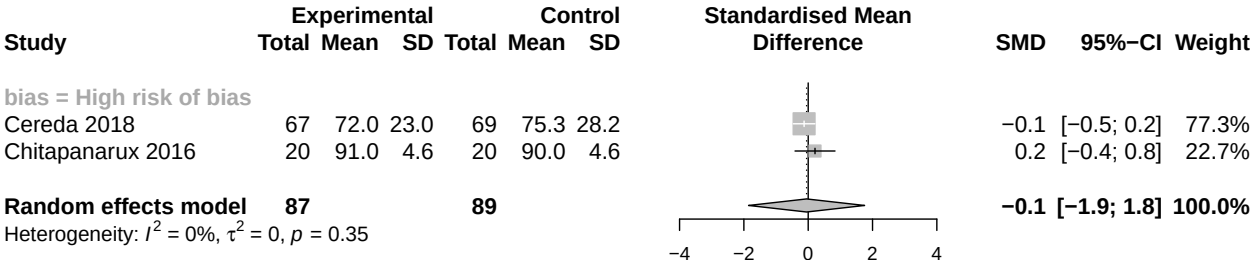
4.3.3.4 Diarrhoea



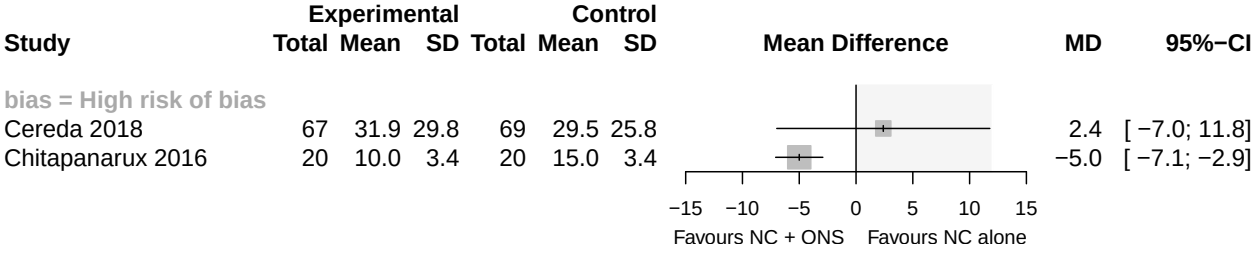
4.3.3.5 Dyspnoea



4.3.3.6 Emotional



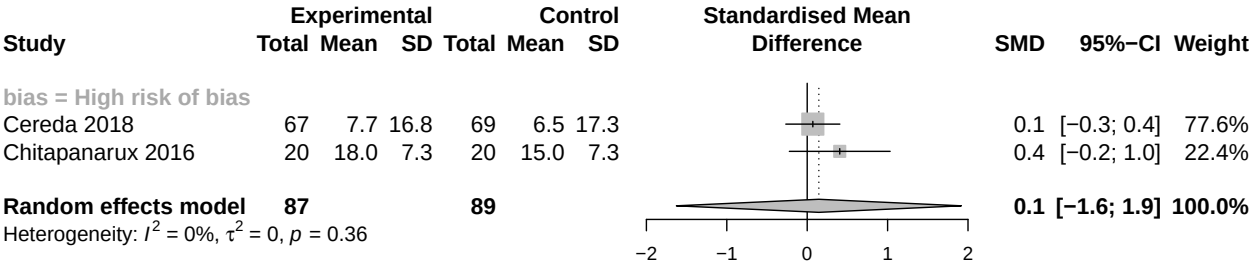
4.3.3.7 Fatigue



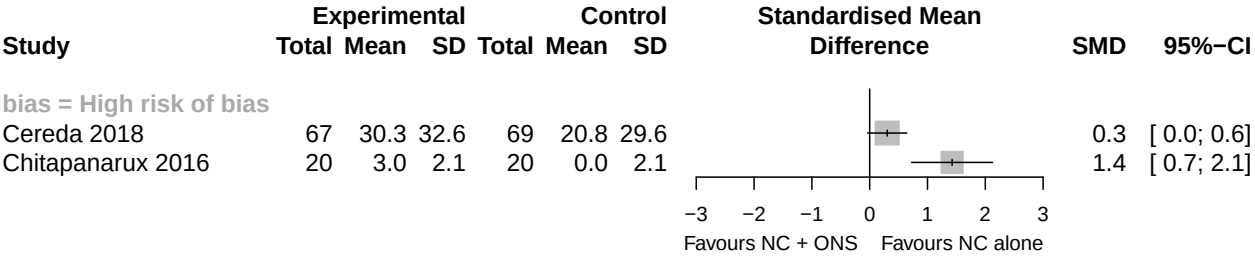
MID: 12.0 (deteriorate)

Musoro J, Coens C, Fiteni F, et al. Minimally important differences for interpreting EORTC QLQ-C30 scores in melanoma, breast cancer and head and neck cancer patients on behalf of the EORTC breast, Head and Neck, Melanoma and Quality of life groups. ISPOR Europe 2018 Barcelona, November, 2018.

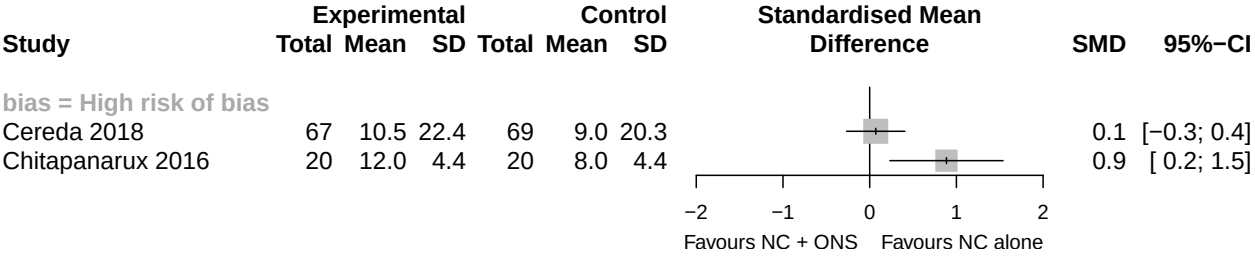
4.3.3.8 Financial



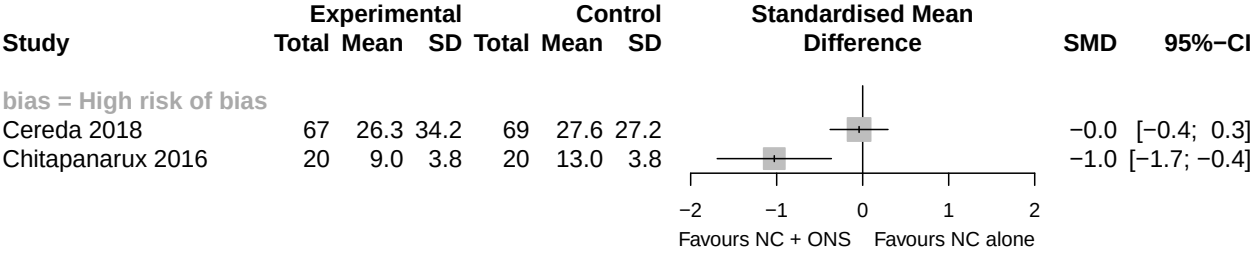
4.3.3.9 Insomnia



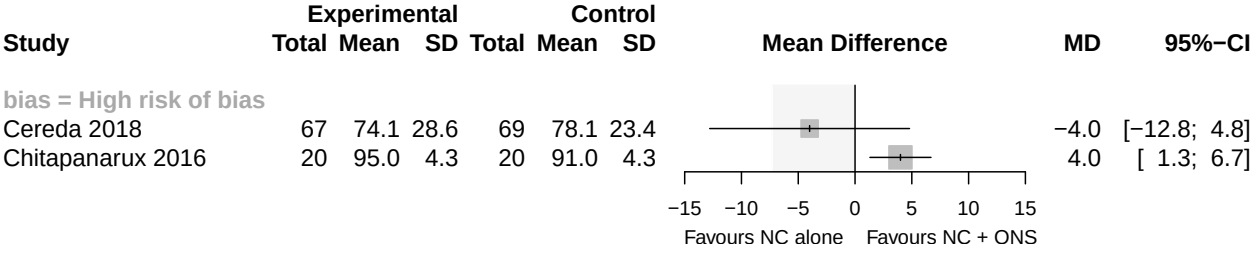
4.3.3.10 Nausea



4.3.3.11 Pain

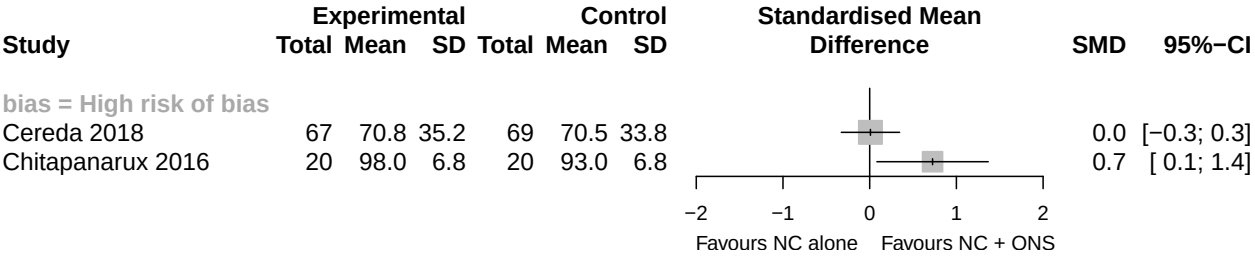


4.3.3.12 Physical

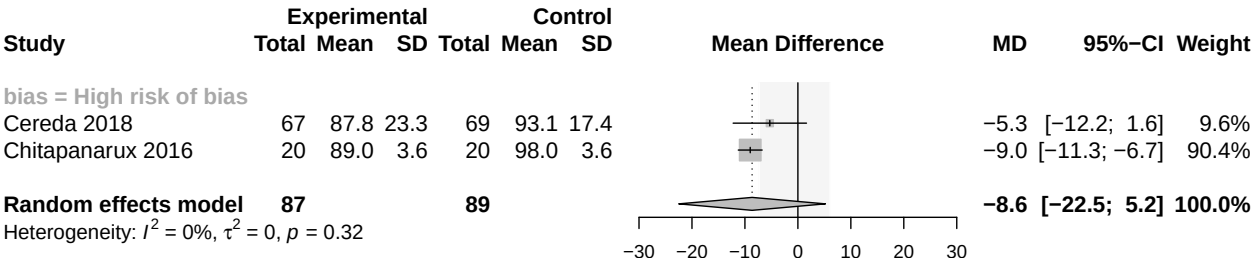


MID: -7.3 (deteriorate)

4.3.3.13 Role



4.3.3.14 Social

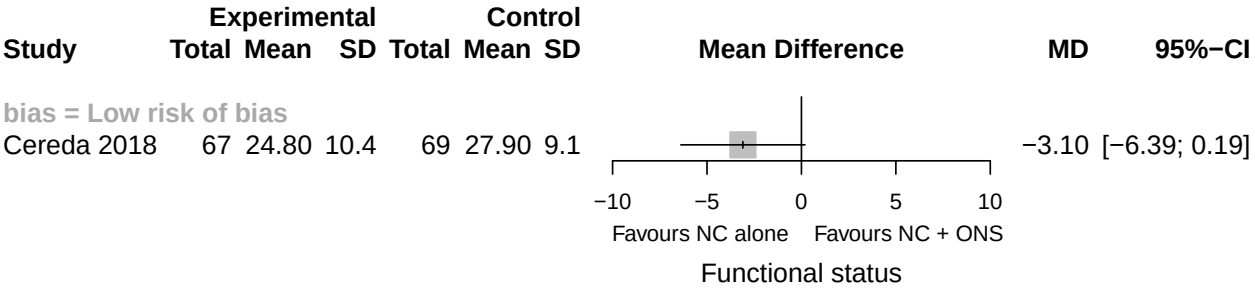


MIDs for the social functioning (SF) scale for improvement (deterioration) were SF: 6.1 (- 7.3) in HNC

Musoro J, Coens C, Fiteni F, et al. Evidence-based approach to determine meaningful change in scores of the EORTC QLQ-C30 in breast and head and neck cancer: on behalf of the EORTC Breast, Head and Neck and Quality of Life Groups. 25th annual conference of the international society for quality of life research, Dublin, Ireland. Qual Life Res 2018;27 (Suppl 1): ab101.4, 18. https://doi.org/10.1007/s11136-018-1946-9

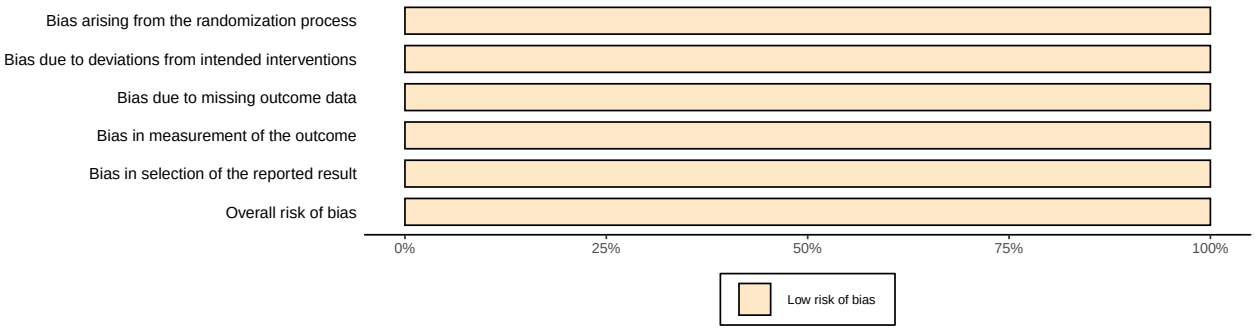
4.4 Functional status (end of treatment)

4.4.1 Forest plot

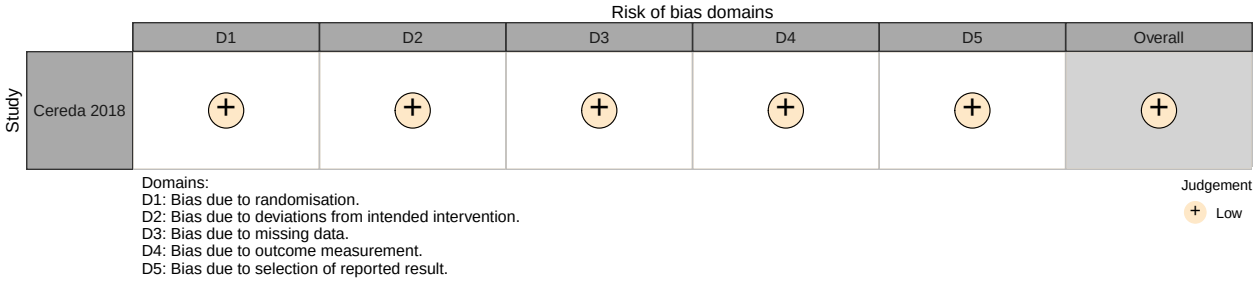


4.4.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



4.4.3 Risk of bias assessments by study

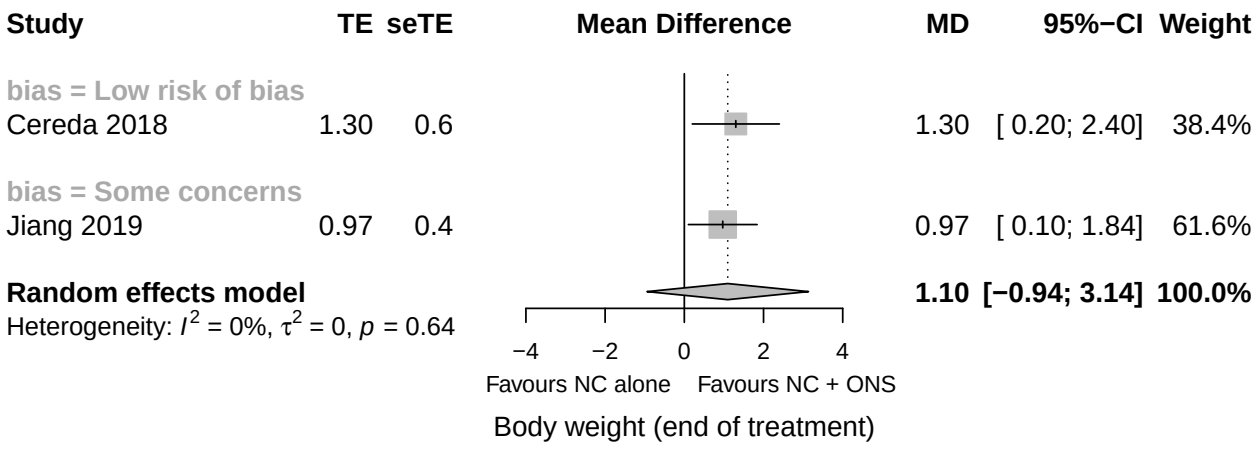


4.5 Body weight (end of treatment)

4.5.1 Main analysis

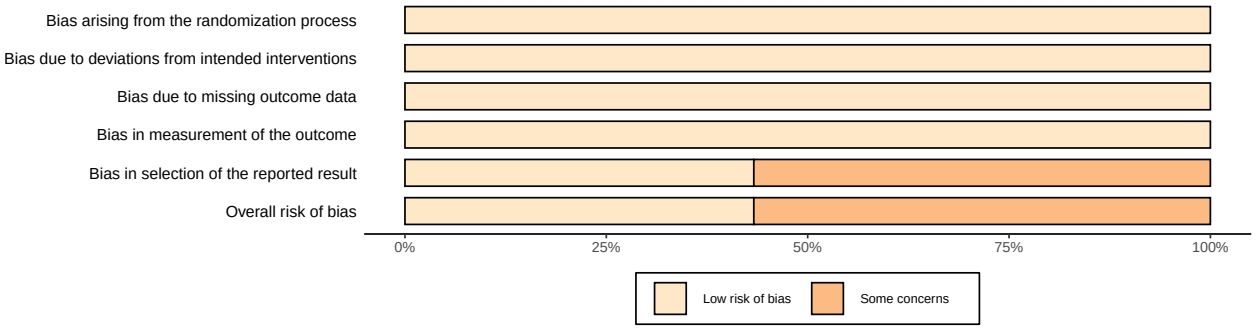
Including only results at most at some concerns of bias.

4.5.1.1 Forest plot



4.5.1.2 Proportion of information at each level of risk of bias

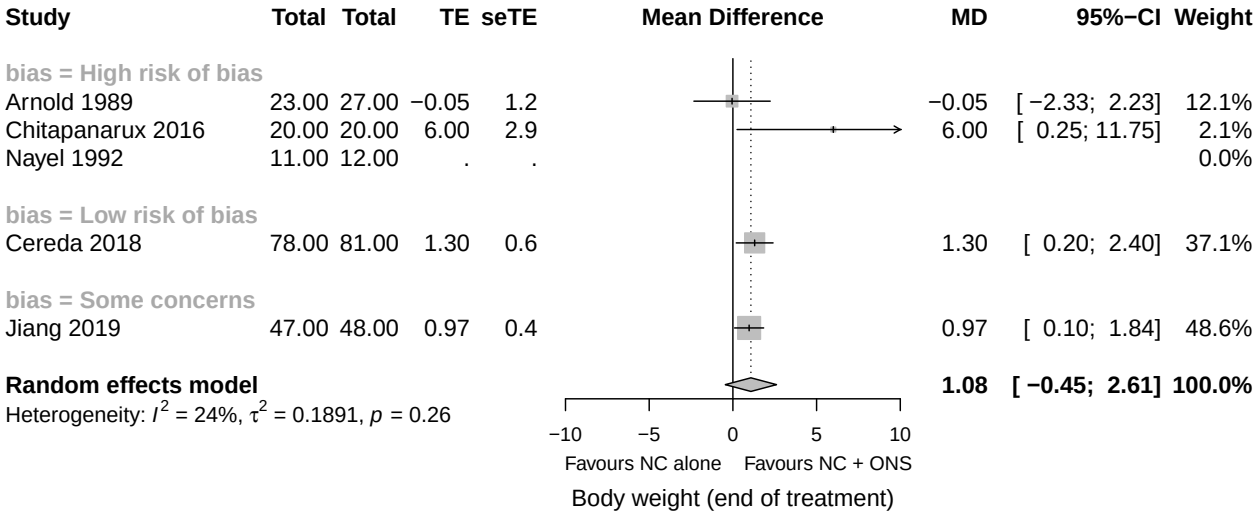
Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



4.5.2 Sensitivity analysis 1

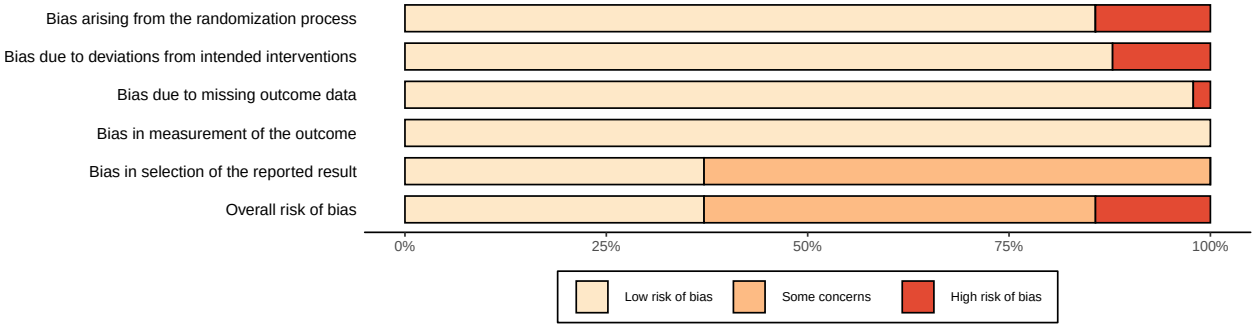
Including all available results.

4.5.2.1 Forest plot

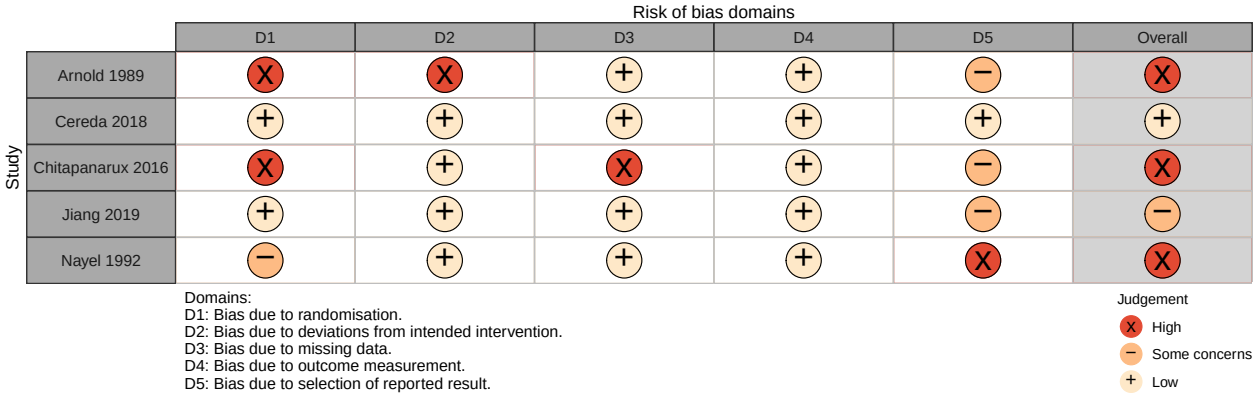


4.5.2.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



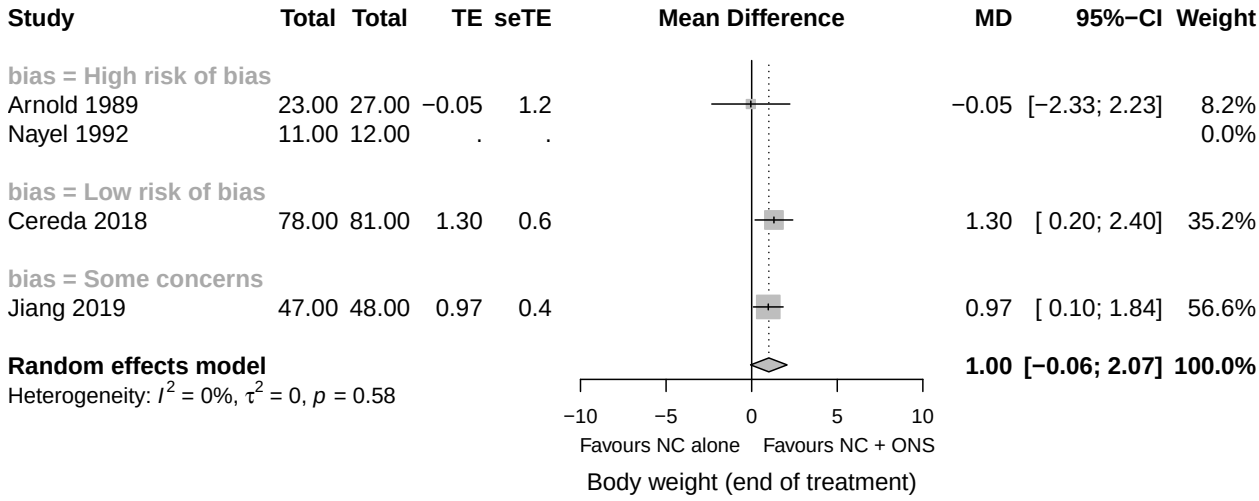
4.5.2.3 Risk of bias assessments by study



4.5.3 Sensitivity analysis 2

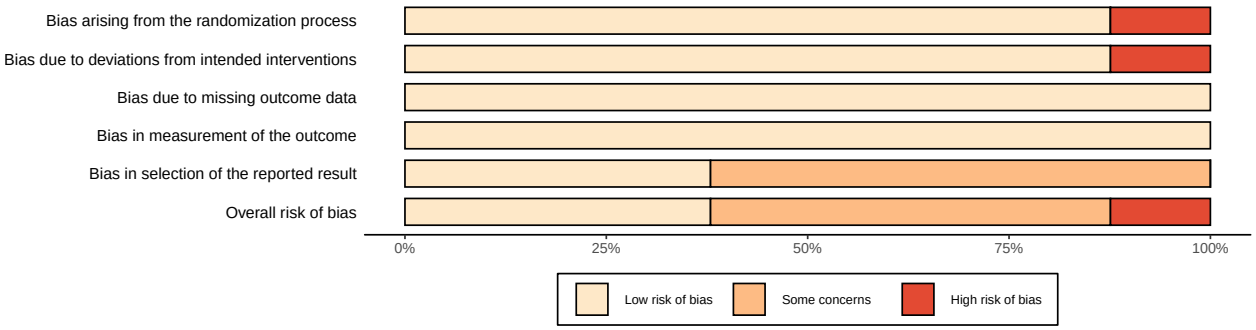
Excluding Chitapanarux 2016, because mean and standard deviation for this study were inputted (as described in the methods section of the primary report).

4.5.3.1 Forest plot

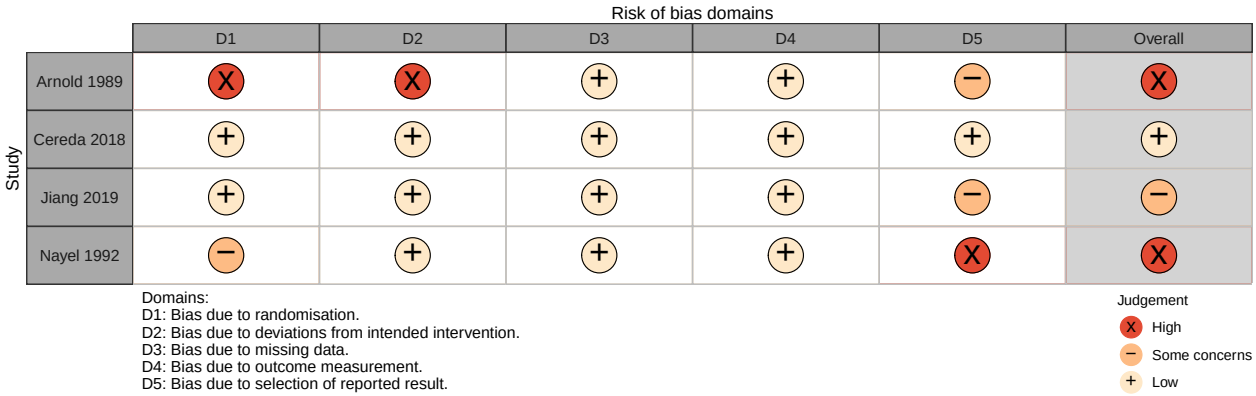


4.5.3.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

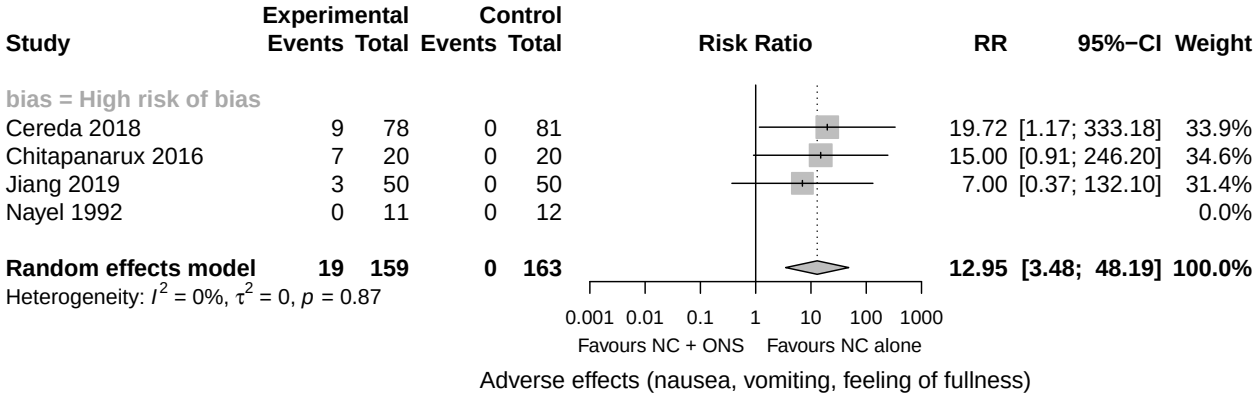


4.5.3.3 Risk of bias assessments by study



4.6 Adverse effects

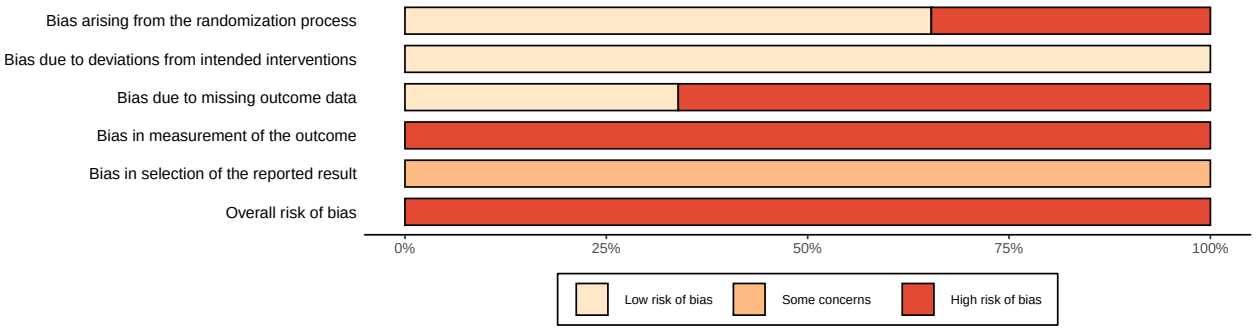
4.6.1 Forest plot



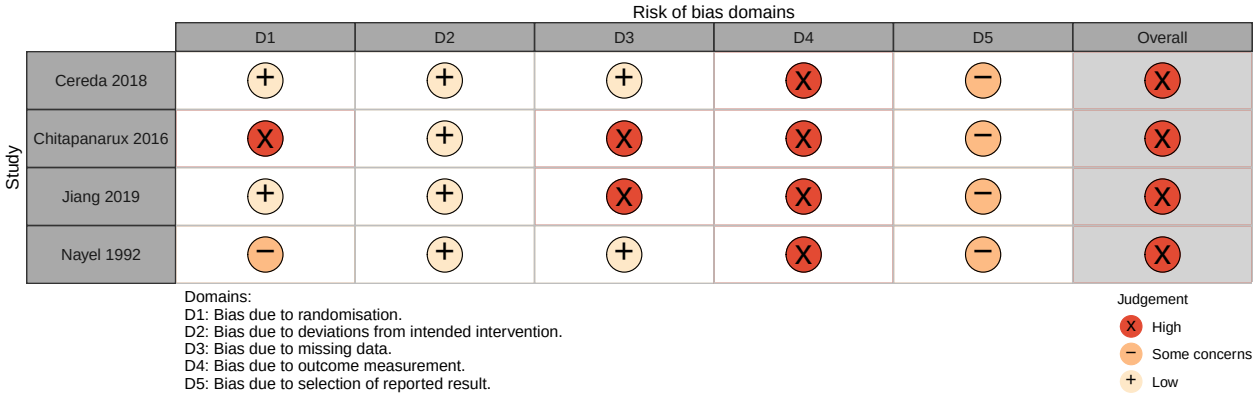
Adverse effects (nausea, vomiting, feeling of fullness)

4.6.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



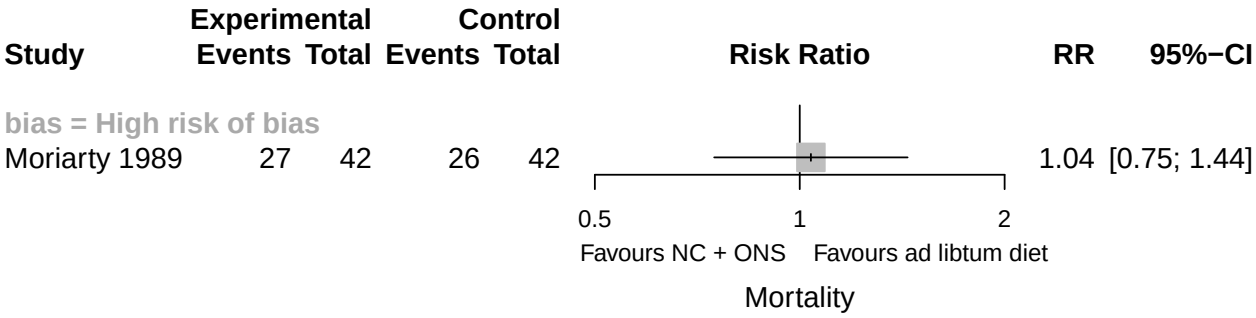
4.6.3 Risk of bias assessments by study



5 Comparison 2

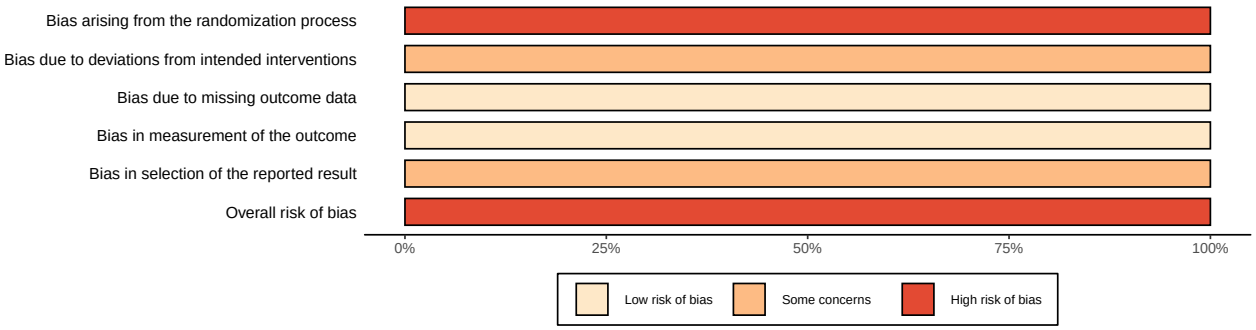
5.1 Mortality

5.1.1 Forest plot

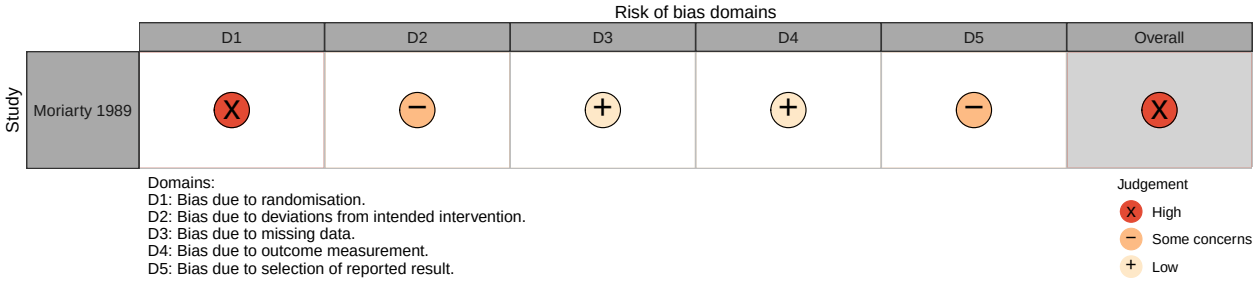


5.1.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



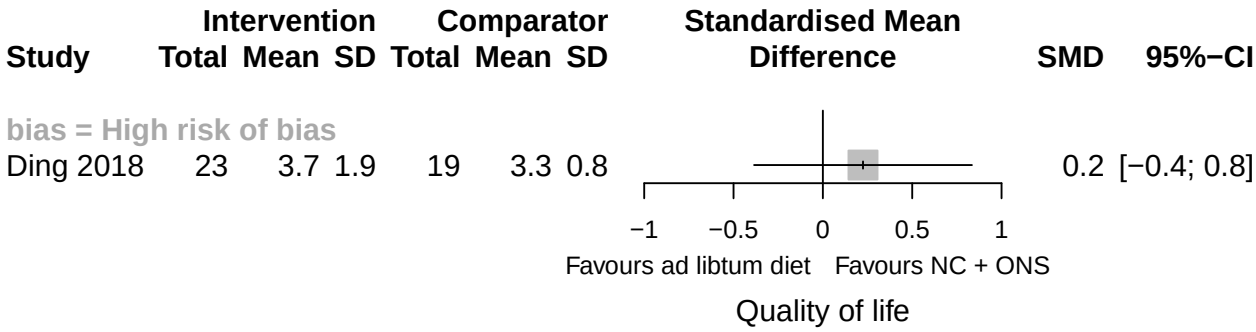
5.1.3 Risk of bias assessments by study



5.2 Quality of life (end of treatment)

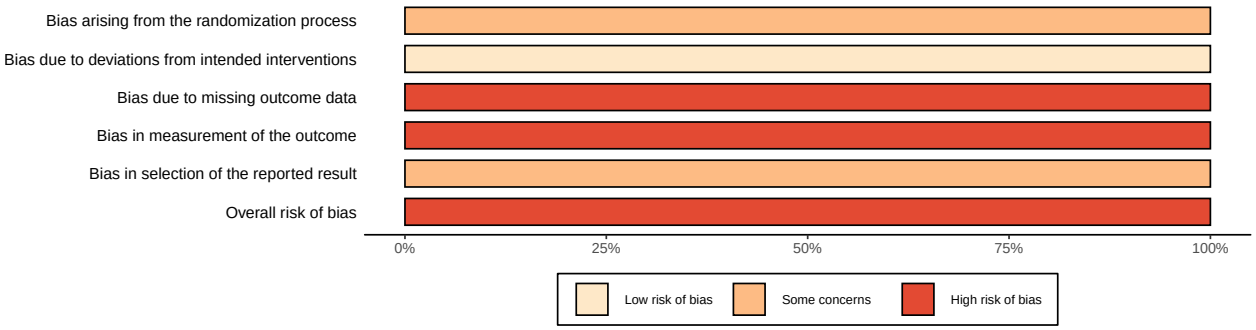
5.2.1 Global quality of life

5.2.1.1 Forest plot

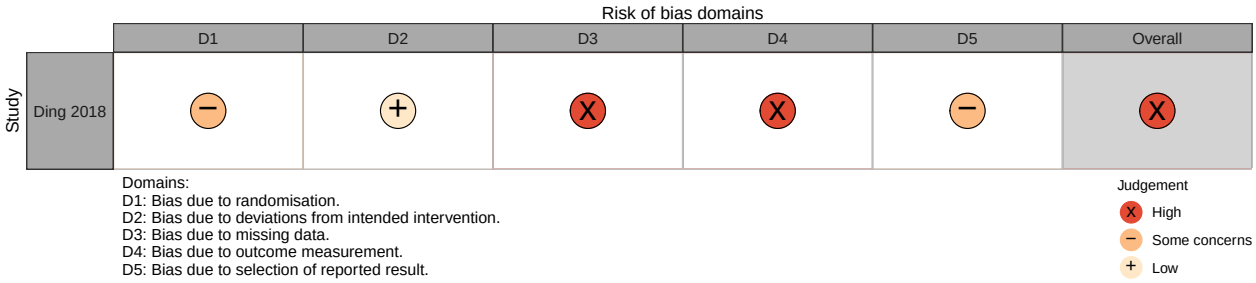


5.2.1.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

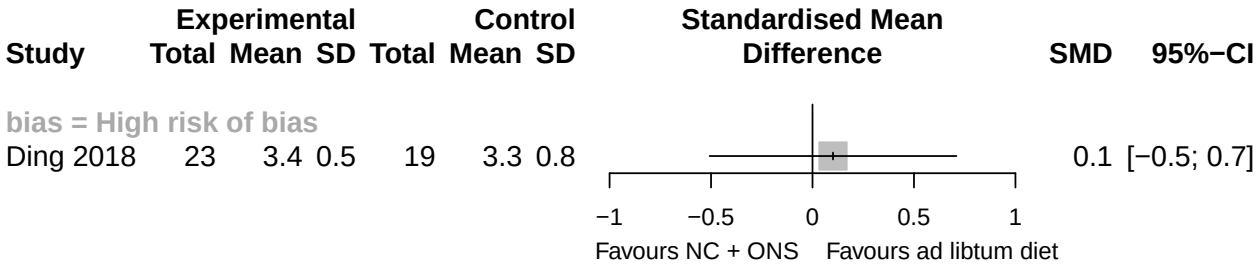


5.2.1.3 Risk of bias assessments by study

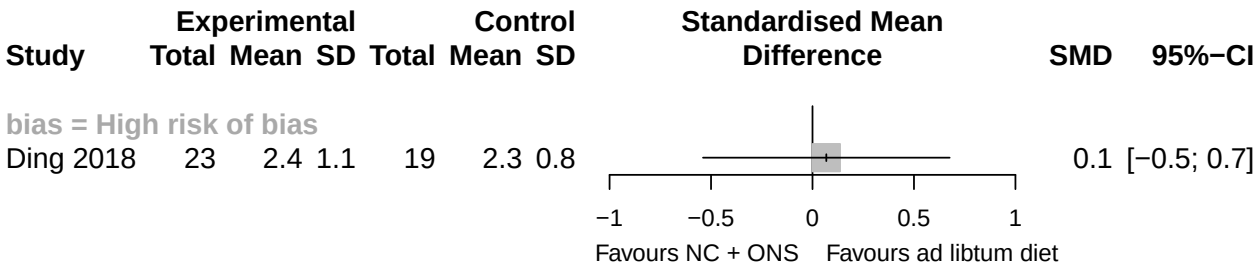


5.2.2 Quality of life subscales

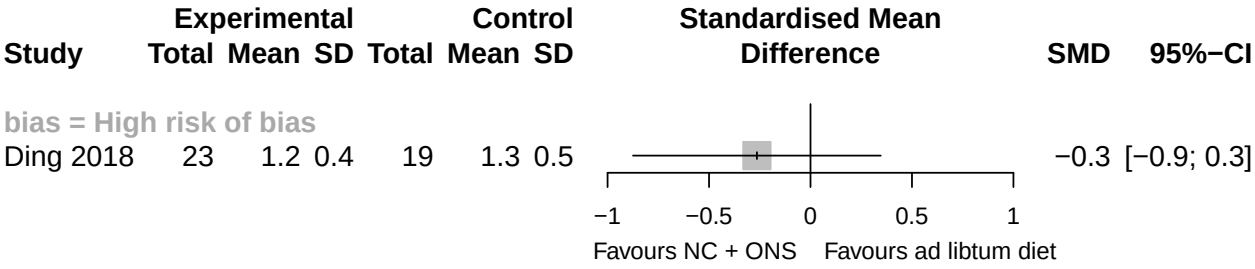
5.2.2.1 Appetite loss



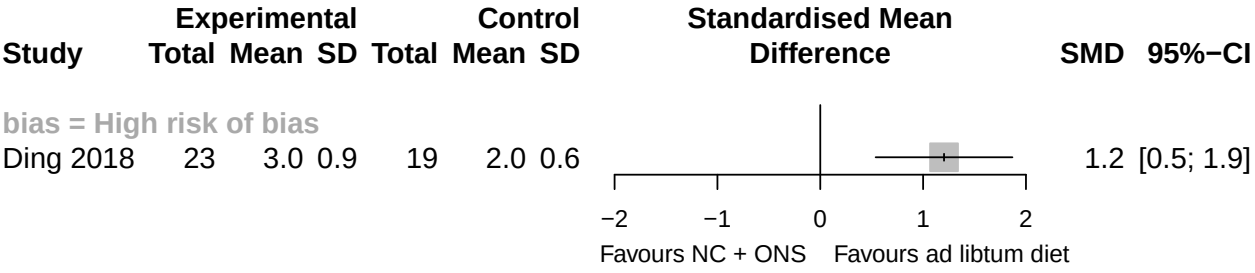
5.2.2.2 Constipation



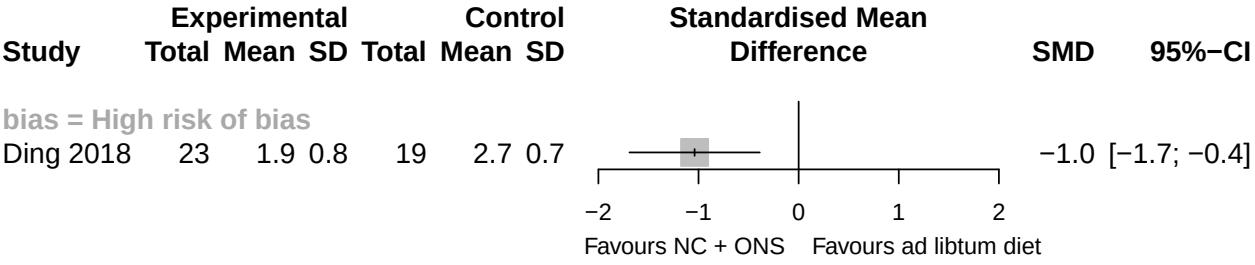
5.2.2.3 Diarrhoea



5.2.2.4 Nausea

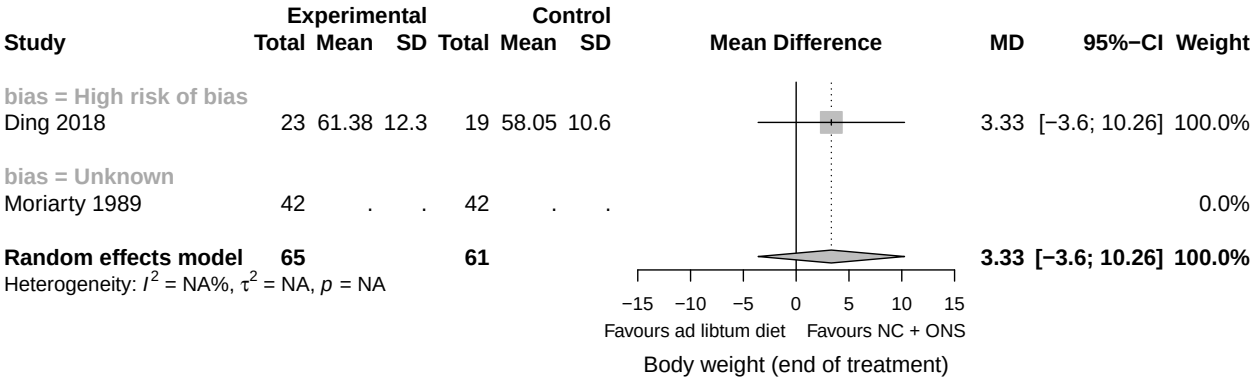


5.2.2.5 Pain



5.3 Body weight (end of treatment)

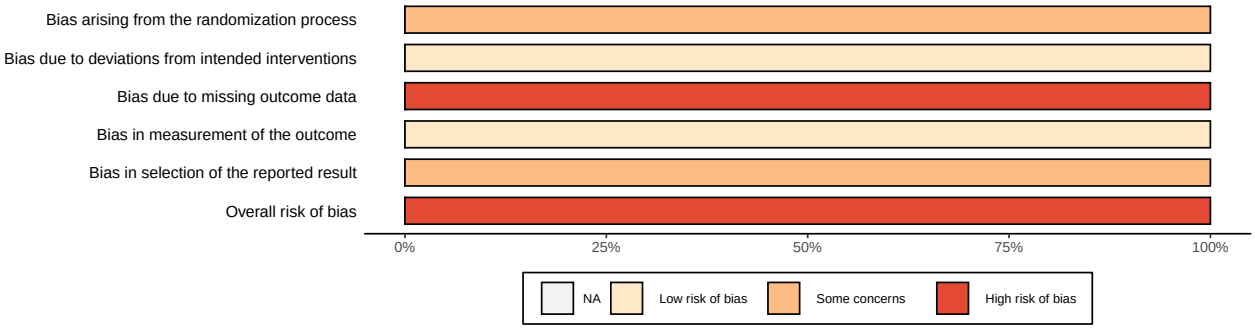
5.3.1 Forest plot



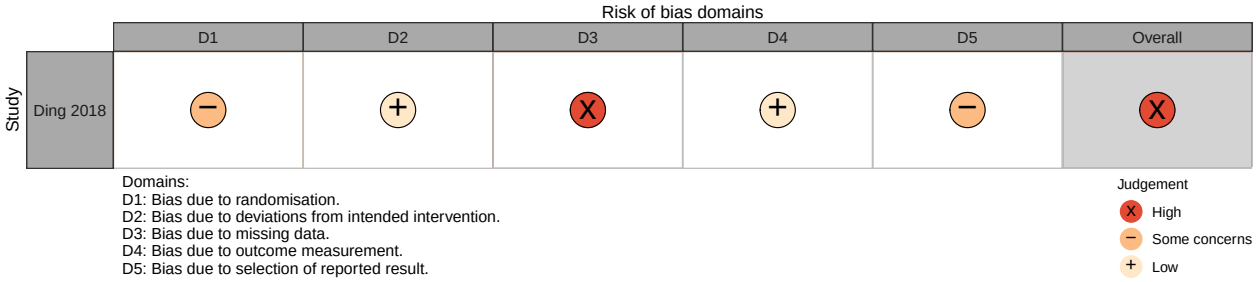
Moriarty 1981 measured body weight but only reported the result as statistically non-significant, so it could not be included in a meta-analysis.

5.3.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



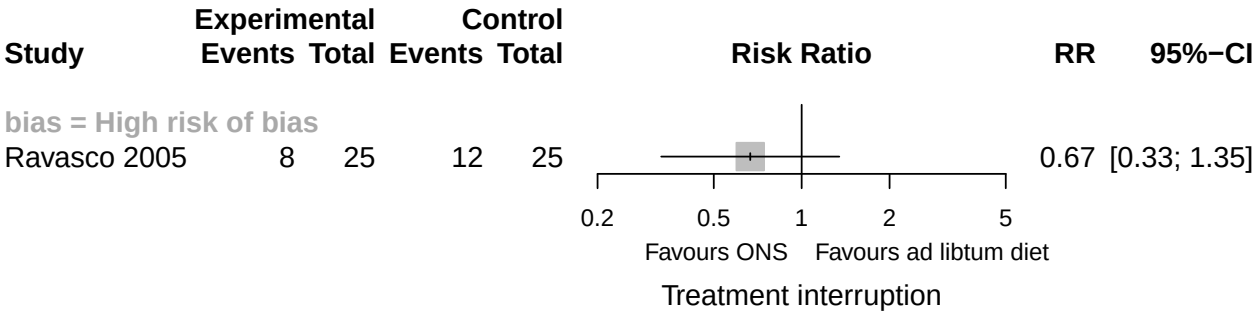
5.3.3 Risk of bias assessments by study



6 Comparison 3

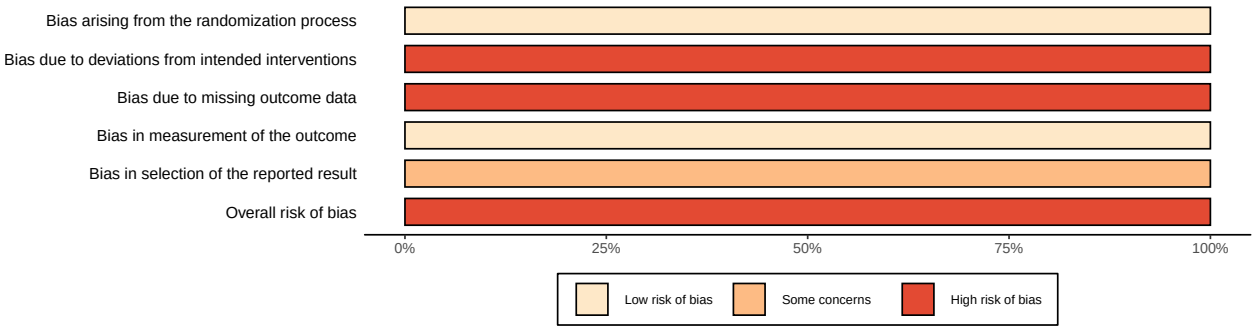
6.1 Mortality

6.1.1 Forest plot

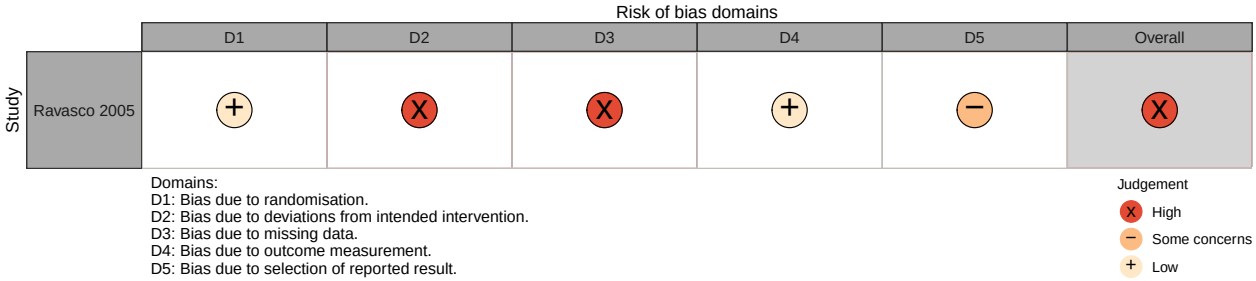


6.1.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

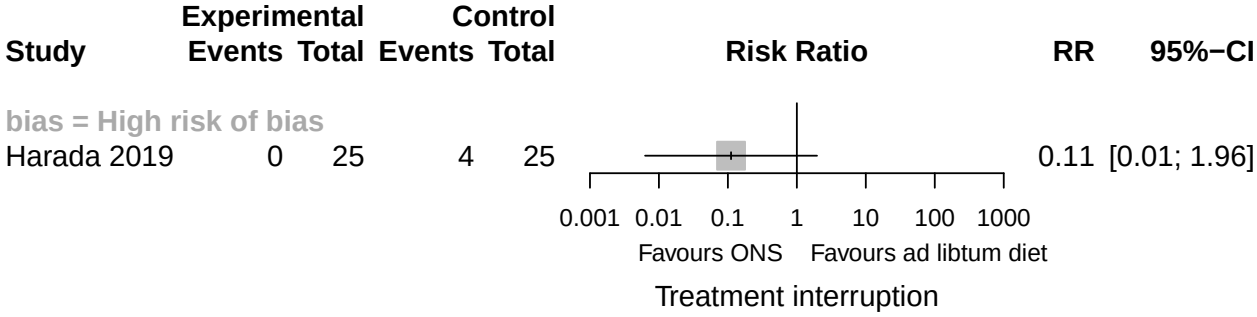


6.1.3 Risk of bias assessments by study



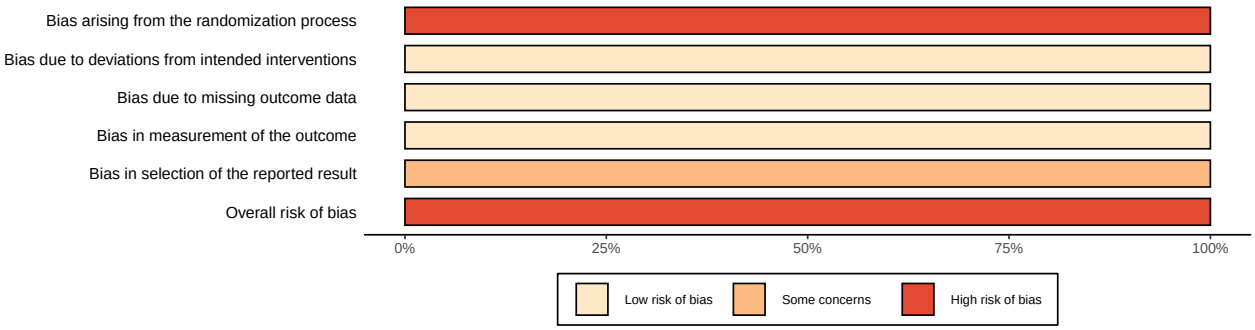
6.2 Interruption of treatment

6.2.1 Forest plot

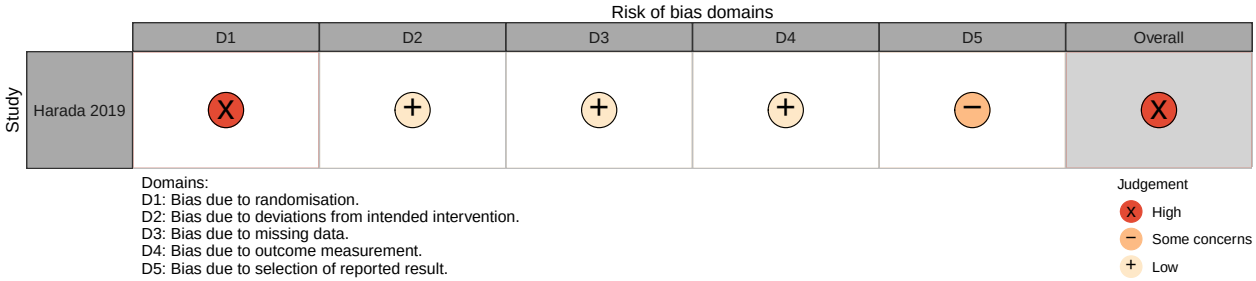


6.2.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

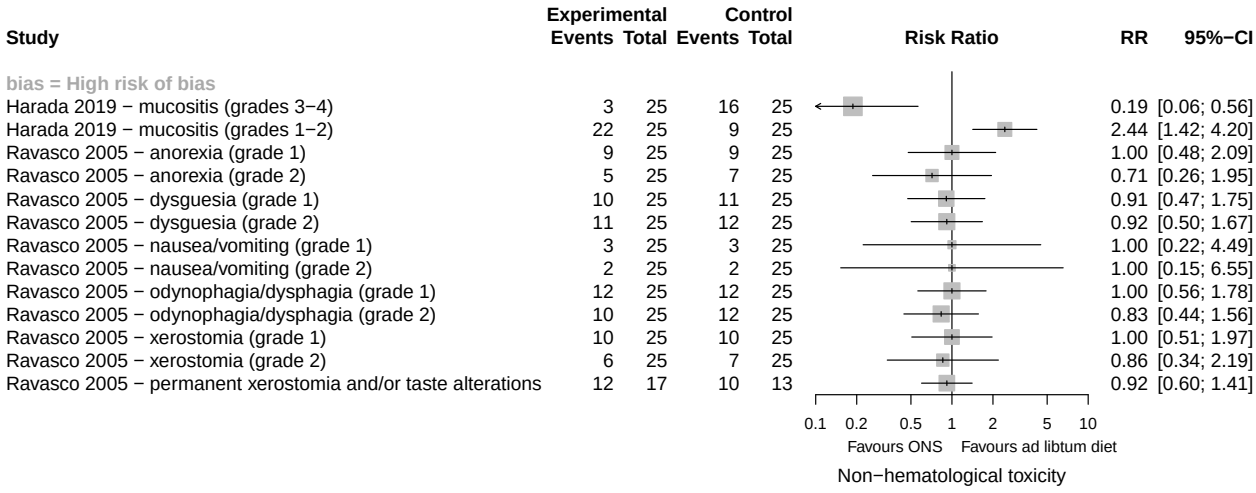


6.2.3 Risk of bias assessments by study

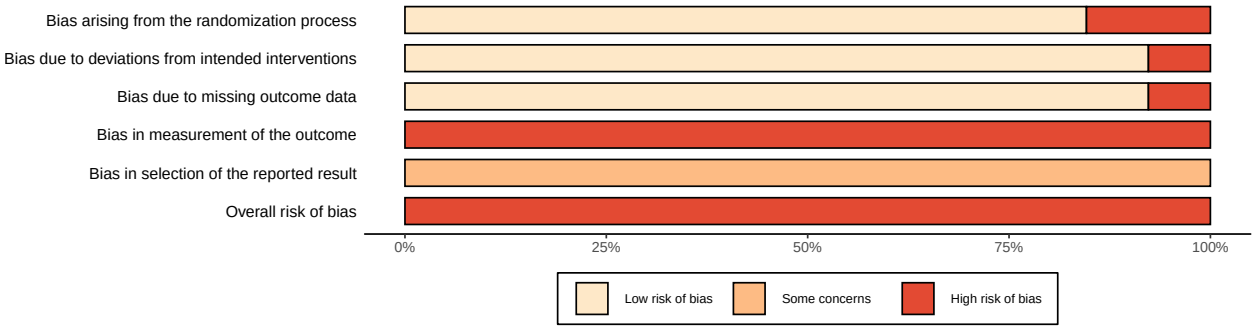


6.3 Summary of non-hematological toxicity outcomes

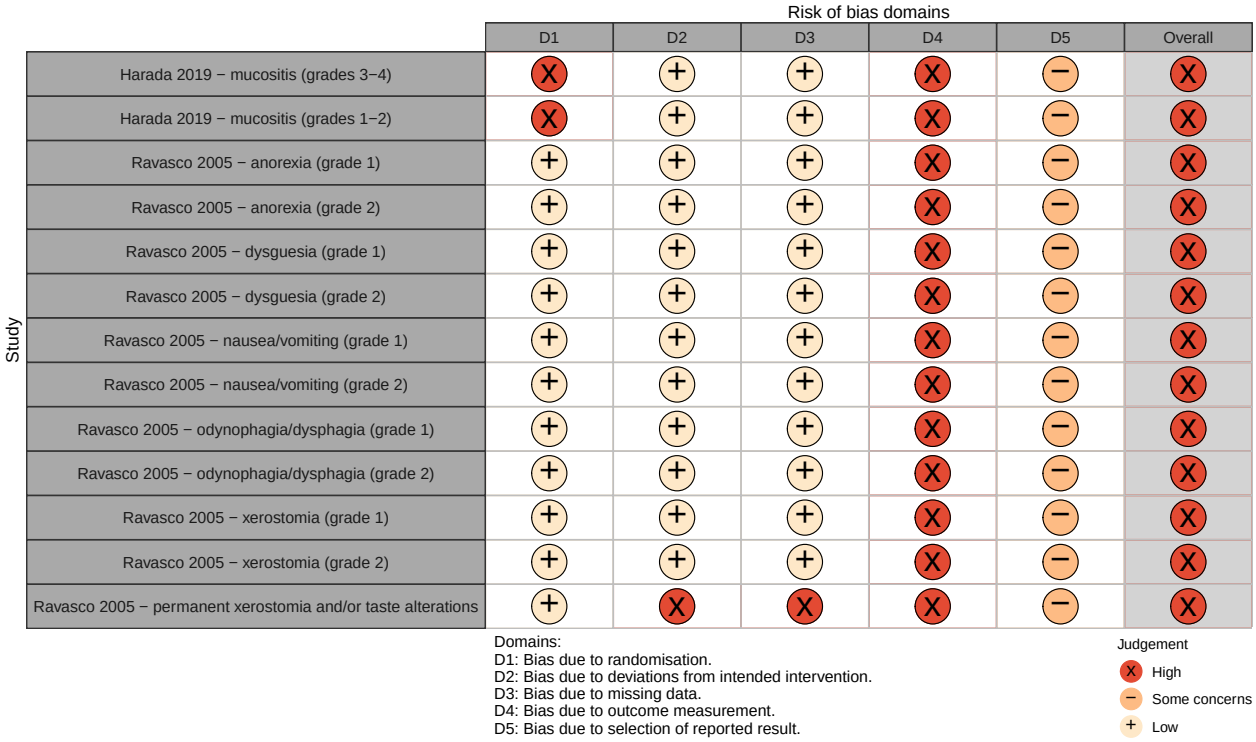
6.3.1 Forest plot



6.3.2 Proportion of the summary at each level of risk of bias

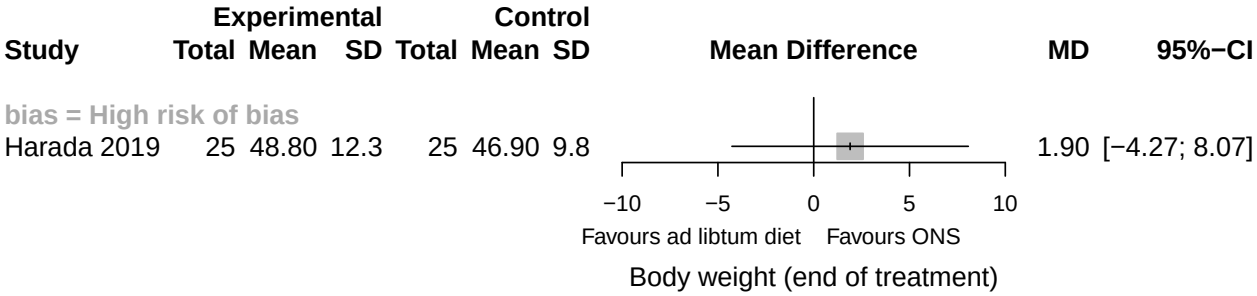


6.3.3 Risk of bias assessments by study



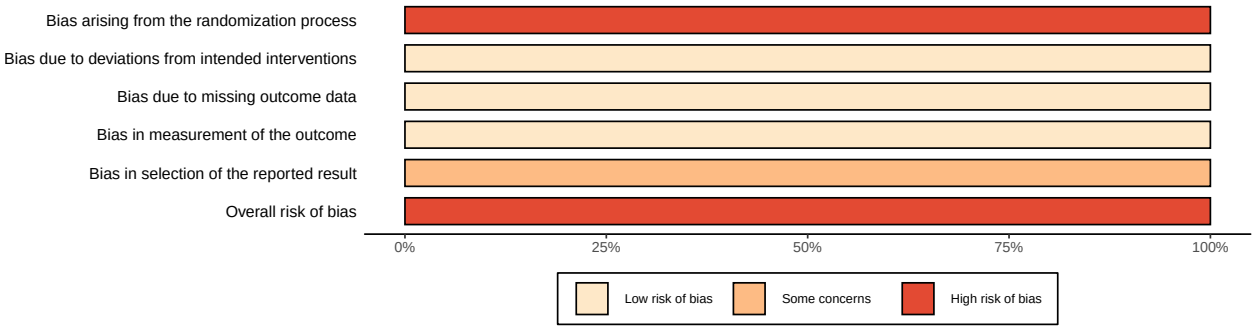
6.4 Body weight (end of treatment)

6.4.1 Forest plot

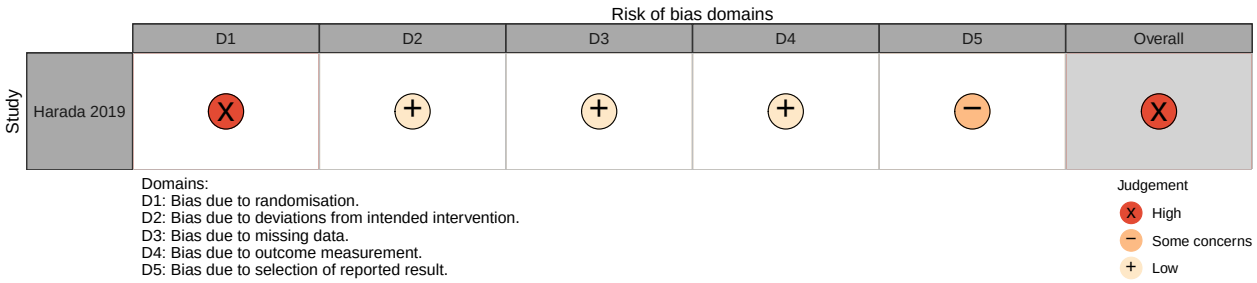


6.4.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)



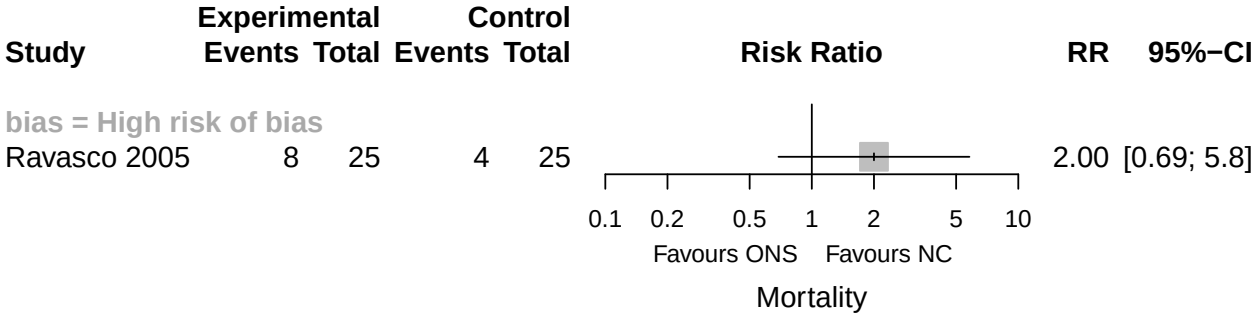
6.4.3 Risk of bias assessments by study



7 Comparison 4

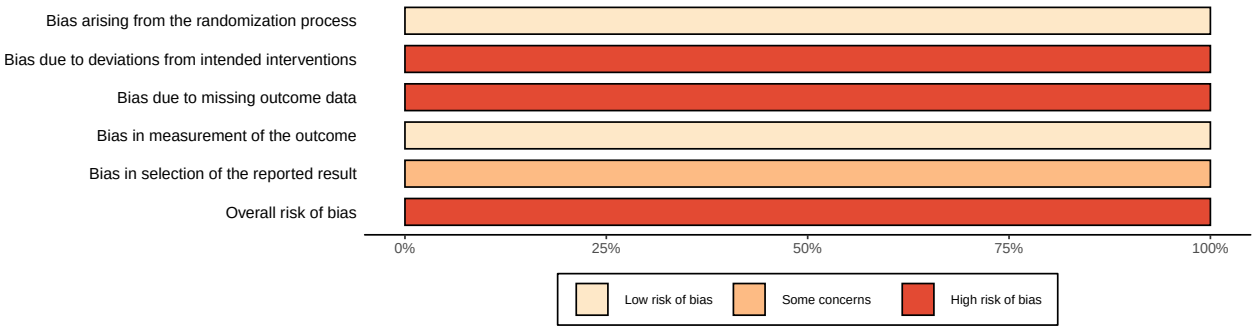
7.1 Mortality

7.1.1 Forest plot

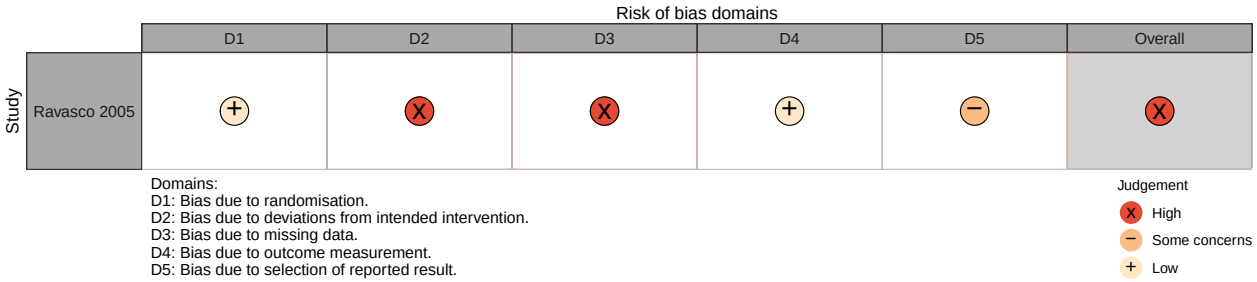


7.1.2 Proportion of information at each level of risk of bias

Risk of bias assessments are weighted by the relative contribution of each study to the meta-analysis result (when applicable)

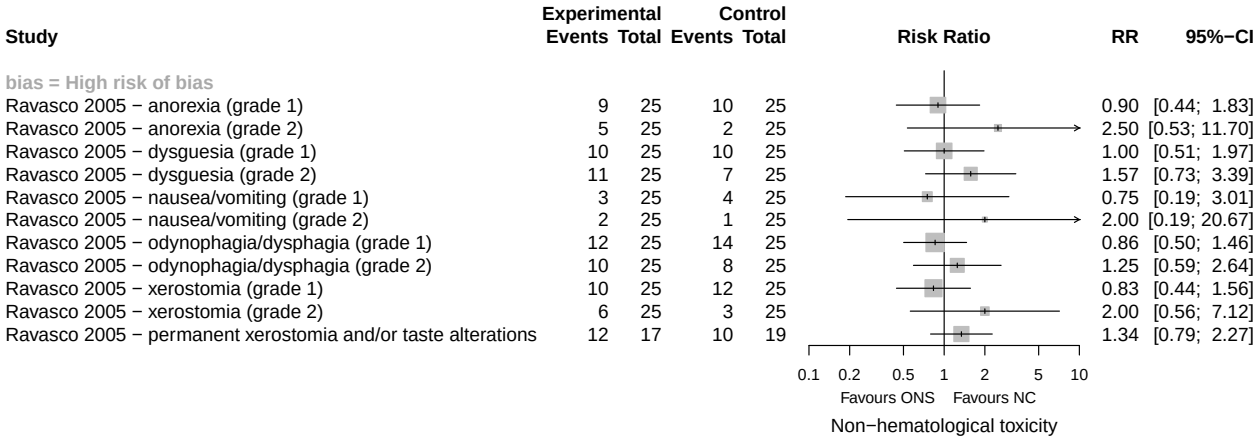


7.1.3 Risk of bias assessments by study

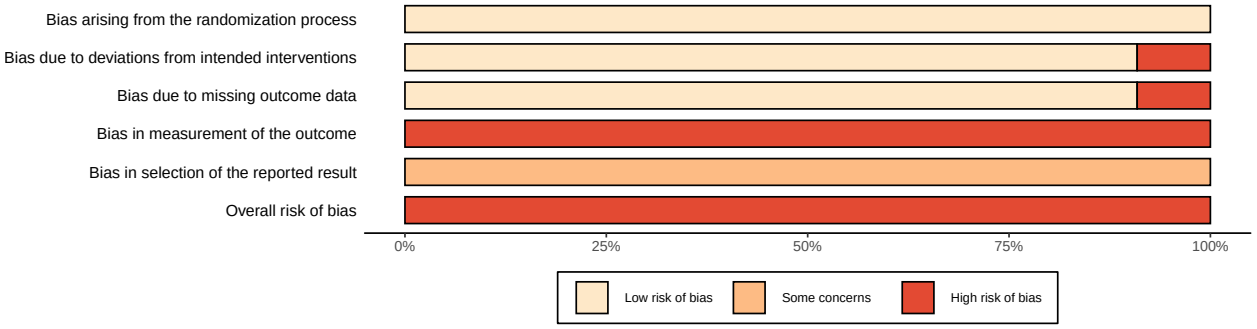
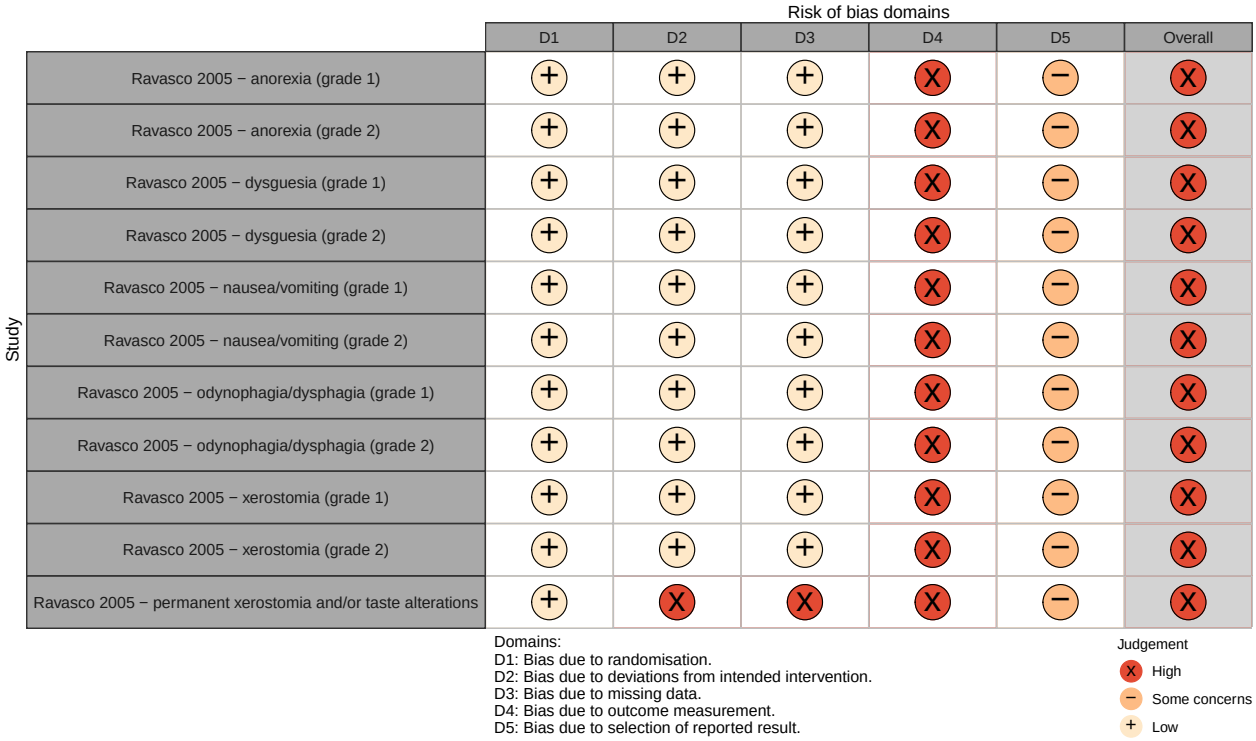


7.2 Summary of non-hematological toxicity outcomes

7.2.1 Forest plot



7.2.2 Proportion of the summary at each level of risk of bias



7.2.3 Risk of bias assessments by study