'Summary of findings' tables in network meta-analysis (NMA)

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Outline

Part 1. Learning objective and introduction to NMA

- Objective
- What is an NMA
- Ranking of treatments
- NMA certainty in evidence assessment
- Summary of Findings (SoF) tables in Systematic Reviews and Meta-analysis
Outline

Part 2. NMA-SoF table
   Introduction to the NMA-SoF table project

Part 3. NMA-SoF table examples

Part 4. Q&A
Part 1

LEARNING OBJECTIVE AND INTRODUCTION TO NMA
Learning objective

• To gain familiarity in interpreting findings of network meta-analysis (NMA) through NMA ‘Summary of findings’ (SoF) tables developed based on principles of the GRADE approach to rating certainty of evidence from NMAs
WHAT IS AN NMA?
Introduction to NMA

Absence of direct comparison between A and B

A
Bupropion

B
Nicotine replacement therapy

C
Placebo
Introduction to NMA

A
Bupropion

B
Bupropion

C
Nicotine replacement therapy

28 RCTs
OR = 0.90 (0.61-1.34)

1 RCT
OR = 0.48 (0.28-0.82)

19 RCTs
OR = 0.57 (0.48-0.67)

Combined Direct vs. Indirect
OR = 0.68 (0.37-1.25)

9 RCTs
OR = 0.51 (0.36-0.73)

Placebo

8
WHAT ARE RANKING TREATMENTS?
Ranking Treatments

Graphical
Ranking Treatments

### Numerical

<table>
<thead>
<tr>
<th>Rank</th>
<th>Treatment</th>
<th>SUCRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Balanced crystalloid</td>
<td>84.1%</td>
</tr>
<tr>
<td>2</td>
<td>Albumin</td>
<td>74.5%</td>
</tr>
<tr>
<td>3</td>
<td>Heavy starch</td>
<td>45.4%</td>
</tr>
<tr>
<td>4</td>
<td>Gelatin</td>
<td>37.7%</td>
</tr>
<tr>
<td>5</td>
<td>Saline</td>
<td>34.2%</td>
</tr>
<tr>
<td>6</td>
<td>Light starch</td>
<td>24.0%</td>
</tr>
</tbody>
</table>

*SUCRA surface under the cumulative ranking curve*

<table>
<thead>
<tr>
<th>Nodes and Fluids</th>
<th>Median ranks (95% CrI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Six node analysis</td>
<td></td>
</tr>
<tr>
<td>Balanced crystalloid</td>
<td>2.00 (1.00, 4.00)</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.00 (1.00, 5.00)</td>
</tr>
<tr>
<td>Heavy starch</td>
<td>4.00 (2.00, 6.00)</td>
</tr>
<tr>
<td>Gelatin</td>
<td>4.00 (1.00, 6.00)</td>
</tr>
<tr>
<td>Saline</td>
<td>5.00 (3.00, 6.00)</td>
</tr>
<tr>
<td>Light starch</td>
<td>5.00 (1.00, 6.00)</td>
</tr>
</tbody>
</table>

Median and 95% CrI for the rank of each treatment
HOW TO ASSESS NMA CERTAINTY (QUALITY) IN EVIDENCE WITH GRADE?
• Grading system in health-care to assess the quality (or certainty) of evidence and strength of recommendations
Determinants of certainty in a body of evidence

• A body of evidence starts as: high | ☐☐☐☐☐

• 5 factors that can lower quality

1. Risk of bias criteria
   • Lack of randomization (non-randomized or observational studies) lowers confidence to low

2. Inconsistency (or heterogeneity)

3. Indirectness (PICO and applicability)

4. Imprecision

5. Publication bias
Determinants of certainty in a body of evidence:

- 3 factors can increase quality
  1. large magnitude of effect
  2. opposing plausible residual bias or confounding
  3. dose-response gradient
NMA certainty in evidence

High certainty and *direct* evidence contributes as much as indirect evidence.

**Rate CiE *direct* estimates**
- Risk of Bias
- Inconsistency
- Indirectness
- Publication bias

**Rate CiE *indirect* estimates**
- Transitivity
- Lowest of the ratings of the two direct comparisons forming the most dominant first-order loop

**Rate CiE NMA estimates**
- Incoherence
- Imprecision

Not sufficient evidence, moderate, low or very low certainty.
SUMMARY of FINDINGS (SoF) TABLES IN SYSTEMATIC REVIEWS AND META-ANALYSES
SoF tables in Systematic Reviews and Meta-analysis

Elements of a GRADE SoF table

### Probiotics compared to no probiotics in INFANTS for the prevention of allergies

<table>
<thead>
<tr>
<th>Patient or population: INFANTS for the prevention of allergies</th>
<th>Setting: outpatient</th>
<th>Intervention: probiotics</th>
<th>Comparison: no probiotics</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Certainty</th>
<th>What happens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma / wheezing - infants follow up: range 6 to 24 months to N of participants: 412 (3 RCTs)</td>
<td>RR 1.04 (0.63 to 1.70)</td>
<td>12.1%</td>
<td>12.6% (7.6 to 20.6)</td>
<td>0.5% more (4.5 fewer to 8.5 more)</td>
</tr>
<tr>
<td>Adverse effects follow up: range 6 to 24 months to N of participants: 187 (2 RCTs)</td>
<td>RR 1.27 (0.51 to 3.18)</td>
<td>53.2%</td>
<td>67.6% (27.1 to 100.0)</td>
<td>14.4% more (26.1 fewer to 116 more)</td>
</tr>
</tbody>
</table>

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio; SMD: Standardised mean difference

### GRADE Working Group grades of evidence

- **High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect.
- **Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- **Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
- **Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

### Explanations

a. Concerns with high risk of bias for allocation concealment and blinding. Unclear risk of bias in random allocation and adequate follow-up.
b. Clinical heterogeneity due to high risk vs average risk of allergies and different probiotics among studies.
c. Confidence interval does not exclude appreciable benefit or harm.
d. One study with unclear description of randomization process, allocation concealment, blinding and follow-up.
# SoF tables in Systematic Reviews and Meta-analysis

## Elements of a GRADE SoF table

**Probiotics compared to no probiotics in INFANTS for the prevention of allergies**

**Bibliography:** WAO systematic review

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>N of participants (studies) Follow-up</th>
<th>Certainty of the evidence (GRADE)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma / wheezing - infants follow up: range 6 to 24 months</td>
<td>412 (3 RCTs)</td>
<td>✖️✖️✖️ ➤ VERY LOW</td>
<td>RR 1.04 (0.63 to 1.70)</td>
<td>121 per 1,000</td>
</tr>
<tr>
<td>Adverse effects follow up: range 6 to 24 months</td>
<td>187 (2 RCTs)</td>
<td>✖️✖️✖️ ➤ VERY LOW</td>
<td>RR 1.27 (0.51 to 3.18)</td>
<td>532 per 1,000</td>
</tr>
</tbody>
</table>

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).*

CI: Confidence interval; RR: Risk ratio; SMD: Standardised mean difference

**GRADE Working Group grades of evidence**

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**Explanations**

- a. Concerns with high risk of bias for allocation concealment and blinding. Unclear risk of bias in random allocation and adequate follow-up
- b. Clinical heterogeneity due to high risk vs average risk of allergies and different probiotics among studies.
- c. Confidence interval does not exclude appreciable benefit or harm
- d. One study with unclear description of randomization process, allocation concealment, blinding and follow-up
SoF tables in Systematic Reviews and Meta-analysis

Elements of a SoF table

<table>
<thead>
<tr>
<th>Probiotics compared to no probiotics in INFANTS for the prevention of allergies</th>
</tr>
</thead>
</table>
| **Patient or population:** INFANTS for the prevention of allergies
**Setting:** outpatient
**Intervention:** probiotics
**Comparison:** no probiotics |

<table>
<thead>
<tr>
<th>Outcomes</th>
<th><strong>Anticipated absolute effects</strong>* (95% CI)</th>
<th><strong>Relative effect (95% CI)</strong></th>
<th><strong>No of participants (studies)</strong></th>
<th><strong>Certainty of the evidence (GRADE)</strong></th>
<th><strong>Comments</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma / wheezing - infants follow up: range 6 to 24 months to</td>
<td>121 per 1,000 (76 to 206)</td>
<td><strong>RR 1.04</strong> (0.63 to 1.70)</td>
<td>412 (3 RCTs)</td>
<td>☒○○○○ VERY LOW a,b,c</td>
<td></td>
</tr>
<tr>
<td>Adverse effects follow up: range 6 to 24 months to</td>
<td>532 per 1,000 (271 to 1,000)</td>
<td><strong>RR 1.27</strong> (0.51 to 3.18)</td>
<td>187 (2 RCTs)</td>
<td>☒○○○○ VERY LOW b,c,d</td>
<td></td>
</tr>
</tbody>
</table>

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

**CI:** Confidence interval; **RR:** Risk ratio; **SMD:** Standardised mean difference

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**GRADE Working Group grades of evidence**

**High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

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**Explanations**

a. Concerns with high risk of bias for allocation concealment and blinding. Unclear risk of bias in random allocation and adequate follow-up
b. Clinical heterogeneity due to high risk vs average risk of allergies and different probiotics among studies.
c. Confidence interval does not exclude appreciable benefit or harm
d. One study with unclear description of randomization process, allocation concealment, blinding and follow-up
Part 2

NMA-SOF TABLE

Introduction to the NMA-SoF table project
NMA [GRADE] SoF table format
NMA-SoF TABLE: WHY?
Introduction NMA-SoF table project

- No standardized Network metaanalysis (NMA) Summary of Findings (SoF) table format

Presentational approaches used in the UK for reporting evidence synthesis using indirect and mixed treatment comparisons

Sze Huey Tan¹, Sylwia Bujkiewicz², Alexander Sutton³, Pascale Dequen⁴ and Nicola Cooper⁵

Reporting of results from network meta-analyses: methodological systematic review

Aida Bahia PhD student¹, Ludovic Trinquart postdoctoral research fellow¹ ² ³ ⁴, Raphaële Seror associate professor of rheumatology¹ ³ ⁴, Philippe Ravaud professor of epidemiology and director¹ ² ³ ⁴

What Guidance Are Researchers Given on How to Present Network Meta-Analyses to End-Users such as Policymakers and Clinicians? A Systematic Review

Shannon M. Sullivan¹, Doug Coyle², George Wells¹ ²

Characteristics and knowledge synthesis approach for 456 network meta-analyses: a scoping review

Wasifa Zarin¹, Areti Angeliki Veroniki¹, Vera Ninačić¹, Afshin Vafaei¹, Emily Reymen¹, Sanobir S. Motiwala¹, Jesmin Antony¹, Shannon M. Sullivan¹, Patricia Rios¹, Caitlin Daly¹, Joycelyn Ewisie¹, Maria Petropoulou², Adriani Nikolakopoulou², Anna Chaimani², Georgia Salanti² ³ ⁴, Sharon E. Straus¹ ³ ⁴ and Andrea C. Tricco¹ ² ⁴
WHAT IS THE OPTIMAL PRESENTATION OF RESULTS OF NMA REPORTS?
PICO information

Interpretation of findings

Ranking treatments

Certainty of evidence

NMA graphic

Data presentation
NMA-SoF TABLE FORMAT
# NMA-SoF table example 1

## Estimates of effects, credible intervals, and certainty of the evidence for comparison fluid resuscitation in patients with sepsis

**Bayesian NMA-SoF table**

<table>
<thead>
<tr>
<th>Patient or population:</th>
<th>Critically ill patients with severe sepsis or septic shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventions:</td>
<td>Balanced crystalloid (BC), Albumin, High-molecular-weight hydroxyethyl starch (H-HES), Saline solution, Gelatin</td>
</tr>
<tr>
<td>Comparator (reference):</td>
<td>Low-molecular weight hydroxyethyl starch (L-HES)</td>
</tr>
<tr>
<td>Outcome:</td>
<td>Mortality: range of follow up between 24 hours to 90 days</td>
</tr>
<tr>
<td>Setting(s):</td>
<td>Inpatient</td>
</tr>
</tbody>
</table>

### Total studies: 6 RCT Total Participants: 8303

<table>
<thead>
<tr>
<th>Relative effect** (95% CI)</th>
<th>Anticipated absolute effect*** (95% CI)</th>
<th>Certainty of evidence</th>
<th>Ranking**** (95% CI)</th>
<th>Interpretation of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Without intervention</strong></td>
<td><strong>With intervention</strong></td>
<td><strong>Difference</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balanced crystalloid</td>
<td>0.75 (0.56 to 0.97) Network estimate</td>
<td>180 per 1000</td>
<td>141 per 1000</td>
<td>Moderate Due to Inconsistencyf</td>
</tr>
<tr>
<td>(2 RCT; 846 participants)</td>
<td></td>
<td></td>
<td>39 per 1000 fewer</td>
<td>(from 67 fewer to 5 fewer)</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.79 (0.59 to 1.06) Network estimate</td>
<td>180 per 1000</td>
<td>148 per 1000</td>
<td>Low Due to Inconsistencyf</td>
</tr>
<tr>
<td>(No direct evidence, indirect evidence)</td>
<td></td>
<td></td>
<td>32 per 1000 fewer</td>
<td>(from 65 fewer to 88 more)</td>
</tr>
<tr>
<td>H-HES</td>
<td>0.91 (0.63 to 1.30) Network estimate</td>
<td>180 per 1000</td>
<td>164 per 1000</td>
<td>Low Due to Inconsistencyf</td>
</tr>
<tr>
<td>(No direct evidence, indirect evidence)</td>
<td></td>
<td></td>
<td>16 per 1000 fewer</td>
<td>(from 59 fewer to 46 more)</td>
</tr>
<tr>
<td>Saline solution</td>
<td>1.04 (0.87 to 1.25) Network estimate</td>
<td>180 per 1000</td>
<td>166 per 1000</td>
<td>Moderate Due to Inconsistencyf</td>
</tr>
<tr>
<td>(4 RCT; 7642 participants)</td>
<td></td>
<td></td>
<td>6 per 1000 fewer</td>
<td>(from 29 fewer to 35 more)</td>
</tr>
<tr>
<td>Gelatin</td>
<td>1.00 (0.44 to 2.21) Network estimate</td>
<td>180 per 1000</td>
<td>180 per 1000</td>
<td>Very Low Due to Inconsistencyf</td>
</tr>
<tr>
<td>(No direct evidence, indirect evidence)</td>
<td></td>
<td></td>
<td>9 per 1000 fewer</td>
<td>(from 52 fewer to 146 more)</td>
</tr>
<tr>
<td>L-HES</td>
<td>Reference Comparator</td>
<td>No estimable</td>
<td>No estimable</td>
<td>Reference Comparator</td>
</tr>
</tbody>
</table>

### NMA-SoF Table definitions

* Solid lines represent direct comparisons

** Network Meta-analysis (NMA) estimates are reported as odds ratio. CI: credible interval. Results are expressed in credible intervals as opposed to the confidence intervals (CI) since a Bayesian analysis has been conducted.**** Median and credible intervals are presented. Rank statistics is defined as the probabilities that a treatment out of n treatments in a network meta-analysis is the best, the second, the third and so on until the least effective treatment.

** Explanation:**

**GRADE Working Group grades of evidence (or certainty in the evidence)**

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate quality:** We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different from the estimate of the effect.

**Low quality:** We have some concerns that the true effect is different from the estimate of the effect.

**Very low quality:** We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.

**Explanatory Footnotes:**

1 Mortality is reported from a large randomized control trial where critically ill patients admitted to an intensive care unit (ICU) received fluid resuscitation with hydroxyethyl starch (HES).
2 Serious indirectness: The indirect evidence for this comparison goes through a second order loop via heavy starch and saline.
3 Serious indirectness: Due to wide confidence intervals in the indirect estimate.
4 Serious indirectness: The indirect evidence for this comparison goes through a first order loop via saline and saline vs. light starch.
5 Serious indirectness: Due to there was significant heterogeneity in the direct comparison of light starch vs. balanced crystalloid.
6 Serious indirectness: The indirect evidence for this comparison goes through a second order loop via balance crystalloid and heavy starch.
NMA-SoF table example 1

Estimates of effects, credible intervals, and certainty of the evidence for comparison fluid resuscitation in patients with sepsis

**Patient or population:** Critically ill patients with severe sepsis or septic shock  

**Interventions:** Balanced crystalloid (BC), Albumin, High-molecular weight hydroxyethyl starch (H-HES), Saline solution, Gelatin  

**Comparator (reference):** Low-molecular weight hydroxyethyl starch (L-HES)  

**Outcome:** Mortality; range of follow up between 24 hours to 90 days  

**Setting(s):** Inpatient

<table>
<thead>
<tr>
<th>Total studies: 6 RCT</th>
<th>Relative effect** (95% CrI)</th>
<th>Anticipated absolute effect*** (95% CrI)</th>
<th>Certainty of evidence</th>
<th>Ranking**** (95% CrI)</th>
<th>Interpretation of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without intervention</td>
<td>With intervention</td>
<td>Difference</td>
<td></td>
</tr>
<tr>
<td>Balanced crystalloid</td>
<td>0.75</td>
<td>(0.58 to 0.97)</td>
<td>180 per 1000</td>
<td>141 per 1000</td>
<td>39 per 1000 fewer (from 67 fewer to 5 fewer)</td>
</tr>
<tr>
<td>(2 RCT; 846 participants)</td>
<td>Network estimate</td>
<td></td>
<td>180 per 1000</td>
<td>141 per 1000</td>
<td>39 per 1000 fewer (from 67 fewer to 5 fewer)</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.79</td>
<td>(0.59 to 1.06)</td>
<td>180 per 1000</td>
<td>141 per 1000</td>
<td>32 per 1000 fewer (from 65 fewer to 88 more)</td>
</tr>
<tr>
<td>(No direct evidence, Indirect evidence only)</td>
<td>Network estimate</td>
<td></td>
<td>180 per 1000</td>
<td>141 per 1000</td>
<td>32 per 1000 fewer (from 65 fewer to 88 more)</td>
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<tr>
<td>H-HES</td>
<td>0.91</td>
<td>(0.63 to 1.33)</td>
<td>180 per 1000</td>
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</tr>
<tr>
<td>(No direct evidence, Indirect evidence only)</td>
<td>Network estimate</td>
<td></td>
<td>180 per 1000</td>
<td>141 per 1000</td>
<td>16 per 1000 fewer (from 59 fewer to 46 more)</td>
</tr>
</tbody>
</table>
# NMA-SoF table example 1

<table>
<thead>
<tr>
<th></th>
<th>1.04 (0.87 to 1.25)</th>
<th>180 per 1000(^1)</th>
<th>186 per 1000</th>
<th>6 per 1000 more (from 20 fewer to 35 more)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Saline solution</strong></td>
<td>Network estimate</td>
<td>4.00 (1.00 to 6.00)</td>
<td>moderately</td>
<td>Definitely inferior</td>
</tr>
<tr>
<td><em>(4 RCT; 7642 participants)</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gelatin</strong></td>
<td>1.00 (0.44 to 2.21)</td>
<td>180 per 1000(^1)</td>
<td>180 per (\times 000)</td>
<td>0 per 1000 fewer (from 92 fewer to 146 more)</td>
</tr>
<tr>
<td><em>(No direct evidence, indirect evidence only)</em></td>
<td>Network estimate</td>
<td>5.00 (3.00 to 6.00)</td>
<td>moderately</td>
<td>Definitely inferior</td>
</tr>
<tr>
<td><strong>L-HES</strong></td>
<td>Reference Comparator</td>
<td>No estimable</td>
<td>No estimable</td>
<td>No estimable</td>
</tr>
</tbody>
</table>

### Explanatory Footnotes

1. Mortality is reported from a large randomized control trial where critically ill patients admitted to an intensive care unit (ICU) required fluid resuscitation with hydroxyethyl starch (HES).
2. Serious indirectness. The indirect evidence for this comparison goes through a second order loop via heavy starch and saline.
3. Serious imprecision. Due to wide confidence intervals in the indirect estimate.
4. Serious indirectness. The indirect evidence for this comparison goes through a first order loop via saline and saline vs. light starch.
5. Serious inconsistency. Due to there was significant heterogeneity in the direct comparison of light starch vs. balanced crystalloid.
6. Serious indirectness. The indirect evidence for this comparison goes through a second order loop via balance crystalloid and heavy starch.

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### NMA-SoF table definitions

* Solid lines represent direct comparisons

** Network Metaanalysis (NMA) estimates are reported as odds ratio. CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence intervals (CI) since a Bayesian analysis has been conducted.

*** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risk of the intervention group with the risk of the control group.

**** Median and credible intervals are presented. Rank statistics is defined as the probabilities that a treatment out of \(n\) treatments in a network meta-analysis is the best, the second, the third and so on until the least effective treatment.

† Information is reported from studies included in the network metaanalysis for the comparison displays.

### GRADE Working Group grades of evidence (or certainty in the evidence)

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

**Very low quality:** We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect
## NMA-SoF table example 2

### Estimates of effects, credible intervals, and certainty of the evidence for chemoprevention of colorectal cancer in individuals with previous colorectal neoplasia

#### Benefits

**Patient or population:** Individuals with previous colorectal neoplasia  
**Interventions:** Low and high dose aspirin, nonaspirin non-steroidal anti-inflammatory drugs (NSAIDs), calcium, vitamin D, folic acid  
**Comparator (reference):** Placebo  
**Outcome:** Prevention of advanced neoplasia; range of follow up between three to five years  
**Setting:** Outpatient

#### Bayesian NMA-SoF table

<table>
<thead>
<tr>
<th>Total studies: 21 RCT</th>
<th>Relative effect** (95% Cr)</th>
<th>Anticipated absolute effect*** (95% Cr)</th>
<th>Certainty of evidence</th>
<th>Ranking**** (95% Cr)</th>
<th>Interpretation of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Participants: 12,088</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin + calcium + vitamin D (1 RCT, 427 participants)</td>
<td>0.71 (0.6 to 0.84)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>53 per 1,000**</td>
<td>Low Due to imprecision</td>
</tr>
<tr>
<td>Calcium + vitamin D (1 RCT, 1,028 participants)</td>
<td>0.91 (0.82 to 1.02)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>67 per 1,000**</td>
<td>Low Due to imprecision</td>
</tr>
<tr>
<td>Aspirin + folic acid (3 RCT, 916 participants)</td>
<td>0.73 (0.43 to 1.2)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>54 per 1,000**</td>
<td>Low Due to imprecision</td>
</tr>
<tr>
<td>Aspirin, high dose (3 RCT, 917 participants)</td>
<td>0.81 (0.56 to 1.28)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>65 per 1,000**</td>
<td>Low Due to imprecision</td>
</tr>
<tr>
<td>Aspirin, low dose (3 RCT, 623 participants)</td>
<td>0.71 (0.41 to 1.23)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>53 per 1,000**</td>
<td>Low Due to imprecision</td>
</tr>
<tr>
<td>Nonaspirin NSAIDs (4 RCT, 3,486 participants)</td>
<td>0.67 (0.24 to 0.55)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>27 per 1,000**</td>
<td>High** (1 to 2)</td>
</tr>
<tr>
<td>Vitamin D (1 RCT, 764 participants)</td>
<td>1.19 (0.55 to 2.2)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>88 per 1,000**</td>
<td>Low Due to imprecision</td>
</tr>
<tr>
<td>Calcium (3 RCT, 2,500 participants)</td>
<td>0.80 (0.49 to 1.26)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>74 per 1,000**</td>
<td>Low Due to imprecision</td>
</tr>
<tr>
<td>Folate (3 RCT, 1,224 participants)</td>
<td>1.32 (0.85 to 2.05)</td>
<td>Network estimate</td>
<td>74 per 1,000**</td>
<td>51 per 1,000**</td>
<td>Low Due to imprecision</td>
</tr>
<tr>
<td>Placebo Reference comparator</td>
<td>Reference comparator</td>
<td>No estimate</td>
<td>No estimate</td>
<td>No estimate</td>
<td>Reference comparator</td>
</tr>
</tbody>
</table>

#### NMA-SoF table definitions

* Line represents direct comparisons  
** Estimates are reported as odds ratio. CI: credible interval. Results are expressed as credible intervals as opposed to the confidence intervals (CI) since a Bayesian analysis has been conducted.  
*** Anticipated absolute effect. Anticipated absolute effect comparison two arms by calculating the difference between the risks of the intervention group with the risks of the control group.  
**** Surface under the cumulative (SUCRA) ranking and credible intervals for efficacy are presented. Rank statistic is defined as the probabilities that a treatment out of n treatments in a network meta-analysis is the best, second, the third and so on until the least effective treatment. 

#### GRADE Working Group grades of evidence (or certainty in the evidence)

- **High quality:** We are very confident that the true effect lies close to that of the estimate of the effect. 
- **Moderate quality:** We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different from the estimate of the effect. 
- **Low quality:** Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect. 

#### Exploratory Factors

- Baseline risks (assumed control risk) obtained from the National Cancer Institute pooling project.  
- Very serious imprecision since 95% CI overlaps with 1, and with wide credible intervals suggesting high possibility of harm.  
- Very serious imprecision since 95% CI overlapping with 1, and with wide credible intervals suggesting high possibility of harm.  
- Very serious imprecision since 95% CI overlapping with 1, and with wide credible intervals suggesting high possibility of harm.  
- Very serious imprecision since 95% CI overlapping with 1, and with wide credible intervals suggesting high possibility of harm.

---

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# NMA-SoF table example 2

Estimates of effects, credible intervals, and certainty of the evidence for chemoprevention of colorectal cancer in individuals with previous colorectal neoplasia

**BENEFITS**

**Patient or population:** Individuals with previous colorectal neoplasia

**Interventions:** Low and high dose aspirin, nonaspirin non-steroidal anti-inflammatory drugs (NSAIDs), calcium, vitamin D, folic acid

**Comparator (reference):** Placebo

**Outcome:** Prevention of advanced neoplasia; range of follow up between three to five years

**Setting:** Outpatient

<table>
<thead>
<tr>
<th>Total studies: 21 RCT</th>
<th>Relative effect** (95% Crl)</th>
<th>Anticipated absolute effect*** (95% Crl)</th>
<th>Certainty of evidence</th>
<th>Ranking**** (95% Crl)</th>
<th>Interpretation of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin + calcium + vitamin D</td>
<td>0.71 (0.18 to 2.49)</td>
<td>Without intervention: 74 per 1000&lt;sup&gt;1&lt;/sup&gt;</td>
<td>21 fewer per 1000 (61 fewer to 110 more)</td>
<td>Low Due to Imprecision&lt;sup&gt;2,5&lt;/sup&gt;</td>
<td>3 (1 to 10)</td>
</tr>
<tr>
<td>(1 RCT; 427 participants)</td>
<td>Network estimate</td>
<td>With intervention: 53 per 1000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium + vitamin D</td>
<td>0.91 (0.52 to 1.63)</td>
<td>Without intervention: 74 per 1000&lt;sup&gt;1&lt;/sup&gt;</td>
<td>7 fewer per 1000 (36 fewer to 47 more)</td>
<td>Low Due to Imprecision&lt;sup&gt;2,5&lt;/sup&gt;</td>
<td>6 (1 to 10)</td>
</tr>
<tr>
<td>(1 RCT; 1028 participants)</td>
<td>Network estimate</td>
<td>With intervention: 67 per 1000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin + folate</td>
<td>0.73 (0.43 to 1.19)</td>
<td>Without intervention: 74 per 1000&lt;sup&gt;1&lt;/sup&gt;</td>
<td>20 fewer per 1000 (42 fewer to 14 more)</td>
<td>Low Due to Imprecision&lt;sup&gt;2,5&lt;/sup&gt;</td>
<td>4 (2 to 8)</td>
</tr>
<tr>
<td>(2 RCT; 916 participants)</td>
<td>Network estimate</td>
<td>With intervention: 54 per 1000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin, high dose</td>
<td>0.81 (0.50 to 1.28)</td>
<td>Without intervention: 74 per 1000&lt;sup&gt;1&lt;/sup&gt;</td>
<td>14 fewer per 1000 (37 fewer to 21 more)</td>
<td>Low Due to Imprecision&lt;sup&gt;2,5&lt;/sup&gt;</td>
<td>5 (2 to 9)</td>
</tr>
<tr>
<td>(3 RCT; 917 participants)</td>
<td>Network estimate</td>
<td>With intervention: 60 per 1000</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
## NMA-SoF table example 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Odds Ratio (95% CI)</th>
<th>Network estimate</th>
<th>74 per 1000</th>
<th>53 per 1000</th>
<th>21 fewer per 1000 (44 fewer to 17 more)</th>
<th>GRADE</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin, low dose</td>
<td>0.71 (0.41 to 1.23)</td>
<td>Network estimate</td>
<td>74 per 1000</td>
<td>53 per 1000</td>
<td>21 fewer per 1000 (44 fewer to 17 more)</td>
<td>Low</td>
<td>3</td>
<td>(2 to 9)</td>
<td>Probably inferior</td>
</tr>
<tr>
<td>(3 RCT; 823 participants)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonaspirin NSAIDs</td>
<td>0.37 (0.24 to 0.53)</td>
<td>Network estimate</td>
<td>74 per 1000</td>
<td>27 per 1000</td>
<td>47 fewer per 1000 (56 fewer to 35 fewer)</td>
<td>High</td>
<td>1</td>
<td>(1 to 2)</td>
<td>Definitely superior</td>
</tr>
<tr>
<td>(4 RCT; 3486 participants)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>1.19 (0.65 to 2.15)</td>
<td>Network estimate</td>
<td>74 per 1000</td>
<td>88 per 1000</td>
<td>14 more per 1000 (26 fewer to 85 more)</td>
<td>Low</td>
<td>9</td>
<td>(3 to 10)</td>
<td>Probably inferior</td>
</tr>
<tr>
<td>(1 RCT; 764 participants)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>1.00 (0.66 to 1.52)</td>
<td>Network estimate</td>
<td>74 per 1000</td>
<td>74 per 1000</td>
<td>0 fewer per 1000 (25 fewer to 38 more)</td>
<td>Low</td>
<td>7</td>
<td>(3 to 10)</td>
<td>Probably inferior</td>
</tr>
<tr>
<td>(3 RCT; 2503 participants)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Folate</td>
<td>1.32 (0.85 to 2.00)</td>
<td>Network estimate</td>
<td>74 per 1000</td>
<td>51 per 1000</td>
<td>23 more per 1000 (11 fewer to 74 more)</td>
<td>Low</td>
<td>9</td>
<td>(5 to 10)</td>
<td>Probably inferior</td>
</tr>
<tr>
<td>(3 RCT; 1224 participants)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>Reference comparator</td>
<td>No estimable</td>
<td>No estimable</td>
<td>No estimable</td>
<td>No estimable</td>
<td>Reference comparator</td>
<td>7</td>
<td>(4 to 9)</td>
<td>Reference comparator</td>
</tr>
</tbody>
</table>

### NMA-SoF table definitions

* Lines represent direct comparisons
** Estimates are reported as odds ratio. CrI: credible interval. Results are expressed in credible intervals as opposed to the confidence intervals (CI) since a Bayesian analysis has been conducted.
*** Anticipated absolute effect. Anticipated absolute effect compares two risks by calculating the difference between the risks of the intervention group with the risk of the control group.
**** Surface under the cumulative (SUCRA) ranking and credible intervals for efficacy are presented. Rank statistics is defined as the probabilities that a treatment out of n treatments in a network meta-analysis is the best, the second, the third and so on until the least effective treatment.

### GRADE Working Group grades of evidence (or certainty in the evidence)

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect.

**Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

**Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

**Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

### Explanatory Footnotes

1 Baseline risks (assumed control risk) obtained from the National Cancer Institute pooling project.
2 Very serious imprecision since 95% CrI crosses unity, and with wide credible intervals suggesting high possibility of harm.
3 Very serious imprecision since RR>1 (suggesting greater likelihood of harm than benefit), and with wide credible intervals.
4 Very serious imprecision since RR is one (suggesting no evidence of benefit) and wide credible intervals suggesting high possibility of harm.
5 Conceptually, there was no significant inconsistency, with comparable distribution of plausible effect modifiers across trials of different chemopreventive agents.
# NMA-SoF table example 2

Estimates of effects, credible intervals, and certainty of the evidence for chemoprevention of colorectal cancer in individuals with previous colorectal neoplasia

**HARMS**

**Patient or population:** Individuals with previous colorectal neoplasia

**Interventions:** Low and high dose aspirin, nonaspirin non-steroidal anti-inflammatory drugs (NSAIDs), calcium, vitamin D, folic acid

**Comparator (reference):** Placebo

**Outcome:** Serious adverse events; range of follow up between three to five years

**Setting:** Outpatient

<table>
<thead>
<tr>
<th>Total studies: 21 RCT</th>
<th>Total Participants: 14135</th>
<th>Relative effect** (95% Crl)</th>
<th>Anticipated absolute effect*** (95% Crl)</th>
<th>Certainty of evidence</th>
<th>Ranking**** (95% Crl)</th>
<th>Interpretation of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>Relative estimate</strong></td>
<td><strong>Without intervention</strong></td>
<td><strong>With intervention</strong></td>
<td><strong>Difference</strong></td>
<td><strong>Evidence</strong></td>
</tr>
<tr>
<td>Aspirin + calcium + vitamin D</td>
<td>(1 RCT; 714 participants)</td>
<td>0.90 (0.54 to 1.51)</td>
<td>Network estimate</td>
<td>187 per 1000¹</td>
<td>89 per 1000</td>
<td>15 more per 1000 (71 more to 77 fewer)</td>
</tr>
<tr>
<td>Calcium + vitamin D</td>
<td>(1 RCT; 1125 participants)</td>
<td>1.11 (0.76 to 1.70)</td>
<td>Network estimate</td>
<td>187 per 1000¹</td>
<td>203 per 1000</td>
<td>16 more per 1000 (38 fewer to 94 more)</td>
</tr>
<tr>
<td>Aspirin + folate</td>
<td>(3 RCT; 1017 participants)</td>
<td>1.21 (0.83 to 1.77)</td>
<td>Network estimate</td>
<td>187 per 1000¹</td>
<td>218 per 1000</td>
<td>31 more per 1000 (27 fewer to 102 more)</td>
</tr>
<tr>
<td>Aspirin, high dose</td>
<td>(3 RCT; 1507 participants)</td>
<td>1.06 (0.76 to 1.49)</td>
<td>Network estimate</td>
<td>187 per 1000¹</td>
<td>196 per 1000</td>
<td>9 more per 1000 (38 fewer to 68 more)</td>
</tr>
</tbody>
</table>
# NMA-SoF table example 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>OR (95% CI)</th>
<th>Network estimate</th>
<th>Effect Size</th>
<th>CI Lower</th>
<th>CI Upper</th>
<th>Relative risk</th>
<th>Grade</th>
<th>Participants</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin, low dose</td>
<td>0.78 (0.43 to 1.38)</td>
<td>187 per 1000&lt;sup&gt;1&lt;/sup&gt;, 152 per 1000</td>
<td>35 fewer per 1000 (54 more to 97 fewer)</td>
<td>Low</td>
<td>8 (3 to 10)</td>
<td>Probably inferior</td>
<td>(2 RCT; 794 participants)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonaspirin NSAIDs</td>
<td>1.23 (0.95 to 1.64)</td>
<td>187 per 1000&lt;sup&gt;1&lt;/sup&gt;, 221 per 1000</td>
<td>34 more per 1000 (8 fewer to 87 more)</td>
<td>Low</td>
<td>2 (1 to 9)</td>
<td>Probably inferior</td>
<td>(3 RCT; 3964 participants)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>1.10 (0.74 to 1.70)</td>
<td>187 per 1000&lt;sup&gt;1&lt;/sup&gt;, 212 per 1000</td>
<td>25 more per 1000 (20 fewer to 78 more)</td>
<td>Low</td>
<td>5 (2 to 10)</td>
<td>Probably inferior</td>
<td>(1 RCT; 835 participants)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>1.38 (1.07 to 1.89)</td>
<td>187 per 1000&lt;sup&gt;1&lt;/sup&gt;, 238 per 1000</td>
<td>51 more per 1000 (22 more to 82 more)</td>
<td>High</td>
<td>8 (3 to 10)</td>
<td>Probably superior</td>
<td>(4 RCT; 2669 participants)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Folate</td>
<td>0.85 (0.59 to 1.22)</td>
<td>187 per 1000&lt;sup&gt;1&lt;/sup&gt;, 165 per 1000</td>
<td>22 fewer per 1000 (21 more to 59 fewer)</td>
<td>Low</td>
<td>6 (2 to 10)</td>
<td>Probably inferior</td>
<td>(3 RCT; 1511 participants)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td>Reference comparator</td>
<td>No estimable</td>
<td>No estimable</td>
<td>Reference comparator</td>
<td>3 (1 to 10)</td>
<td>Reference comparator</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NMA-SoF table definitions**
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- **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

**Explanatory Footnotes**
1 Based on assumed control risk of 18.7% (corresponding to pooled 18.7% risk of SAEs in placebo-treated patients of included trials)
2 Very serious imprecision since 95% CI crosses unity, and with wide credible intervals suggesting uncertainty in the estimate.
3 Conceptually, there was no significant intransitivity, with comparable distribution of plausible effect modifiers across trials of different chemopreventive agents.
Drawing conclusions from NMA

1. Direct estimate
   - Risk of bias
   - Inconsistency
   - Indirectness
   - Publication bias

2. Indirect evidence
   - Lowest at the ratings of the two direct comparisons forming the most dominant first order loop
   - Intransitivity

3. NMA certainty in the Evidence
   - Rating of direct estimate OR
   - Rating the estimate that contributes the most OR
   - Highest between direct and indirect rating
   - Incoherence (inconsistency)
   - Imprecision

   High
   Moderate
   Low
   Very Low

4. Uncertainty in Treatment Rankings: Reanalysis of Network Meta-analyses of Randomized Trials
   - 58 network meta-analyses involving 1308 randomized trials
   - “No evidence showed a difference between the best-ranked intervention and the second and third best-ranked interventions in 90% and 71% of comparisons, respectively.”

<table>
<thead>
<tr>
<th>NMA estimate (95% CrI)</th>
<th>NMA Certainty in the Evidence</th>
<th>Median ranks (95% CrI)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance crystalli</td>
<td>0.75 (0.58-0.97)</td>
<td>Moderate i</td>
<td>2.00 (1.00-3.00)</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.79 (0.59-1.00)</td>
<td>Low i</td>
<td>2.00 (1.00-3.00)</td>
</tr>
<tr>
<td>H-HES</td>
<td>0.91 (0.63-1.20)</td>
<td>Low i</td>
<td>4.00 (2.00-6.00)</td>
</tr>
<tr>
<td>Galactin</td>
<td>1.20 (0.44-2.21)</td>
<td>Very Low i</td>
<td>4.00 (2.00-6.00)</td>
</tr>
<tr>
<td>Saline</td>
<td>1.04 (0.87-1.25)</td>
<td>Moderate i</td>
<td>5.00 (3.00-6.00)</td>
</tr>
<tr>
<td>L-HES</td>
<td>-</td>
<td>-</td>
<td>5.00 (3.00-6.00)</td>
</tr>
</tbody>
</table>

*CrI: credibility interval; H-HES: high-molecular-weight hyaluronic acid; L-HES: low-molecular-weight hyaluronic acid
1. Rated down for imprecision
2. Rated down for inconsistency
3. Rated down for imprecision
4. Rated down for inconsistency
5. Rated down for inconsistency
6. Rated down for imprecision
Estimates of effects, credible intervals, and certainty of the evidence for chemoprevention of colorectal cancer in individuals with previous colorectal neoplasia

**Patient or population:** Individuals with previous colorectal neoplasia

**Interventions:** Low and high dose aspirin, nonaspirin non-steroidal anti-inflammatory drugs (NSAIDs), calcium, vitamin D, folic acid

**Comparator (reference):** Placebo

**Follow-up:** range of follow up between three to five years

**Setting:** Outpatient

### Prevention of advanced neoplasia

<table>
<thead>
<tr>
<th>Total studies: 21 RCT</th>
<th>Total Participants: 12088</th>
<th>Relative effect** (95% Crl)</th>
<th>Anticipated absolute effect*** (95% Crl)</th>
<th>Certainty of evidence</th>
<th>Ranking**** (95% Crl)</th>
<th>Interpretation of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without intervention</td>
<td>With intervention</td>
<td>Difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonaspirin NSAIDs</td>
<td>0.37 (0.24 to 0.53)</td>
<td>74 per 1000(^1)</td>
<td>27 per 1000</td>
<td>47 fewer per 1000 (56 fewer to 35 fewer)</td>
<td>☑☑☑☑☑ High(^2)</td>
<td>1 (1 to 2)</td>
</tr>
<tr>
<td>(4 RCT; 3466 participants)</td>
<td></td>
<td>Network estimate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin, low dose</td>
<td>0.71 (0.41 to 1.23)</td>
<td>74 per 1000(^1)</td>
<td>53 per 1000</td>
<td>21 fewer per 1000 (44 fewer to 17 more)</td>
<td>☑☑☑☑ Low Due to Imprecision(^1)</td>
<td>3 (2 to 9)</td>
</tr>
<tr>
<td>(3 RCT; 823 participants)</td>
<td></td>
<td>Network estimate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin + calcium + vitamin D</td>
<td>0.71 (0.18 to 2.49)</td>
<td>74 per 1000(^1)</td>
<td>53 per 1000</td>
<td>21 fewer per 1000 (61 fewer to 110 more)</td>
<td>☑☑☑☐ Low Due to Imprecision(^1)</td>
<td>3 (1 to 10)</td>
</tr>
<tr>
<td>(1 RCT; 427 participants)</td>
<td></td>
<td>Network estimate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Serious adverse events

<table>
<thead>
<tr>
<th>Total studies: 21 RCT</th>
<th>Total Participants: 14135</th>
<th>Relative effect** (95% Crl)</th>
<th>Anticipated absolute effect*** (95% Crl)</th>
<th>Certainty of evidence</th>
<th>Ranking**** (95% Crl)</th>
<th>Interpretation of Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Without intervention</td>
<td>With intervention</td>
<td>Difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>1.38 (1.07 to 1.89)</td>
<td>187 per 1000(^2)</td>
<td>238 per 1000</td>
<td>51 more per 1000 (22 more to 82 more)</td>
<td>☑☑☑☑ High(^3)</td>
<td>8 (3 to 10)</td>
</tr>
<tr>
<td>(4 RCT; 2669 participants)</td>
<td></td>
<td>Network estimate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium + vitamin D</td>
<td>1.11 (0.76 to 1.70)</td>
<td>187 per 1000(^2)</td>
<td>203 per 1000</td>
<td>16 more per 1000 (38 fewer to 94 more)</td>
<td>☑☑☑☐ Low Due to Imprecision(^1)</td>
<td>2 (1 to 7)</td>
</tr>
<tr>
<td>(1 RCT; 1125 participants)</td>
<td></td>
<td>Network estimate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonaspirin NSAIDs</td>
<td>1.23 (0.95 to 1.64)</td>
<td>187 per 1000(^2)</td>
<td>221 per 1000</td>
<td>34 more per 1000 (8 less to 67 more)</td>
<td>☑☑☑☐ Low Due to Imprecision(^1)</td>
<td>2 (1 to 9)</td>
</tr>
<tr>
<td>(3 RCT; 3964 participants)</td>
<td></td>
<td>Network estimate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Explanatory Footnotes**

1 Baseline risks (assumed control risk) obtained from the National Cancer Institute pooling project.
2 Very serious imprecision since 95% CrI crosses unity, and with wide credible intervals suggesting high possibility of harm.
3 Very serious imprecision since RR > 1 (suggesting greater likelihood of harm than benefit), and with wide credible intervals.
4 Very serious imprecision since RR < 1 (suggesting no evidence of benefit) and wide credible intervals suggesting high possibility of harm.
5 Conceptually, there was no significant intravariety, with comparable distribution of plausible effect modifiers across trials of different chemopreventive agents.
6 Based on assumed control risk of 18.7% (corresponding to pooled 18.7% risk of SAEs in placebo-treated patients of included trials).
7 Very serious imprecision since 95% CrI crosses unity, and with wide credible intervals suggesting uncertainty in the estimate.
8 Conceptually, there was no significant intravariety, with comparable distribution of plausible effect modifiers across trials of different chemopreventive agents.
Wrapping up
• Our NMA-SoF table captures the complexity of the information reported in a NMA publication while maximizing simplicity to achieve a user-friendly presentation.

• In a single NMA-SoF table we report relevant information that the literature described as important for NMA findings, including certainty of evidence, and ranking.

• Further experience with users may result in modifications to the current table, or the development of alternative formats.
Learning objective

• To gain familiarity in interpreting findings of network meta-analysis (NMA) through NMA ‘Summary of findings’ (SoF) tables developed based on principles of the GRADE approach to rating certainty of evidence from NMAs.
Part 4

QUESTIONS
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References


References