

### G.9.1.9 Nutrition

#### Ginkgo biloba versus placebo (Alzheimer's disease)

| Number of RCTs   | Risk of bias | Inconsistency        | Indirectness | Imprecision          | Sample size | Effect size (95% CI)   | Quality  |
|--|--------------|----------------------|--------------|----------------------|-------------|------------------------|----------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 1 (Mazza 2006)   | Not serious  | N/A                  | Not serious  | Serious <sup>1</sup> | 51          | MD 0.85 (-2.39, 4.09)  | Moderate |
| <b>Cognition: all measures (post-intervention) – higher numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 4  | Not serious  | Serious <sup>2</sup> | Not serious  | Serious <sup>3</sup> | 619         | SMD 0.08 (-0.19, 0.35) | Low      |
| <b>ADL: all measures (post-intervention) – higher numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 1 (Schneider 2005)   | Not serious  | N/A                  | Not serious  | Serious <sup>1</sup> | 343         | MD 0.00 (-0.21, 0.21)  | Moderate |
| <b>Global assessment: MMSE (post-intervention) – higher numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 1 (Le Bars 1997)   | Not serious  | N/A                  | Not serious  | Serious <sup>1</sup> | 236         | MD 0.00 (-0.26, 0.26)  | Moderate |
| <ol style="list-style-type: none"> <li>1. Non-significant result</li> <li>2. <math>i^2 &gt; 40\%</math></li> <li>3. 95% CI crosses 1 line of a defined MID interval</li> </ol> |              |                      |              |                      |             |                        |          |

#### Ginkgo biloba versus placebo (Alzheimer's disease or vascular dementia)

| Number of RCTs  | Risk of bias | Inconsistency        | Indirectness | Imprecision          | Sample size | Effect size (95% CI)  | Quality |
|---|--------------|----------------------|--------------|----------------------|-------------|-----------------------|---------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour intervention</b> |              |                      |              |                      |             |                       |         |
| 6   | Not serious  | Serious <sup>1</sup> | Not serious  | Serious <sup>2</sup> | 1,922       | SMD 0.60 (0.06, 1.13) | Low     |

| Number of RCTs   | Risk of bias | Inconsistency        | Indirectness | Imprecision          | Sample size | Effect size (95% CI)     | Quality  |
|--|--------------|----------------------|--------------|----------------------|-------------|--------------------------|----------|
| <b>ADL: all measures (post-intervention) – higher numbers favour intervention</b>              |              |                      |              |                      |             |                          |          |
| 6  | Not serious  | Serious <sup>1</sup> | Not serious  | Serious <sup>2</sup> | 1,922       | SMD 0.41 (0.11, 0.71)    | Low      |
| <b>BPSD: NPI (post-intervention) – lower numbers favour intervention</b>                       |              |                      |              |                      |             |                          |          |
| 4  | Not serious  | Serious <sup>1</sup> | Not serious  | Not serious          | 1,598       | MD -3.88 (-7.63, -0.14)  | Moderate |
| <b>BPSD: all measures (post-intervention) – lower numbers favour intervention</b>              |              |                      |              |                      |             |                          |          |
| 4  | Not serious  | Serious <sup>1</sup> | Not serious  | Serious <sup>2</sup> | 1,598       | SMD -0.67 (-1.31, -0.03) | Low      |
| <b>Global assessment: all measures (post-intervention) – lower numbers favour intervention</b> |              |                      |              |                      |             |                          |          |
| 4  | Not serious  | Serious <sup>1</sup> | Not serious  | Serious <sup>2</sup> | 1,597       | SMD 0.74 (0.14, 1.33)    | Low      |
| <b>Quality of life: all measures (post-intervention) – lower numbers favour intervention</b>   |              |                      |              |                      |             |                          |          |
| 2  | Not serious  | Not serious          | Not serious  | Serious <sup>2</sup> | 806         | SMD 0.24 (0.11, 0.38)    | Moderate |
| 1. $i^2 > 40\%$<br>2. 95% CI crosses 1 line of a defined MID interval                          |              |                      |              |                      |             |                          |          |

### Omega-3 fatty acids (DHA and EPA) versus placebo

| Number of RCTs  | Risk of bias | Inconsistency | Indirectness | Imprecision          | Sample size | Effect size (95% CI)   | Quality  |
|---|--------------|---------------|--------------|----------------------|-------------|------------------------|----------|
| <b>Cognition: MMSE (post-intervention) - higher numbers favour intervention</b>       |              |               |              |                      |             |                        |          |
| 3   | Not serious  | Not serious   | Not serious  | Serious <sup>1</sup> | 604         | MD 0.17 (-0.38, 0.72)  | Moderate |
| <b>ADL: ADCS-ADL (post-intervention) - higher numbers favour intervention</b>         |              |               |              |                      |             |                        |          |
| 1 (Quinn 2010)  | Not serious  | N/A           | Not serious  | Serious <sup>1</sup> | 400         | MD 1.08 (-1.70, 3.86)  | Moderate |
| <b>ADL: all measures (post-intervention) - higher numbers favour intervention</b>     |              |               |              |                      |             |                        |          |
| 2   | Not serious  | Not serious   | Not serious  | Serious <sup>2</sup> | 426         | SMD 0.04 (-0.15, 0.24) | Moderate |
| <b>BPSD: NPI (post-intervention) - lower numbers favour intervention</b>              |              |               |              |                      |             |                        |          |
| 1 (Quinn 2010)  | Not serious  | N/A           | Not serious  | Serious <sup>1</sup> | 400         | MD -2.16 (-5.42, 1.10) | Moderate |
| <b>Dementia severity: CDR (post-intervention) - lower numbers favour intervention</b> |              |               |              |                      |             |                        |          |
| 2   | Not serious  | Not serious   | Not serious  | Serious <sup>1</sup> | 578         | MD -0.07 (-0.63, 0.48) | Moderate |
| 1. Non-significant result<br>2. 95% CI crosses 1 line of a defined MID interval       |              |               |              |                      |             |                        |          |

### Souvenaid versus placebo

| Number of RCTs   | Risk of bias | Inconsistency        | Indirectness | Imprecision          | Sample size | Effect size (95% CI)   | Quality  |
|--|--------------|----------------------|--------------|----------------------|-------------|------------------------|----------|
| <b>Cognition: MMSE (post-intervention) - higher numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 1 (Scheltens 2010)   | Not serious  | N/A                  | Not serious  | Serious <sup>1</sup> | 195         | MD 0.30 (-0.56, 1.16)  | Moderate |
| <b>Cognition: all measures (post-intervention) - higher numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 3  | Not serious  | Serious <sup>2</sup> | Not serious  | Serious <sup>3</sup> | 879         | SMD 0.10 (-0.12, 0.32) | Low      |
| <b>ADL: ADCS-ADL (post-intervention) - higher numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 3  | Not serious  | Not serious          | Not serious  | Serious <sup>1</sup> | 651         | MD 0.13 (-1.32, 1.58)  | Moderate |
| <b>Quality of life: QoL-AD (post-intervention) - higher numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 1 (Scheltens 2010)   | Not serious  | N/A                  | Not serious  | Serious <sup>1</sup> | 200         | MD -0.40 (-1.59, 0.79) | Moderate |
| <b>Dementia severity: CDR (post-intervention) - lower numbers favour intervention</b>  |              |                      |              |                      |             |                        |          |
| 1 (Shah 2013)  | Not serious  | N/A                  | Not serious  | Serious <sup>1</sup> | 450         | MD 0.08 (-0.28, 0.44)  | Moderate |
| <ol style="list-style-type: none"> <li>1. Non-significant result</li> <li>2. <math>i^2 &gt; 40\%</math></li> <li>3. 95% CI crosses 1 line of a defined MID interval</li> </ol> |              |                      |              |                      |             |                        |          |

### Huperzine A versus placebo or no treatment

| Number of RCTs  | Risk of bias              | Inconsistency        | Indirectness | Imprecision          | Sample size | Effect size (95% CI)    | Quality  |
|---|---------------------------|----------------------|--------------|----------------------|-------------|-------------------------|----------|
| <b>Cognition: MMSE (post-intervention) - higher numbers favour Huperzine</b>        |                           |                      |              |                      |             |                         |          |
| 7   | Very serious <sup>1</sup> | Serious <sup>3</sup> | Not serious  | Not serious          | 648         | MD 2.80 (1.61, 3.99)    | Very low |
| <b>ADL: ADCS-ADL (post-intervention) - higher numbers favour Huperzine</b>          |                           |                      |              |                      |             |                         |          |
| 1 (Rafii 2011)  | Not serious               | N/A                  | Not serious  | Serious <sup>2</sup> | 210         | MD 1.63 (-0.84, 4.09)   | Moderate |
| <b>ADL: all measures (post-intervention) - higher numbers favour Huperzine</b>      |                           |                      |              |                      |             |                         |          |
| 7   | Very serious <sup>1</sup> | Serious <sup>3</sup> | Not serious  | Not serious          | 648         | SMD 0.54 (0.23, 0.85)   | Very low |
| <b>Dementia severity: CDR (post-intervention) - higher numbers favour Huperzine</b> |                           |                      |              |                      |             |                         |          |
| 1 (Yang 2003)   | Very serious <sup>1</sup> | N/A                  | Not serious  | Not serious          | 65          | MD -0.80 (-0.95, -0.65) | Low      |
| <b>BPSD:NPI (post-intervention) – higher numbers favour Huperzine</b>               |                           |                      |              |                      |             |                         |          |
| 1 (Rafii 2011)  | Not serious               | N/A                  | Not serious  | Serious <sup>2</sup> | 210         | MD 0.15 (-2.35, 2.66)   | Moderate |

1. Individual studies at high risk of bias, and data not available from some studies only reported in Chinese
2. Non-significant result
3.  $i^2 > 40\%$

### Tailored nutritional guidance versus normal community care

| Number of RCTs  | Risk of bias         | Inconsistency | Indirectness | Imprecision | Sample size | Effect size (95% CI) | Quality  |
|---|----------------------|---------------|--------------|-------------|-------------|----------------------|----------|
| <b>Quality of life: 15D (post-intervention) – higher numbers favour tailored nutritional guidance</b> |                      |               |              |             |             |                      |          |
| 1 (Suominen 2015)   | Serious <sup>1</sup> | N/A           | Not serious  | Not serious | 78          | MD 0.04 (0.01, 0.07) | Moderate |
| 1. Intention to treat analysis not carried out  |                      |               |              |             |             |                      |          |

### Multivitamins versus placebo

| Number of RCTs  | Risk of bias         | Inconsistency | Indirectness | Imprecision          | Sample size | Effect size (95% CI)   | Quality |
|---|----------------------|---------------|--------------|----------------------|-------------|------------------------|---------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour tailored nutritional guidance</b>    |                      |               |              |                      |             |                        |         |
| 1 (Sun 2007)  | Serious <sup>1</sup> | N/A           | Not serious  | Serious <sup>2</sup> | 89          | MD -0.26 (-2.16, 1.64) | Low     |
| <b>ADL: Barthel Index (post-intervention) – higher numbers favour tailored nutritional guidance</b> |                      |               |              |                      |             |                        |         |
| 1 (Sun 2007)  | Serious <sup>1</sup> | N/A           | Not serious  | Serious <sup>2</sup> | 89          | MD -0.14 (-0.91, 0.63) | Low     |
| 1. No details of randomisation method or assessor blinding reported                                 |                      |               |              |                      |             |                        |         |
| 2. Non-significant result   |                      |               |              |                      |             |                        |         |

### Vitamin E versus placebo

| Number of RCTs   | Risk of bias | Inconsistency        | Indirectness | Imprecision          | Sample size | Effect size (95% CI)   | Quality  |
|--|--------------|----------------------|--------------|----------------------|-------------|------------------------|----------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour vitamin E</b> |              |                      |              |                      |             |                        |          |
| 1 (Dysken 2014)  | Not serious  | Serious <sup>2</sup> | Not serious  | Serious <sup>1</sup> | 561         | MD 0.22 (-0.13, 0.87)  | Moderate |
| <b>ADL:ADCS-ADL (post-intervention) – higher numbers favour vitamin E</b>    |              |                      |              |                      |             |                        |          |
| 1 (Dysken 2014)  | Not serious  | Not serious          | Not serious  | Serious <sup>1</sup> | 561         | MD 1.46 (-1.84, 4.76)  | Moderate |
| <b>BPSD:NPI (post-intervention) – higher numbers favour vitamin E</b>        |              |                      |              |                      |             |                        |          |
| 1 (Dysken 2014)  | Not serious  | Not serious          | Not serious  | Serious <sup>1</sup> | 561         | MD -0.77 (-2.74, 1.19) | Moderate |
| 1. Not serious   |              |                      |              |                      |             |                        |          |

| Number of RCTs  | Risk of bias | Inconsistency | Indirectness | Imprecision | Sample size | Effect size (95% CI) | Quality |
|-----------------|--------------|---------------|--------------|-------------|-------------|----------------------|---------|
| 2. $i^2 > 40\%$ |              |               |              |             |             |                      |         |

### Folic Acid, B12 and B6 versus placebo

| Number of RCTs  | Risk of bias | Inconsistency | Indirectness | Imprecision          | Sample size | Effect size (95% CI)   | Quality  |
|---|--------------|---------------|--------------|----------------------|-------------|------------------------|----------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour intervention</b>       |              |               |              |                      |             |                        |          |
| 1 (Aisen 2008)  | Not serious  | N/A           | Not serious  | Serious <sup>1</sup> | 409         | MD -0.43 (-1.32, 0.46) | Moderate |
| <b>ADL: ADCSL-ADL (post-intervention) – higher numbers favour intervention</b>        |              |               |              |                      |             |                        |          |
| 1 (Aisen 2008)  | Not serious  | N/A           | Not serious  | Serious <sup>1</sup> | 409         | MD -0.96 (-3.25, 1.33) | Moderate |
| <b>Dementia severity: CDR (post-intervention) – lower numbers favour intervention</b> |              |               |              |                      |             |                        |          |
| 1 (Aisen 2008)  | Not serious  | N/A           | Not serious  | Serious <sup>1</sup> | 409         | MD 0.07 (-0.41, 0.55)  | Moderate |
| 1. Non-significant result   |              |               |              |                      |             |                        |          |

### Folic acid, B12, Hcy, SAM, SAH and donepezil versus donepezil

| Number of RCTs  | Risk of bias         | Inconsistency | Indirectness | Imprecision               | Sample size | Effect size (95% CI)   | Quality  |
|---|----------------------|---------------|--------------|---------------------------|-------------|------------------------|----------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour intervention</b>   |                      |               |              |                           |             |                        |          |
| 2   | Serious <sup>1</sup> | Not serious   | Not serious  | Serious <sup>2</sup>      | 162         | MD 0.26 (-1.22, 1.74)  | Low      |
| <b>ADL: all measures (post-intervention) – higher numbers favour intervention</b> |                      |               |              |                           |             |                        |          |
| 2   | Serious <sup>1</sup> | N/A           | Not serious  | Very serious <sup>3</sup> | 162         | SMD 0.28 (-0.38, 0.95) | Very low |
| 1. Intention to treat analysis not carried out                                    |                      |               |              |                           |             |                        |          |
| 2. Non-significant result   |                      |               |              |                           |             |                        |          |
| 3. 95% CI crosses 2 lines of a defined MID interval                               |                      |               |              |                           |             |                        |          |

### Oral nutritional supplements versus standard dietetic advice

| Number of RCTs  | Risk of bias | Inconsistency | Indirectness | Imprecision          | Sample size | Effect size (95% CI)  | Quality  |
|---|--------------|---------------|--------------|----------------------|-------------|-----------------------|----------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour intervention</b> |              |               |              |                      |             |                       |          |
| 2   | Not serious  | Not serious   | Not serious  | Serious <sup>1</sup> | 58          | MD 0.68 (-0.96, 2.31) | Moderate |
| <b>Cognition: MMSE (follow-up) – higher numbers favour intervention</b>         |              |               |              |                      |             |                       |          |

| Number of RCTs   | Risk of bias | Inconsistency | Indirectness | Imprecision               | Sample size | Effect size (95% CI)   | Quality  |
|--|--------------|---------------|--------------|---------------------------|-------------|------------------------|----------|
| 2  | Not serious  | Not serious   | Not serious  | Serious <sup>1</sup>      | 55          | MD 0.39 (-1.55, 2.33)  | Moderate |
| <b>ADL: all measures (post-intervention) – higher numbers favour intervention</b>  |              |               |              |                           |             |                        |          |
| 2  | Not serious  | Not serious   | Not serious  | Very serious <sup>2</sup> | 115         | SMD 0.07 (-0.30, 0.44) | Low      |
| <b>ADL: all measures (follow-up) – higher numbers favour intervention</b>  |              |               |              |                           |             |                        |          |
| 1 (Lauque 2004)  | Not serious  | N/A           | Not serious  | Very serious <sup>2</sup> | 80          | SMD 0.08 (-0.35, 0.51) | Low      |
| <ol style="list-style-type: none"> <li>1. Non-significant result</li> <li>2. 95% CI crosses 2 lines of a defined MID interval</li> </ol> |              |               |              |                           |             |                        |          |

#### Whole formula diet (based on lyophilised (dried) foods) versus standard dietetic advice

| Number of RCTs  | Risk of bias         | Inconsistency | Indirectness | Imprecision               | Sample size | Effect size (95% CI)    | Quality  |
|---|----------------------|---------------|--------------|---------------------------|-------------|-------------------------|----------|
| <b>Cognition: all measures (post-intervention) – higher numbers favour intervention</b>   |                      |               |              |                           |             |                         |          |
| 1 (Salas-Salvado 2004)  | Serious <sup>1</sup> | N/A           | Not serious  | Very serious <sup>2</sup> | 38          | SMD -0.38 (-1.04, 0.28) | Very low |
| <ol style="list-style-type: none"> <li>1. Intention to treat analysis not carried out</li> <li>2. 95% CI crosses 2 lines of a defined MID interval</li> </ol> |                      |               |              |                           |             |                         |          |

#### Ginseng versus placebo

| Number of RCTs   | Risk of bias         | Inconsistency | Indirectness | Imprecision          | Sample size | Effect size (95% CI)  | Quality |
|--|----------------------|---------------|--------------|----------------------|-------------|-----------------------|---------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour intervention</b>                          |                      |               |              |                      |             |                       |         |
| 3  | Serious <sup>1</sup> | N/A           | Not serious  | Serious <sup>2</sup> | 226         | MD 0.31 (-0.52, 1.15) | Low     |
| <ol style="list-style-type: none"> <li>1. Open-label study</li> <li>2. Non-significant result</li> </ol> |                      |               |              |                      |             |                       |         |

#### Chinese herbal formula (Yishen Huazhuo decoction) and donepezil versus placebo and donepezil

| Number of RCTs  | Risk of bias | Inconsistency | Indirectness         | Imprecision          | Sample size | Effect size (95% CI)  | Quality |
|---|--------------|---------------|----------------------|----------------------|-------------|-----------------------|---------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour intervention</b> |              |               |                      |                      |             |                       |         |
| 1 (Zhang 2015)  | Not serious  | N/A           | Serious <sup>1</sup> | Serious <sup>2</sup> | 144         | MD 0.45 (-0.34, 1.24) | Low     |

| Number of RCTs  | Risk of bias | Inconsistency | Indirectness         | Imprecision          | Sample size | Effect size (95% CI)    | Quality  |
|---|--------------|---------------|----------------------|----------------------|-------------|-------------------------|----------|
| <b>Cognition: MMSE (follow-up) – higher numbers favour intervention</b>   |              |               |                      |                      |             |                         |          |
| 1 (Zhang 2015)  | Not serious  | N/A           | Serious <sup>1</sup> | Not serious          | 144         | MD 0.97 (0.25, 1.69)    | Moderate |
| <b>ADL: all measures (post-intervention) – higher numbers favour intervention</b>   |              |               |                      |                      |             |                         |          |
| 1 (Zhang 2015)  | Not serious  | N/A           | Serious <sup>1</sup> | Serious <sup>3</sup> | 144         | SMD -0.01 (-0.34, 0.31) | Low      |
| <b>ADL: all measures (follow-up) – higher numbers favour intervention</b>   |              |               |                      |                      |             |                         |          |
| 1 (Zhang 2015)  | Not serious  | N/A           | Serious <sup>1</sup> | Serious <sup>2</sup> | 144         | SMD -0.23 (-0.56, 0.10) | Low      |
| <b>BPSD: NPI (post-intervention) – lower numbers favour intervention</b>  |              |               |                      |                      |             |                         |          |
| 1 (Zhang 2015)  | Not serious  | N/A           | Serious <sup>1</sup> | Serious <sup>2</sup> | 144         | MD -0.17 (-0.85, 0.51)  | Low      |
| <b>BPSD: NPI (follow-up) – lower numbers favour intervention</b>  |              |               |                      |                      |             |                         |          |
| 1 (Zhang 2015)  | Not serious  | N/A           | Serious <sup>1</sup> | Serious <sup>2</sup> | 144         | MD -0.09 (-0.71, 0.53)  | Low      |
| <ol style="list-style-type: none"> <li>1. Not a relevant intervention in the UK</li> <li>2. Non-significant result</li> <li>3. 95% CI crosses 1 line of a defined MID interval</li> </ol> |              |               |                      |                      |             |                         |          |

### Chinese Traditional medicine (Yokukansan) versus placebo

| Number of RCTs   | Risk of bias         | Inconsistency | Indirectness         | Imprecision          | Sample size | Effect size (95% CI)   | Quality  |
|--|----------------------|---------------|----------------------|----------------------|-------------|------------------------|----------|
| <b>Cognition: MMSE (post-intervention) – higher numbers favour intervention</b>  |                      |               |                      |                      |             |                        |          |
| 1 (Farukawa 2017)  | Serious <sup>1</sup> | N/A           | Serious <sup>2</sup> | Serious <sup>3</sup> | 137         | MD -0.30 (-1.78, 1.18) | Very low |
| <b>BPSD: NPI (post-intervention) – lower numbers favour intervention</b>   |                      |               |                      |                      |             |                        |          |
| 1 (Farukawa 2017)  | Serious <sup>1</sup> | N/A           | Serious <sup>2</sup> | Serious <sup>3</sup> | 142         | MD -0.40 (-1.84, 1.04) | Very low |
| <ol style="list-style-type: none"> <li>1. No details of randomisation method or assessor blinding reported</li> <li>2. Not a relevant intervention in the UK</li> <li>3. Non-significant result</li> </ol> |                      |               |                      |                      |             |                        |          |

### Chinese traditional medicine (Di-Huang-Yi-Zhi) and donepezil versus placebo and donepezil

| Number of RCTs   | Risk of bias | Inconsistency | Indirectness | Imprecision | Sample size | Effect size (95% CI) | Quality |
|--|--------------|---------------|--------------|-------------|-------------|----------------------|---------|
| <b>Mini Mental State Examination – higher numbers favour Di-Huang-Yi-ZHI (@6 months)</b> |              |               |              |             |             |                      |         |

| Number of RCTs   | Risk of bias              | Inconsistency | Indirectness         | Imprecision          | Sample size | Effect size (95% CI)    | Quality  |
|--|---------------------------|---------------|----------------------|----------------------|-------------|-------------------------|----------|
| 1 (Gu 2015)  | Serious <sup>1</sup>      | N/A           | Serious <sup>1</sup> | Serious <sup>2</sup> | 60          | MD 0.85 (-0.72, 2.42)   | Very low |
| <b>Activities of Daily Living – lower numbers favour Di-Huang-Yi-ZHI (@6 months)</b>   |                           |               |                      |                      |             |                         |          |
| 1 (Gu 2015)  | Very serious <sup>4</sup> | N/A           | Serious <sup>1</sup> | Not serious          | 60          | MD -6.54 (-9.84, -3.24) | Very low |
| <ol style="list-style-type: none"> <li>1. No details of randomisation method or assessor blinding reported</li> <li>2. Not a relevant intervention in the UK</li> <li>3. Non-significant result</li> <li>4. No details of randomisation method or assessor blinding reported; unclear what outcome measure used for ADL</li> </ol> |                           |               |                      |                      |             |                         |          |

### Nutritional Formulation versus placebo

| Number of RCTs   | Risk of bias         | Inconsistency | Indirectness | Imprecision          | Sample size | Effect size (95% CI)   | Quality |
|--|----------------------|---------------|--------------|----------------------|-------------|------------------------|---------|
| <b>Neuropsychiatric Inventory – lower numbers favour nutritional formulation (@3 months)</b>   |                      |               |              |                      |             |                        |         |
| 1 (Remington 2014)   | Serious <sup>1</sup> | N/A           | Not Serious  | Serious <sup>2</sup> | 83          | MD 0.40 (-4.49, 5.29)  | Low     |
| <b>Activities of Daily Living – lower numbers favour nutritional formulation (@3 months)</b>   |                      |               |              |                      |             |                        |         |
| 1 (Remington 2014)   | Serious <sup>1</sup> | N/A           | Not Serious  | Serious <sup>2</sup> | 83          | MD 2.30 (-5.51, 10.11) | Low     |
| <ol style="list-style-type: none"> <li>1. High number of participants lost to follow up</li> <li>2. Non-significant result</li> </ol> <p>Nutritional formulation consist of - 400µg folic acid, 6µg B1, 30I.U. alpha-tocopherol,400g SAM (200mg active ion), 600mg NAC and 500mg ALCAR</p> |                      |               |              |                      |             |                        |         |