Appendix S4 GRADE summary for efficacy of probiotics on mental health in patients with multiple sclerosis

(a) EDSS scores

Probiotic compared to Placebo for Multiple sclerosis

Patient or population: patients with Multiple sclerosis
Settings:
Intervention: Probiotic
Comparison: Placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Placebo	Corresponding risk Probiotic				
EDSS scores Follow-up: 3 months		The mean edss scores in the intervention groups was **1.22 standard deviations lower** (2.4 to 0.03 lower)		173 (3 studies)	⊕⊖⊖⊖ **very low**[1,2,3]	SMD -1.22 (-2.4 to -0.03)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] serious inconsistency due to high heterogeneity with 75%<12.
[2] serious indirectness due to different strains and intervention time in all studies.
[3] serious imprecision due to the small sample size（< 400 individuals）and wide confidence interval.

(b) BDI scores

Probiotic compared to Placebo for Multiple sclerosis

Patient or population: patients with Multiple sclerosis
Settings:
Intervention: Probiotic
Comparison: Placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Placebo	Corresponding risk Probiotic				
BDI scores Follow-up: 3 months		The mean bdi scores in the intervention groups was **1.58 standard deviations lower** (3.03 to 0.12 lower)		173 (3 studies)	⊕⊖⊖⊖ **very low**[1,2,3]	SMD -1.58 (-3.03 to -0.12)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] serious inconsistency due to high heterogeneity with 75%<12.
[2] serious indirectness due to different strains and intervention time in all studies.
[3] serious imprecision due to the small sample size（< 400 individuals）and wide confidence interval.

(c) GHQ scores

Probiotic compared to Placebo for Multiple sclerosis

Patient or population: patients with Multiple sclerosis
Settings:
Intervention: Probiotic
Comparison: Placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Placebo	Corresponding risk Probiotic				
GHQ scores Follow-up: 3 months		The mean ghq scores in the intervention groups was **0.71 standard deviations lower** (1.02 to 0.4 lower)		173 (3 studies)	⊕⊕⊖⊖ **low**[1,2]	SMD -0.71 (-1.02 to -0.4)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] serious indirectness due to different strains and intervention time in all studies.
[2] serious imprecision due to the small sample size（< 400 individuals）and wide confidence interval.

(d) DASS scores

Probiotic compared to Placebo for Multiple sclerosis

Patient or population: patients with Multiple sclerosis
Settings:
Intervention: Probiotic
Comparison: Placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk Placebo	Corresponding risk Probiotic				
DASS scores Follow-up: 3 months		The mean dass scores in the intervention groups was **0.72 standard deviations lower** (1.12 to 0.33 lower)		108 (2 studies)	⊕⊖⊖⊖ **very low**[1,2]	SMD -0.72 (-1.12 to -0.33)

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] serious indirectness due to different strains and intervention time the two studies.
[2] very serious imprecision due to the small sample size（< 400 individuals）and wide confidence interval.