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| --- | --- | --- | --- | --- | --- | --- | --- |
| Outcome | Participants (studies) | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Overall certainty of evidence |
| KL-6 | 16 observational studies | Serious1 | Serious2 | Not serious | Not serious | Plausible confounding3 |  VERY LOW |
| SP-D | 10 observational studies | Serious1 | Serious2 | Not serious | Not serious | Plausible confounding3 |  VERY LOW |
| SP-A | 5 observational studies | Serious1 | Serious2 | Not serious | Not serious | Plausible confounding3 |  VERY LOW |
| RAGEs | 5 observational studies | Serious1 | Serious2 | Not serious | Not serious | Plausible confounding3 |  VERY LOW |

**1Serious risk of bias due to the NOS score (5-6)**

**2Serious inconsistency due to significant heterogeneity (I2＞50%)**

**3all plausible residual confounding would reduce the demonstrated effect. Some of the studies do not match the basic information of two groups, like age, sex ratio and so on.**