**Table S4**. Bias analysis in clinical studies according to the Downs and Black Quality Index\*.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Studies**  **Signaling questions** | **Botoni et al. 2007** | **Khoury et al. 1996** | **Szajnbok et al. 1993** | **Robert et al. 1992** |
| Is the hypothesis/aim/objective of the study clearly described? | 1 | 1 | 1 | 1 |
| Main outcomes were clearly described in the Introduction or Methods? | 0 | 0 | 0 | 0 |
| Are the characteristics of the patients included in the study clearly described? | 1 | 1 | 1 | 1 |
| Interventions were clearly described? | 1 | 1 | 1 | 1 |
| Distributions of confounders in each group compared was clearly described? | 0 | 0 | 0 | 0 |
| Are the main findings of the study clearly described? | 1 | 1 | 1 | 1 |
| Provide estimates of the random variability in the data for the main outcomes? | 1 | 1 | 1 | 1 |
| The important adverse events that may be a consequence of the intervention been reported? | 1 | 0 | 1 | 1 |
| The characteristics of patients lost to follow-up been described? | 1 | 1 | 1 | 1 |
| Have actual probability values been reported for the main outcomes? | 1 | 1 | 1 | 1 |
| The subjects were representative of the entire population from which they were recruited? | 0 | 0 | 0 | 0 |
| **Partial score/items (n)** | 8 | 7 | 8 | 8 |
| **Partial score/items (%)** | 72 | 63 | 72 | 72 |

**Table S4 *(continuation).*** Bias analysis in clinical studies according to the Downs and Black Quality Index\*.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Studies**  **Signaling questions** | **Botoni et al. 2007** | **Khoury et al. 1996** | **Szajnbok et al. 1993** | **Robert et al. 1992** |
| Were the subjects prepared to participate representative of the entire population from which they were recruited? | 1 | 1 | 1 | 1 |
| Were the staff, places, and facilities, representative of the treatment the majority of patients receive? | 1 | 1 | 1 | 1 |
| Was an attempt made to blind study subjects to the intervention? | 1 | 0 | 0 | 1 |
| Was an attempt made to blind those measuring the main outcomes of the intervention? | 0 | 1 | 0 | 0 |
| Results based on “data dredging”, were clearly reported? | 1 | 1 | 1 | 1 |
| Do the analyses adjust for different lengths (follow-up or period between the intervention and outcome)? | 1 | 1 | 1 | 1 |
| Were the statistical tests used to assess the main outcomes appropriate? | 1 | 1 | 1 | 1 |
| Was compliance with intervention/s reliable? | 1 | 1 | 1 | 1 |
| Were the main outcome measures used accurate (valid and reliable)? | 1 | 1 | 1 | 1 |
| Were the patients in different groups or were the cases and controls recruited from the same population? | 1 | 1 | 1 | 1 |
| Were study subjects in different groups or were the cases and controls recruited over the same period of time? | 1 | 1 | 1 | 1 |
| Were study subjects randomized in groups? | 1 | 0 | 1 | 1 |
| Randomized intervention assignment concealed from patients and health care staff until recruitment was complete? | 0 | 0 | 0 | 1 |
| **Partial score/items (n)** | **10** | **9** | **9** | **11** |
| **Partial score/items (%)** | **77** | **69** | **69** | **84** |

**Table S4 *(continuation).*** Bias analysis of clinical studies according to the Downs and Black Quality Index\*.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Studies**  **Signaling questions** | **Botoni et al. 2007** | **Khoury et al. 1996** | **Szajnbok et al. 1993** | **Robert et al. 1992** |
| Adequate adjustment for confounding from which the main findings were drawn? | 0 | 0 | 0 | 0 |
| Losses of patients were considered? | 1 | 1 | 1 | 1 |
| **Partial score/items (n)** | 1 | 1 | 1 | 1 |
| **Partial score/items (%)** | 50 | 50 | 50 | 50 |
| **Quality Score/items (n)** | **19** | **17** | **18** | **20** |
| **Quality Score/items (%)** | **73** | **65** | **69** | **77** |

\* Downs and Black Measuring Quality in randomized and non-randomized clinical assays (*Journal of Epidemiology and Community Health* 52:377-384, 1998).