**Additional file 3: Categories of quality of evidence based on GRADE**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Domain of certainty of included articles** | | | | | | **Factor that increase certainty included articles** | | | | **Overall quality** |
| Number of studies | Study design | Publication bias | Indirectness | Inconsistency /heterogeneity | Imprecision | Risk bias | Magnitude of effect | Dose response gradient | Effect of confounding variables |  | |
| 49 | Observational studies (evidence of certainty assessment started at low because of the design) | Not serious (No evidence of publication bias based on funnel plot and egger’s test) | Not serious (all studies the outcome variable objectively) | Serious (significant heterogeneity detected) | Not serious (all included studies have good sample size, narrow confidence interval of the estimate) | Serious (few number of studies included, the method employed in the study is cross-sectional, prone to bias) | Large magnitude of effect is observed in this meta-analysis | Not applicable for observational studies | All included studies have  controlled the effect of confounding | Low | |

**Additional file 3 continued: detailed explanations how to assess the GRADE**

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| --- | --- |
| **Rank** | **Description of the rank** |
| High ++++ | Further research is very unlikely to change our confidence in the estimate effect |
| Moderate +++ | Further research is likely to have an important impact in our confidence in the estimate of effect and change the estimate |
| Low ++ | Further research is very likely to have an important impact in our confidence in the estimate effect is likely to change the estimate |
| Very low + | Any estimate of effect is very uncertain |
| **Grade assessment** | |
| Study limitations: If most trials at low ROB = no downgrade for limitations of design; If most trials at unclear ROB = downgrade for limitations of design by 1 level; If most trials at high ROB = downgrade for limitations of design by 2 levels. | |
| Inconsistency: 1 or 2 levels of downgrade depending on clinical & methodological heterogeneity (PICO), statistical heterogeneity, Confidence interval overlap | |
| Indirectness: 1 or 2 levels of downgrade depending on whether or not head-to-head comparisons were used | |
| Imprecision: 1 or 2 levels of downgrade depending on statistical heterogeneity, CI overlap and inclusion of benefits and harms in the CI | |
| Publication bias: suspected or unsuspected based on completeness of search strategy, formal statistical assessment and SR authors’ comments | |
| Outcome Importance: not important; important but not critical; critical. Refers to selected outcome and based on importance relative to intervention. i.e. implant failure critical but clinical attachment loss may be important but not | |
| Effect size: if effect is strong applicable for observational studies RR>2 or <0.5; RR>5 or RR<0.2 | |
| GRADE rating in this review: High, moderate, low, very low | |
| GRADE reported by SR authors (if provided): High, moderate, low, very low | |
| SR = Systematic review; ROB = Risk of bias; CI = Confidence interval; OR = Odds ratio; Risk ratio | |