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| --- | --- | --- | --- | --- | --- | --- |
| ***Study (1st Author, Year)*** | **Crujeiras et al** | **Harvie et al** | **Pinhel et al 2017 and 2018** | **Rendo-Urteaga et al** | **Samblas et al** | **vanBussel et al** |
| *Q1* | Y | N | Y | Y | Y | Y |
| *Q2* | Y | Y | Y | Y | Y | Y |
| *Q3* | N | Y | N | Y | Y | Y |
| *Q4* | NA | NA | Y | NA | NA | Y |
| *Q5* | NA | NA | N | NA | NA | NA |
| *Q6* | N | Y | Y | Y | Y | Y |
| *Q7* | N | Y | Y | Y | Y | Y |
| *Q8* | N | N | N | N | N | N |
| *Q9* | NA | NA | NA | NA | NA | NA |
| *Q10* | N | Y | Y | Y | Y | Y |
| *Q11* | N | Y | Y | Y | Y | Y |
| *Q12* | N | N | N | Y | N | Y |
| *Q13*  | N | Y | N | Y | Y | Y |
| *Q14*  | N | N | N | N | N | N |
| *Q15* | Y | Y | Y | Y | Y | Y |
| **Overall** | NEG | P | NEU | P | NEU | P |

Additional file 1. Quality and Risk of Bias Assessment for included studies. If “Yes” were answered for 8 or more questions studies were designated Positive, if 8 or more answers were “No” the studies were designated Negative otherwise studies were designated Neutral. Adapted from (1).

The following questions were used for quality assessment and risk of bias:

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| **VALIDITY QUESTIONS - PRIMARY STUDIES** |
| *1. Was the research question clearly stated?* |
| *2. Was the study design clearly stated?* |
| *3. Was the selection of study subjects/patients free from bias? Was the eligibility criteria clearly stated along with the sources and methods of selection of participants/cases* |
| *4. Were study groups comparable?* |
| *5. If studies were matched was the matching criteria clearly outlined?* |
| *6. Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?* |
| *7. Were outcomes clearly defined and the measurements valid and reliable?* |
| *8. Was method of handling withdrawals described?* |
| *9. Was blinding used to prevent introduction of bias?* |
| *10. Were statistical methods appropriately described?* |
| *11. Was the statistical analysis appropriate for the study design and type of outcome indicators?* |
| *12. Were appropriate quality control checks performed on expression data and clearly reported?* |
| *13. Were conclusions supported by results with biases and limitations taken into consideration?*  |
| *14. Was the direction and magnitude of any potential biases discussed?*  |
| *15. Is bias due to study’s funding or sponsorship unlikely?* |
|  |
| **Negative/Neutral/Positive (N/0/P)** |
| **If most (eight or more) of the answers to the above validity questions are “No,” the report should be designated negative** |
| **If the answers to validity criteria questions 3, 4, 6, and 7 do not indicate that the study is exceptionally strong, the report should be designated neutral** |
| **If most of the answers to the above validity questions are “Yes” (including criteria 2, 3, 6, 7 and at least one additional “Yes”), the report should be designated positive** |

References:

1. Day KJ, Adamski MM, Dordevic AL, Murgia C. Genetic variations as modifying factors to dietary zinc requirements—A systematic review. Nutrients. 2017;9(2):148.