| Gorostiaga et al 2005 | Score |
|--|-------|
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the | 1 |
| introduction or methods section? | |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a | 0 |
| consequence of the intervention been reported? | |
| 9. Have the characteristics of patients lost to follow-up been described? | 0 |
| 10. Have actual probability values been reported for the main | 0 |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative of the entire sample from which they were recruited? | 1 |
| 12. Were those subjects who were prepared to participated representative of the entire population from which they were recruited? | 0 |
| 13. Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive? | 1 |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention they received? | 0 |
| 15. Was an attempt made to blind those measuring the main outcomes of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? | 1 |
| 18. Were the statistical tests used to assess the main outcomes appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and reliable? | 0 |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control | 1 |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |

| cohort studies) or were the cases and controls (case-control | |
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| studies) recruited over the same time? | 1 |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | |
| irrevocable? | 0 |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | 0 |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power 27. Did the study have sufficient power to detect a clinically. | 1 |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being due to chance is $< 5\%$ | |
| <i>Holm et al 2004</i> | Score |
| | Scole |
| Reporting 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
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| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
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| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
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| 4. Are the intervention of interest clearly described?5. Are the distributions of principal confounder in each group of | <u> </u> |
| | 1 |
| subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | <u> </u> |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 |
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| 8. Have all of the important adverse events that may be a | 0 |
| 9. Have the characteristics of patients lost to follow-up been | 0 |
| described? | 0 |
| 10. Have actual probability values been reported for the main | 0 |
| outcomes except where the probability value is less than 0.001? | 0 |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 1 |
| of the entire sample from which they were recruited? | 1 |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | 0 |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | 1 |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | ~ |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | ~ |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | ~ |
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| 17. In trials and cohort studies, do the analyses adjust for different | 1 |

| time period between the intervention and outcome the same for cases and controls? | |
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| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 0 |
| reliable? | |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited over the same time? | |
| 23. Were study subjects randomized to intervention groups? | 1 |
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| patients and health care staff until recruitment was complete and | |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | 0 |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | 1 |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being the technical $\frac{1}{2}$ | |
| due to chance is < 5% Oxyzoglou et al 2007 | Coore |
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| Reporting | |
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| <i>Reporting</i> Is the hypothesis/aim/objective of the study clearly described? Are the main outcomes to be measured clearly described in the introduction or methods section? Are the characteristics of the patients included in the study clearly described? Are the intervention of interest clearly described? Are the distributions of principal confounder in each group of subjects to be compared clearly described? Are the main findings of the study clearly described? Does the study provide estimates of the random variability in the data for the main outcomes? Have all of the important adverse events that may be a consequence of the intervention been reported? Have the characteristics of patients lost to follow-up been described? | 1 1 1 1 1 1 1 1 0 1 1 |
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| Reporting 1. Is the hypothesis/aim/objective of the study clearly described? 2. Are the main outcomes to be measured clearly described in the introduction or methods section? 3. Are the characteristics of the patients included in the study clearly described? 4. Are the intervention of interest clearly described? 5. Are the distributions of principal confounder in each group of subjects to be compared clearly described? 6. Are the main findings of the study clearly described? 7. Does the study provide estimates of the random variability in the data for the main outcomes? 8. Have all of the important adverse events that may be a consequence of the intervention been reported? 9. Have the characteristics of patients lost to follow-up been described? 10. Have actual probability values been reported for the main outcomes except where the probability value is less than 0.001? External validity | 1 1 1 1 1 1 1 1 0 1 1 0 |
| Reporting 1. Is the hypothesis/aim/objective of the study clearly described? 2. Are the main outcomes to be measured clearly described in the introduction or methods section? 3. Are the characteristics of the patients included in the study clearly described? 4. Are the intervention of interest clearly described? 5. Are the distributions of principal confounder in each group of subjects to be compared clearly described? 6. Are the main findings of the study clearly described? 7. Does the study provide estimates of the random variability in the data for the main outcomes? 8. Have all of the important adverse events that may be a consequence of the intervention been reported? 9. Have the characteristics of patients lost to follow-up been described? 10. Have actual probability values been reported for the main outcomes except where the probability value is less than 0.001? External validity 11. Were the subjects asked to participate in the study representative of the entire sample from which they were recruited? 12. Were those subjects who were prepared to participated | 1 1 1 1 1 1 1 1 0 1 1 0 |
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| 13. Were the staff, places, and facilities where the patients were | 1 |
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| treated, representative of the treatment the majority of patients | |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | - |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | Ĩ |
| time period between the intervention and outcome the same for | |
| cases and controls? | |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 0 |
| reliable? | |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited over the same time? | |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | - |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is < 5% | C |
| Ettema et al 2008 | Score |
| Reporting | 1 |
| 1. Is the hypothesis/aim/objective of the study clearly described? | <u>1</u> 1 |
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
| 3. Are the characteristics of the patients included in the study clearly | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
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| data for the main outcomes? | Ŧ |
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| 8. Have all of the important adverse events that may be a | 0 |
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| consequence of the intervention been reported? | |
| 9. Have the characteristics of patients lost to follow-up been described? | 1 |
| 10. Have actual probability values been reported for the main | 0 |
| outcomes except where the probability value is less than 0.001? | 0 |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 0 |
| of the entire sample from which they were recruited? | 0 |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | 0 |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | 1 |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | 0 |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | 1 |
| time period between the intervention and outcome the same for | |
| cases and controls? | |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 0 |
| reliable? | Ū |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | - |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | _ |
| studies) recruited over the same time? | |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | Ū |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | ~ |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | ~ |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | ÷ |
| due to chance is $< 5\%$ | |
| Gorostiaga et al 1999 | Score |
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| Reporting | |
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| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the | 1 |
| introduction or methods section? | |
| 3. Are the characteristics of the patients included in the study clear | ly 1 |
| described? | , , |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the | e 1 |
| data for the main outcomes? | |
| 8. Have all of the important adverse events that may be a | 0 |
| consequence of the intervention been reported? | |
| 9. Have the characteristics of patients lost to follow-up been | 1 |
| described? | |
| 10. Have actual probability values been reported for the main | 1 |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | e 1 |
| of the entire sample from which they were recruited? | |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | 0 |
| 15. Was an attempt made to blind those measuring the main outcom | es 0 |
| of the intervention? | |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | 1 |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the time pariod between the intervention and outcome the same for | |
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| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 0 |
| reliable? | U |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | 1 |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
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| 23. Were study subjects randomized to intervention groups? | 0 |
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| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is $< 5\%$ | |
| Hermassi et al 2010 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the | 1 |
| introduction or methods section? | |
| 3. Are the characteristics of the patients included in the study clearly | 1 |
| described? | |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the | 1 |
| data for the main outcomes? | |
| 8. Have all of the important adverse events that may be a | 0 |
| consequence of the intervention been reported? | |
| 9. Have the characteristics of patients lost to follow-up been | 0 |
| described? | |
| 10. Have actual probability values been reported for the main | 1 |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 1 |
| of the entire sample from which they were recruited? | |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | - |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | |
| time period between the intervention and outcome the same for | |
| cases and controls? | |

| 18. Were the statistical tests used to assess the main outcomes | 1 |
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| appropriate? 19. Was compliance with the intervention/s reliable? | 0 |
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| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited from the same population? | |
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| cohort studies) or were the cases and controls (case-control | |
| studies) recruited over the same time? | |
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| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is $< 5\%$ | |
| Hermassi et al 2011 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the | 1 |
| introduction or methods section? | |
| 3. Are the characteristics of the patients included in the study clearly | 1 |
| described? | |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the | 1 |
| data for the main outcomes? | 0 |
| 8. Have all of the important adverse events that may be a | 0 |
| consequence of the intervention been reported? | 0 |
| 9. Have the characteristics of patients lost to follow-up been described? | 0 |
| | 1 |
| 10. Have actual probability values been reported for the main | 1 |
| outcomes except where the probability value is less than 0.001? External validity | |
| | 1 |
| 11. Were the subjects asked to participate in the study representative of the entire sample from which they were recruited? | 1 |
| of the entire sample from which they were recruited? | 0 |
| 12. Were those subjects who were prepared to participated representative of the entire population from which they were | U |
| recruited? | |
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| 13. Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients | 1 |

| receive? | |
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| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | |
| time period between the intervention and outcome the same for | |
| cases and controls? | |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 1 |
| reliable? | |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited over the same time? | |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is < 5% | |
| Hermassi et al 2014 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the | 1 |
| introduction or methods section? | |
| 3. Are the characteristics of the patients included in the study clearly | 1 |
| described? | |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the | 1 |
| data for the main outcomes? | |
| | |
| 8. Have all of the important adverse events that may be a | 0 |

| 9. Have the characteristics of patients lost to follow-up been described? | 0 |
|---|-------|
| 10. Have actual probability values been reported for the main | 0 |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 1 |
| of the entire sample from which they were recruited? | |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | - |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | 1 |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | |
| time period between the intervention and outcome the same for | |
| cases and controls? | 1 |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 0 |
| reliable? | 0 |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | 1 |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | - |
| studies) recruited over the same time? | |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is < 5% | |
| Hermassi et al 2015 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |

| 2. Are the main outcomes to be measured clearly described in the | 1 |
|---|---|
| introduction or methods section? | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the | 1 |
| data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a | 0 |
| consequence of the intervention been reported? | |
| 9. Have the characteristics of patients lost to follow-up been | 0 |
| described? | |
| 10. Have actual probability values been reported for the main | 1 |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 1 |
| of the entire sample from which they were recruited? | |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | 0 |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | 1 |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | |
| time period between the intervention and outcome the same for cases and controls? | |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 1 |
| reliable? | 1 |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | - |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| | |
| studies) recruited over the same time? | |
| | 1 |
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| patients and health care staff until recruitment was complete and irrevocable? | |
|--|-------|
| 25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? | 0 |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is < 5% | 1 |
| Marques & González-Badillo 2006 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a consequence of the intervention been reported? | 0 |
| 9. Have the characteristics of patients lost to follow-up been described? | 1 |
| 10. Have actual probability values been reported for the main outcomes except where the probability value is less than 0.001? | 0 |
| External validity | |
| 11. Were the subjects asked to participate in the study representative of the entire sample from which they were recruited? | 1 |
| 12. Were those subjects who were prepared to participated representative of the entire population from which they were recruited? | 0 |
| 13. Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive? | 1 |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention they received? | 0 |
| 15. Was an attempt made to blind those measuring the main outcomes of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? | 1 |
| 18. Were the statistical tests used to assess the main outcomes appropriate? | 1 |

| 19. Was compliance with the intervention/s reliable? 0 20. Were the main outcome measures used accurate (valid and neliable? 0 <i>Confounding (selection bias)</i> 1 21. Were the patients in different intervention groups (trials and necohort studies) or were the cases and controls (case-control studies) recruited from the same population? 1 22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) or were the cases and controls (case-control studies) recruited over the same time? 1 23. Were study subjects randomized to intervention groups? 1 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? 0 | |
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| reliable?Confounding (selection bias)21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) or were the cases and controls (case-control studies) recruited over the same time?23. Were study subjects randomized to intervention groups?124. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?0 | |
| Confounding (selection bias)21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population?122. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time?123. Were study subjects randomized to intervention groups?124. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?0 | |
| 21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population? 1 22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time? 1 23. Were study subjects randomized to intervention groups? 1 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? 0 | |
| cohort studies) or were the cases and controls (case-control studies) recruited from the same population?22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time?23. Were study subjects randomized to intervention groups?124. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? | |
| cohort studies) or were the cases and controls (case-control studies) recruited from the same population?22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time?23. Were study subjects randomized to intervention groups?124. Was the randomized intervention assignment concealed from both | |
| 22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time? 1 23. Were study subjects randomized to intervention groups? 1 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? 0 | |
| cohort studies) or were the cases and controls (case-control studies) recruited over the same time?23. Were study subjects randomized to intervention groups?124. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?0 | |
| studies) recruited over the same time?23. Were study subjects randomized to intervention groups?24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? | |
| 23. Were study subjects randomized to intervention groups?124. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?0 | |
| 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? | |
| patients and health care staff until recruitment was complete and irrevocable? | |
| irrevocable? | |
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| $25 \mathbf{W}_{2} \mathbf{d}_{2} \mathbf{d}_{2$ | |
| 25. Was there adequate adjustment for confounding in the analyses 0 | |
| from which the main findings were drawn? | |
| 26. Were losses of patients to follow-up taken into account? 0 | |
| Power | |
| 27. Did the study have sufficient power to detect a clinically 1 | |
| important effect where the probability value for a difference being | |
| due to chance is $< 5\%$ | |
| Ignjatovic et al 2012 Score | |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | |
| 2. Are the main outcomes to be measured clearly described in the 1 | |
| introduction or methods section? | |
| 3. Are the characteristics of the patients included in the study clearly 1 | |
| described? | |
| 4. Are the intervention of interest clearly described? 1 | |
| 5. Are the distributions of principal confounder in each group of 1 | |
| subjects to be compared clearly described? | |
| 6. Are the main findings of the study clearly described? | |
| 7. Does the study provide estimates of the random variability in the 1 | |
| data for the main outcomes? | |
| 8. Have all of the important adverse events that may be a 0 | |
| consequence of the intervention been reported? | |
| 9. Have the characteristics of patients lost to follow-up been 1 | |
| described? | |
| 10. Have actual probability values been reported for the main0 | |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative 1 | |
| of the entire sample from which they were recruited? | |
| 12. Were those subjects who were prepared to participated 0 | |
| representative of the entire population from which they were | |
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| recruited? | |
| recruited? 13. Were the staff, places, and facilities where the patients were 1 | |
| recruited? 13. Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients | |
| recruited? 13. Were the staff, places, and facilities where the patients were 1 | |

| 14. Was an attempt made to blind study subjects to the intervention they received? | 0 |
|--|-------|
| 15. Was an attempt made to blind those measuring the main outcomes of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? | 1 |
| 18. Were the statistical tests used to assess the main outcomes appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and reliable? | 1 |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population? | 1 |
| 22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time? | 1 |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? | 0 |
| 25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? | 0 |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is < 5% | 1 |
| Caravalho et al 2014 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a consequence of the intervention been reported? | 0 |
| 9. Have the characteristics of patients lost to follow-up been described? | 1 |
| | |

| 10. Have actual probability values been reported for the main | 0 |
|--|-------|
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative of the entire sample from which they were recruited? | 1 |
| 12. Were those subjects who were prepared to participated | 0 |
| | 0 |
| representative of the entire population from which they were recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | 1 |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | 0 |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | 1 |
| time period between the intervention and outcome the same for | |
| cases and controls? | |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 0 |
| reliable? | 0 |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited over the same time? | |
| 23. Were study subjects randomized to intervention groups? | 0 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is $< 5\%$ | |
| Chelly et al 2014 | Score |
| Reporting | |
| | 1 |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| Is the hypothesis/aim/objective of the study clearly described? Are the main outcomes to be measured clearly described in the | 1 |

| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
|---|---|
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a consequence of the intervention been reported? | 0 |
| 9. Have the characteristics of patients lost to follow-up been described? | 1 |
| 10. Have actual probability values been reported for the main outcomes except where the probability value is less than 0.001? | 0 |
| External validity | |
| 11. Were the subjects asked to participate in the study representative of the entire sample from which they were recruited? | 1 |
| 12. Were those subjects who were prepared to participated representative of the entire population from which they were recruited? | 0 |
| 13. Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive? | 1 |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention they received? | 0 |
| 15. Was an attempt made to blind those measuring the main outcomes of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? | 1 |
| 18. Were the statistical tests used to assess the main outcomes appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and reliable? | 0 |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population? | 1 |
| 22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time? | 1 |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? | 0 |

| 25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? | 0 |
|---|-------|
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | 0 |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is $< 5\%$ | |
| Raeder et al 2015 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a consequence of the intervention been reported? | 0 |
| 9. Have the characteristics of patients lost to follow-up been described? | 1 |
| 10. Have actual probability values been reported for the main | 0 |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 1 |
| of the entire sample from which they were recruited? | _ |
| 12. Were those subjects who were prepared to participated representative of the entire population from which they were recruited? | 0 |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | I |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | Ŭ |
| 15. Was an attempt made to blind those measuring the main outcomes of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? | 1 |
| 18. Were the statistical tests used to assess the main outcomes appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| | ~ |

| reliable? | |
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| reliable? | |
| Confounding (selection bias) | 1 |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control atudies) recruited from the same population? | |
| studies) recruited from the same population? | 1 |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control studies) recruited over the same time? | |
| studies) recruited over the same time? | 0 |
| 23. Were study subjects randomized to intervention groups? | 0 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and irrevocable? | |
| | 0 |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | 0 |
| | 1 |
| 27. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being | 1 |
| due to chance is $< 5\%$ | |
| Genevois et al 2014 | Score |
| | Scole |
| Reporting | 1 |
| 1. Is the hypothesis/aim/objective of the study clearly described? | <u> </u> |
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
| | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | <u> </u> |
| subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the | <u> </u> |
| data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a | 0 |
| consequence of the intervention been reported? | 0 |
| 9. Have the characteristics of patients lost to follow-up been | 1 |
| described? | 1 |
| 10. Have actual probability values been reported for the main | 0 |
| outcomes except where the probability value is less than 0.001? | 0 |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 0 |
| of the entire sample from which they were recruited? | U |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | U |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | 1 |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | U |
| | |

| 15. Was an attempt made to blind those measuring the main outcomes of the intervention? | 0 |
|---|-------|
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls? | 1 |
| 18. Were the statistical tests used to assess the main outcomes appropriate? | 1 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and reliable? | 0 |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population? | 1 |
| 22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time? | 1 |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? | 0 |
| 25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? | 0 |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is < 5% | 1 |
| Granados et al 2007 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a consequence of the intervention been reported? | 0 |
| 9. Have the characteristics of patients lost to follow-up been described? | 1 |
| 10. Have actual probability values been reported for the main outcomes except where the probability value is less than 0.001? | 0 |
| | |

| Fut any al coalidity | |
|---|-------|
| External validity | 1 |
| 11. Were the subjects asked to participate in the study representative | 1 |
| of the entire sample from which they were recruited? | 0 |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were recruited? | |
| | 1 |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients receive? | |
| Study bias | |
| | 0 |
| 14. Was an attempt made to blind study subjects to the intervention they received? | - |
| 15. Was an attempt made to blind those measuring the main outcomes of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | |
| time period between the intervention and outcome the same for | |
| cases and controls? | |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | 0 |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and reliable? | 0 |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited over the same time? | |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| patients and health care staff until recruitment was complete and | |
| irrevocable? | |
| 25. Was there adequate adjustment for confounding in the analyses | 0 |
| from which the main findings were drawn? | |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is $< 5\%$ | C |
| Toumi et al 2004 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
| 3. Are the characteristics of the patients included in the study clearly | 1 |
| described? | |
| | |

| 4. Are the intervention of interest clearly described? | 1 |
|--|---|
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the | 1 |
| data for the main outcomes? | |
| 8. Have all of the important adverse events that may be a | 0 |
| consequence of the intervention been reported? | |
| 9. Have the characteristics of patients lost to follow-up been | 1 |
| described? | |
| 10. Have actual probability values been reported for the main | 0 |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 1 |
| of the entire sample from which they were recruited? | |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | |
| 16. If any of the results of the study were based on "data dredging", | 0 |
| was this made clear? | |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | |
| time period between the intervention and outcome the same for | |
| cases and controls? | |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and | 0 |
| reliable? | |
| Confounding (selection bias) | |
| 21. Were the patients in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited from the same population? | |
| 22. Were study subjects in different intervention groups (trials and | 1 |
| cohort studies) or were the cases and controls (case-control | |
| studies) recruited over the same time? | |
| | 1 |
| 25. Were study subjects randomized to micryention groups? | |
| 23. Were study subjects randomized to intervention groups? 24. Was the randomized intervention assignment concealed from both | 0 |
| 24. Was the randomized intervention assignment concealed from both | 0 |
| 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and | 0 |
| 24. Was the randomized intervention assignment concealed from both | 0 |

| 26. Were losses of patients to follow-up taken into account? | 0 |
|---|-------|
| Power 27 Did the study have sufficient neuron to detect a aligically | 1 |
| 27. Did the study have sufficient power to detect a clinically | 1 |
| important effect where the probability value for a difference being | |
| due to chance is < 5% | 9 |
| Muijen et al 1991 | Score |
| Reporting | |
| 1. Is the hypothesis/aim/objective of the study clearly described? | 1 |
| 2. Are the main outcomes to be measured clearly described in the introduction or methods section? | 1 |
| 3. Are the characteristics of the patients included in the study clearly described? | 1 |
| 4. Are the intervention of interest clearly described? | 1 |
| 5. Are the distributions of principal confounder in each group of | 1 |
| subjects to be compared clearly described? | 1 |
| 6. Are the main findings of the study clearly described? | 1 |
| 7. Does the study provide estimates of the random variability in the data for the main outcomes? | 1 |
| 8. Have all of the important adverse events that may be a | 0 |
| consequence of the intervention been reported? | |
| 9. Have the characteristics of patients lost to follow-up been described? | 1 |
| 10. Have actual probability values been reported for the main | 0 |
| outcomes except where the probability value is less than 0.001? | |
| External validity | |
| 11. Were the subjects asked to participate in the study representative | 1 |
| of the entire sample from which they were recruited? | |
| 12. Were those subjects who were prepared to participated | 0 |
| representative of the entire population from which they were | Ū. |
| recruited? | |
| 13. Were the staff, places, and facilities where the patients were | 1 |
| treated, representative of the treatment the majority of patients | 1 |
| receive? | |
| Study bias | |
| 14. Was an attempt made to blind study subjects to the intervention | 0 |
| they received? | 0 |
| 15. Was an attempt made to blind those measuring the main outcomes | 0 |
| of the intervention? | 0 |
| 16. If any of the results of the study were based on "data dredging", was this made clear? | 0 |
| 17. In trials and cohort studies, do the analyses adjust for different | 1 |
| lengths of follow-up of patients, or in case-control studies, is the | |
| time period between the intervention and outcome the same for | |
| cases and controls? | |
| 18. Were the statistical tests used to assess the main outcomes | 1 |
| appropriate? | |
| 19. Was compliance with the intervention/s reliable? | 0 |
| 20. Were the main outcome measures used accurate (valid and reliable? | 0 |
| Confounding (selection bias) | |

| 21. Were the patients in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited from the same population? | 1 |
|--|---|
| 22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same time? | 1 |
| 23. Were study subjects randomized to intervention groups? | 1 |
| 24. Was the randomized intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? | 0 |
| 25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? | 0 |
| 26. Were losses of patients to follow-up taken into account? | 0 |
| Power | |
| 27. Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is < 5% | 1 |