**Overview of this appendix**

Assessments are presented in alphabetical order by study ID. For each study, an assessment was done for each outcome and comparison contributing to the MA.

For each study we report

* the outcome domain for the assessment,
* other outcomes included in MAs for the study (noting if the assessment was the same for these or other comparisons), and
* the study design (parallel, cluster or cross-over).

Where the RoB assessment was the same for all outcomes, only one assessment is reported. If the study reported multiple arms that were combined for analysis (e.g. a sham control and a no intervention control) we reported the rating for the comparison at highest risk of bias.

The assessment includes:

* the overall risk of bias judgement (as reported in forest plots),
* the judgement for each domain, with an explanation provided for each signalling questions for which the response could lead to a judgement of high risk of bias or some concerns, and
* the response to each signalling question (numbered, the questions are reported in full below).

We did not assess studies that were not included for meta-analysis. These were counted as ‘missing results’ (i.e. those studies where the result was judged to be uninterpretable or where there were major concerns about the integrity of the data such that it would be misleading to report the results). In such cases, concerns about bias leading to an under- or over-estimate of effect are inconsequential compared to the impact of major errors in reported data or the interpretation of that data.

**Box E1**. Signalling questions from the revised Cochrane risk of bias (ROB 2) tools for randomised trials (questions in grey cells are specific to the trial design)

| **Parallel (individually randomised)** | **Crossover (XO)** |
| --- | --- |
| **Domain 1.** Bias arising from the randomisation process |  | |
| 1.1 Was the allocation sequence random? | 1.1 Was the allocation sequence random? |
| 1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions? | 1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions? |
| 1.3 Did baseline differences between intervention groups suggest a problem with the randomization process? | 1.3 Did baseline differences between intervention groups at the start of the first period suggest a problem with the randomization process? |
| **Domain 1b.** Timing of identification or recruitment of participants | **Domain S.** Bias arising from period and carryover effects | |
| n/a | S.1 Was the number of participants allocated to each of the two sequences equal or nearly equal? |
| n/a | S.2 If N/PN/Ni to S.1 Were period effects accounted for in the analysis |
| n/a | S.3 Was there sufficient time for any carryover effects to have disappeared before outcome assessment in the second period? |
| **Domain 2.** Bias due to deviations from intended interventions |  | |
| 2.1 Were participants aware of their assigned intervention during the trial? | 2.1 Were participants aware of their assigned intervention during each period of the trial? |
| 2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during the trial? | 2.2 Were carers and people delivering the interventions aware of participants' assigned intervention during each period of the trial? |
| 2.3 If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context? | 2.3 If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention that arose because of the trial context? |
| 2.4 If Y/PY to 2.3 Were these deviations likely to have affected the outcome? | 2.4 If Y/PY to 2.3 Were these deviations likely to have affected the outcome? |
| 2.5 If Y/PY to 2/4: Were these deviations from intended intervention balanced between groups? | 2.5 If Y/PY to 2/4: Were these deviations from intended intervention balanced between groups? |
| 2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention? | 2.6 Was an appropriate analysis used to estimate the effect of assignment to intervention? |
| 2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized? | 2.7 If N/PN/NI to 2.6: Was there potential for a substantial impact (on the result) of the failure to analyse participants in the group to which they were randomized? |
| **Domain 3**. Bias due to missing outcome data |  | |
| 3.1 Were data for this outcome available for all, or nearly all, participants randomized? | 3.1 Were data for this outcome available for all, or nearly all, participants randomized? |
| 3.2 If N/PN/NI to 3.1a or 3.1b: Is there evidence that the result was not biased by missing data? | 3.2 If N/PN/NI to 3.1a or 3.1b: Is there evidence that the result was not biased by missing data? |
| 3.3 If N/PN to 3.2 Could missingness in the outcome depend on its true value? | 3.3 If N/PN to 3.2 Could missingness in the outcome depend on its true value? |
| 3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value? | 3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value? |
| **Domain 4**. Bias in the measurement of the outcome |  | |
| 4.1 Was the method of measuring the outcome inappropriate? | 4.1 Was the method of measuring the outcome inappropriate? |
| 4.2 Could measurement or ascertainment of the outcome have differed between intervention groups? | 4.2 Could measurement or ascertainment of the outcome have differed between interventions within each sequence? |
| 4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants? | 4.3 If N/PN/NI to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants? |
| 4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received? | 4.4 If Y/PY/NI to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received? |
| 4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received? | 4.5 If Y/PY/NI to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received? |
| **Domain 5**. Bias from selection of the reported result |  | |
| 5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? | 5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? |
| *Is the numerical results being assessed likely to have been selected, on the basis of the results from …* | | |
| 5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain? | 5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain? |
| 5.3 ... multiple eligible analyses of the data? | 5.4 Is a result based on data from both periods sought, but unavailable on the basis of carryover having been identified? |

| **Study ID.  Abedini 2022** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Participants were randomised based on medical record numbers (even numbers assigned to intervention group, odd numbers assigned to control group).  No information provided to determine if the person allocating participants to groups could have predicted the allocation sequence, or if they had motivation to change the allocation (excluding participant or delaying enrolment). | N | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual oncology care, so it is likely that participants were aware of their assigned intervention.  The same researcher delivered the intervention and conducted assessments for both arms and it is likely that they were aware of the participants’ assigned intervention  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | PY | PY | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Some concerns | I: 30/36 (17% missing), C: 30/36 (17% missing)  Analysis method did not correct for bias; no sensitivity analysis  An equal proportion of participants withdrew in both groups so this was unlikely due to outcome worsening | N | N | NI | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to inactive forms of usual care that were likely to influence the outcome. | N | PN | NI | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Akkoz Cevik 2021** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | No info on concealment | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | ITT | N | PN | NA | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Reflexology was applied during active labour, same time as outcome assessment  R was delivered as part of pre-labour treatment; participants were less likely to notice or expect the intervention. | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Retrospective registration (2019-03-13) | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Akkoz Cevik 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | No info on concealment | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | ITT | N | PN | NA | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Reflexology was applied during active labour, same time as outcome assessment  R was delivered as part of pre-labour treatment; participants were less likely to notice or expect the intervention. | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Retrospective registration (2019-03-13) | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Aliashraf Jodat 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | PN: Block randomisation, fixed block size (14x2) but only 2 predictable allocations out of 28 | PN | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were aware that they had received R or usual care.  Research staff who delivered the R intervention were not blinded and knew the protocol.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | R group was measured after 20min of R + 10min of rest = 30min after ECT; C group was measured 1h after ECT. 30min are unlikely to cause significant difference in VAS score, plus some buffer time btw ECT, R and outcome measurement can be expected.  Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Anderson 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Patients were assigned to intervention group by random drawing - no further information provided. | PY | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so it is likely that participants were aware of their assigned intervention.  The same researchers were involved in care for both arms and it is likely that they were aware of the participants’ assigned intervention.  Intention-to-treat (ITT) analysis | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | I: 20/20 (0% missing) C: 20/20 (0% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received reflexology or no intervention.  Participants’ knowledge of the intervention they received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to no treatment that were likely to influence the outcome. | PN | PN | PY | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | There is only one possible way in which the outcome can be measured (and at a single timepoint).  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Aslan 2022** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Imbalance in baseline measurement of outcome (statistically significant) | Y | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Aslan 2022** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Attias 2016** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Allocation to complimentary and alternative medicine (CAM) intervention, guided imagery, or standard care appears to be randomised. However participats allocated to CAM intervention were further allocated to one of 5 CAM interventions according to the day of surgery, to align with practitioner work days. | PY | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator group received usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | PY | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to inactive forms of usual care that were likely to influence the outcome. | N | PN | Y | Y | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Attias 2018** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Based on dates when reflexologist was working; predictable and not truly random  Imbalance in gender and laparoscopic surgery, both of which can influence pain | N | N | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | Y | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Aydin 2021** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | PY | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | I: 36/38 (5% missing); C:36/38 (5% missing)  Analysis method did not correct for bias; no sensitivity analysis | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or no intervention  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to no intervention that were likely to influence the outcome. | N | PN | PY | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Azima 2015** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Permuted block randomisation used; random sized blocks so the person allocating participants to their intervention groups was unlikely to be able to predict the allocation sequence | Y | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so it is likely that participants were aware of their assigned intervention.  The same people were involved in care for both arms and it is likely that they were aware of the participants’ assigned intervention.  Use of pharmacological and non-pharmacological pain relief was an exclusion criteria. Use of pain relief was not measured in this population with primary dysmenorrhoea. It is unclear if those in the no intervention group used any/more pain relief than the  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | PY | NI | NA | NA | Y | NA |
| 3. Bias due missing outcome data | High | I: 34/40 (15% missing) C: 34/40 (15% missing)  Analysis method did not correct for bias; no sensitivity analysis  Azima 2015 http://dx.doi.org/10.1016/j.jpag.2015.02.003 (study report of ineligible comparator arms v control) report that some partcipants were excluded due to pain intensity, but no information how many, and from which group. | N | N | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors)  were aware that they had received reflexology or  no intervention.  Relief of dysmenorrhoea pain.  Participants were likely to have had a prior belief about the benefits of reflexology compared to no intervention, hence participant's perception of pain was likely to be influenced. | N | N | Y | Y | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Multiple measures eligible for the meta-analysis of pain are fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Babazadeh 2020** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Some imbalance in baseline characteristics but unlikely to affect outcome | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Did not attend first session of R (n=1)  I: 1; C: 0  Naïve per protocol  1 deviation (1.3%) | Y | Y | Y | PY | N | N | PN |
| 3. Bias due missing outcome data | High | I: 36/40 (10% missing); C: 37/40 (8% missing)  Analysis method did not correct for bias; no sensitivity analysis  3 participants (4%) were LTFU without reasons - not answer referral calls and not interested to participate. It is theoretically possible that those with worse outcome (fatigue) would miss f/u.  Imbalance in reasons for LTFU (that are related to outcomes) btw groups (I: 0/40; C: 3/40) | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Bagheri-Nesami 2014** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | No information to determine if the person allocating participants to groups could have predicted the allocation sequence, or if they had motivation to change the allocation (excluding participant or delaying enrolment). | NI | PN | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | The same researcher was involved in care for both arms and they were aware of the participants’ assigned intervention.  Intention-to-treat (ITT) analysis | PY | Y | PN | NA | NA | PY | NA |
| 3. Bias due missing outcome data | Low | I: 40/40 (0% missing) C: 40/40 (0% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low |  | PN | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Measures eligible for the meta-analysis appear fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Baglama 2019** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Some imbalance in baseline characteristics but likely by chance and unlikely to affect outcome | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Caregivers who delivered the intervention were not blinded.  Did not receive intervention (n=2); intervention not implemented regularly (n=2)  I: 2; C: 2  Naïve per protocol  6 deviations (5%) | Y | Y | Y | PY | Y | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 60/64 (7% missing); C: 60/64 (7% missing)  Analysis method did not correct for bias; no sensitivity analysis  4 participants (3%) were LTFU for reasons unrelated to outcomes (diabetes, surgery, death).  2 participants (2%) were LTFU but not related to outcome - intervention not implemented regularlyy. Patients with worse outcome (anxiety) would have been more likely to attend clinic | PN | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants, caregivers and clinicians (unclear which of these were outcome assessors) were not blinded.  C is reading which can be perceived as equally effective | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Baglama 2019** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Some imbalance in baseline characteristics but likely by chance and unlikely to affect outcome | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Caregivers who delivered the intervention were not blinded.  Did not receive intervention (n=2); intervention not implemented regularly (n=2)  I: 2; C: 2  Naïve per protocol  6 deviations (5%) | Y | Y | Y | PY | Y | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 60/64 (7% missing); C: 60/64 (7% missing)  Analysis method did not correct for bias; no sensitivity analysis  1 participants (1%) were LTFU for reasons related to outcomes (death - could be a result of worsening of cancer) | PN | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants, caregivers and clinicians (unclear which of these were outcome assessors) were not blinded.  C is reading which can be perceived as equally effective | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Baglama 2019** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Some imbalance in baseline characteristics but likely by chance and unlikely to affect outcome | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Caregivers who delivered the intervention were not blinded.  Did not receive intervention (n=2); intervention not implemented regularly (n=2)  I: 2; C: 2  Naïve per protocol  6 deviations (5%) | Y | Y | Y | PY | Y | N | PN |
| 3. Bias due missing outcome data | Low | I: 60/64 (7% missing); C: 60/64 (7% missing)  Analysis method did not correct for bias; no sensitivity analysis  4 participants (3%) were LTFU for reasons unrelated to outcomes (diabetes, surgery, death).  2 participants (2%) were LTFU without reasons - intervention not implemented regularly. Patients with worse outcome would have been more likely to attend clinic | PN | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants, caregivers and clinicians (unclear which of these were outcome assessors) were not blinded.  C is reading which can be perceived as equally effective | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Bahrami 2018** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Bakhshi 2022** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Caregivers who delivered the R intervention were not blinded.  Failure to follow sequence of intervention (n=2)  I: 0; C: 2  Naïve per protocol  2 deviations (3%) | Y | Y | Y | PY | N | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 30/35 (14% missing); C: 30/35 (14% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reason were provided for LTFU but patients with worse outcome (pain) would have been more likely to attend clinic | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants and data collector (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Bakir 2018** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Significant difference in baseline pain | Y | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Not receiving intervention (n=3)  I: 3; C: 0  Naïve per protocol  3 deviations (4%) | PY | PY | Y | PY | N | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 30/34 (12% missing); C: 30/34 (12% missing)  Analysis method did not correct for bias; no sensitivity analysis  2 participants were lost to follow-up for reasons unrelated to outcomes (neuropathy). No reason were provided for LTFU for 3 participants but patients with worse outcome (pain) would have been more likely to attend clinic | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants and data collector (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Bakir 2018** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Significant difference in baseline pain | Y | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Not receiving intervention (n=3)  I: 3; C: 0  Naïve per protocol  3 deviations (4%) | PY | PY | Y | PY | N | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 30/34 (12% missing); C: 30/34 (12% missing)  Analysis method did not correct for bias; no sensitivity analysis  2 participants were lost to follow-up for reasons unrelated to outcomes (neuropathy). No reason were provided for LTFU for 3 participants but patients with worse outcome (sleep quality) would have been more likely to attend clinic | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants and data collector (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Chen 2011** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation. Block number was randomised, mitigating risk of predictable allocation. | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Skipped day 2/3 (n=2)  I: 2/34; C: 0/34  Naïve per protocol  2deviations 3%) which is <=10% | Y | Y | Y | PY | N | N | PN |
| 3. Bias due missing outcome data | Low | I: 32/34 (6% missing); C: 33/34 (3% missing)  Analysis method did not correct for bias; no sensitivity analysis  Measurements were taken during the same hospital stay so outcome severity is unlikely to affect LTFU | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Cicek 2021** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | PY | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so it is likely that participants were aware of their assigned intervention.  Researchers delivering the intervention were aware of the participants’ assigned intervention because the randomised allocation was not concealed.  Intention-to-treat (ITT) analysis | Y | Y | PN | NA | NA | PY | NA |
| 3. Bias due missing outcome data | Low | I: 24/24 (0% missing) C: 24/24 (0% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received reflexology or usual care.  Participants’ knowledge of the intervention they received could have influenced their response.  Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | NI | PN | PY | PY | PY |  |  |
| 5. Bias in the selection of the reported results | High | Results are only available for the overall DPN (diabetic peripheral neuropathy) score for the prioritised outcome, despite it being usual to report all subscale scores (NSS, neuropathy symptom score, and NDS, neuropathy disability score).  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PY | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Close 2016** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, physical function, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | C group received R after the study but before outcome measurement. Effort was made to conceal the true intervention (with foot bath as a sham treatment) but the usual care group would still be aware of a lack of intervention.  Clinical staff who delivered the R intervention were not blinded.  Not completing the study - reasons not provided (n=11)  Author said mITT, but the description fits naïve per protocol (excluding participants who did not complete >3 study weeks)  11 potential deviations (18%) | PY | Y | NI | NA | NA | N | PY |
| 3. Bias due missing outcome data | Low | I: 24/30 (20% missing); C: 25/30 (17% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reason were provided for LTFU but patients with worse outcome (distress) would have been more likely to attend clinic | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | R group completed questionnaire at clinic and C group completed at home, though unlikely to influence results.  Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Close 2016** | **Outcome domain.** physical function | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, physical function, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | C group received R after the study but before outcome measurement. Effort was made to conceal the true intervention (with foot bath as a sham treatment) but the usual care group would still be aware of a lack of intervention.  Clinical staff who delivered the R intervention were not blinded.  Not completing the study - reasons not provided (n=11)  Author said mITT, but the description fits naïve per protocol (excluding participants who did not complete >3 study weeks)  11 potential deviations (18%) | PY | Y | NI | NA | NA | N | PY |
| 3. Bias due missing outcome data | Some concerns | I: 24/30 (20% missing); C: 25/30 (17% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reason were provided for LTFU but patients with worse outcome (mobility) would have been less likely to attend clinic.  No imbalance in no. of LTFU btw groups. | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | R group completed questionnaire at clinic and C group completed at home, though unlikely to influence results.  Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Close 2016** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, physical function, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | C group received R after the study but before outcome measurement. Effort was made to conceal the true intervention (with foot bath as a sham treatment) but the usual care group would still be aware of a lack of intervention.  Clinical staff who delivered the R intervention were not blinded.  Not completing the study - reasons not provided (n=11)  Author said mITT, but the description fits naïve per protocol (excluding participants who did not complete >3 study weeks)  11 potential deviations (18%) | PY | Y | NI | NA | NA | N | PY |
| 3. Bias due missing outcome data | Low | I: 24/30 (20% missing); C: 25/30 (17% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reason were provided for LTFU but patients with worse outcome (pain) would have been more likely to attend clinic | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | R group completed questionnaire at clinic and C group completed at home, though unlikely to influence results.  Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Dashti 2016** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Authors stated no statistical significance but provided no statistics | NI | NI | NI |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | Y | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Dehghanmehr 2019** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | PY | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | PY | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or no intervention  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to no intervention that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Deniz 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Block randomisation. Unsure whether block size was randomised | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were infants.  Research staff who delivered the R intervention were not blinded.  ITT | PN | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Researcher and nurse (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Dikmen 2019** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded.  Research staff who delivered the R intervention were not blinded.  ITT | N | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded. | PN | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | High | Mean+SD was measured but only median+IRQ were reported in a graph. | NI | N | Y |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Dikmen 2019** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded.  Research staff who delivered the R intervention were not blinded.  ITT | N | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded. | PN | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | High | Mean+SD was measured but only median+IRQ were reported in a graph. | NI | N | Y |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Dikmen 2019** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded.  Research staff who delivered the R intervention were not blinded.  ITT | N | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded. | PN | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | High | Mean+SD was measured but only median+IRQ were reported in a graph. | NI | N | Y |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Dilek Dogan 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. same RoB all outcomes: EFMH, fatigue, pain, physical function | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so it is likely that participants were aware of their assigned intervention.  Researchers delivering the intervention were aware of the participants’ assigned intervention because the randomised allocation was not concealed.  Intention-to-treat (ITT) analysis | Y | Y | PN | NA | NA | PY | NA |
| 3. Bias due missing outcome data | Low | I: 30/33 (10% missing) C: 30/33 (10% missing) | PY | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received reflexology or usual care.  Participants’ knowledge of the intervention they received could have influenced their response.  Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | PN | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Multiple measures eligible for the meta-analysis of pain are fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Doğru 2021** | **Outcome domain.** efmh | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | 120 were assessed for eligibility and then randomised using coin flip method. It is unclear how exactly 30 participants were allocated to each of the four groups using this method (very low probability). | PY | PN | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention, so it is likely that participants were aware of their assigned intervention. (Both groups received standard care relating to their procedures).  The same people were involved in care for both arms and it is likely that they were aware of the participants’ assigned intervention.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | PY | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | I: 56/60 (7% missing) C: 56/60 (7% missing) (problems during storage of laboratory samples) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Intervention group received reflexology and comparator no intervention, so it is likely that participants (outcome assessors) were aware of their assigned intervention. (Both groups received standard care relating to their procedures).  Participants’ knowledge of the intervention they received could have influenced their response. However given the context of outcome measurement (participants undergoing angiography), it is less likely their anxiety was influenced by knowledge of the intervention received. | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Multiple measures eligible for the meta-analysis of <outcome> are fully reported in the paper. It is unlikely that there were other results from which these measures were selected.  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Dolatian 2011** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | Y | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. outcome assessors) were not blinded.  R was delivered as part of pre-labour treatment; participants were less likely to notice or expect the intervention. | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | High | Pain scores were only reported for dilation 4-6cm. | NI | PY | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Elbasan 2018** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, physical function | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | PY | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | High | I: 20/25 (20% missing); C: 20/27 (28% missing)  Analysis method did not correct for bias; no sensitivity analysis | N | N | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Parents/caregivers (i.e. outcome assessors) were not blinded.  C is neurodevelopmental therapy which can be perceived as equally effective | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Elbasan 2018** | **Outcome domain.** physical function | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, physical function | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | PY | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | High | I: 20/25 (20% missing); C: 20/27 (28% missing)  Analysis method did not correct for bias; no sensitivity analysis | N | N | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Researchers (i.e. outcome assessors) were not blinded.  C is neurodevelopmental therapy which can be perceived as equally effective | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Fazlollah 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation. Block number was varied and presumably randomised, mitigating risk of predictable allocation | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | PN | NA | NA | N | N |
| 3. Bias due missing outcome data | High | I: 30/33 (10% missing); C: 30/32 (6% missing)  Analysis method did not correct for bias; no sensitivity analysis  5 participants (8%) were LTFU due to postop complications, which would have influenced pain | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded.  R was not the main care that patients sought, but massage was a noticeable addition to postop care | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Fazlollah 2021** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation. Block number was varied and presumably randomised, mitigating risk of predictable allocation | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | PN | NA | NA | N | N |
| 3. Bias due missing outcome data | High | I: 30/33 (10% missing); C: 30/32 (6% missing)  Analysis method did not correct for bias; no sensitivity analysis  5 participants (8%) were LTFU due to postop complications, which would have influenced sleep | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded.  R was not the main care that patients sought, but massage was a noticeable addition to postop care | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Ghaljaei 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were children (mean age 8 years) with leukaemia undergoing chemotherapy. Both groups received usual procedural care. Given the study sample and context, we judged it unlikely that participants were aware of their assigned intervention during the trial.  Intention-to-treat (ITT) analysis | PN | N | NA | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | I: 40/40 (0% missing); C: 40/40 (0% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (outcome assessors) were children (mean age 8 years) with leukaemia undergoing chemotherapy. Both groups received usual procedural care. Given the study sample and context, we judged it unlikely that participants were aware of their assigned intervention during the trial. | N | N | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | There is only one possible way in which the outcome can be measured (and at a single timepoint).  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Ghasemi 2021** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  ITT | N | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | The nurse (i.e. data collector) was blinded. Participants (i.e. outcome assessors) were blinded - placebo was used. | N | N | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Gok Metin 2016** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | Low | I: 17/18 (6%); C: 18/18 (0% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | C group completed the questionnaire via weekly calls. Unclear R group completed the questionnaire via weekly calls or F2F during home visits.  Participants (i.e. outcome assessors) were not blinded. | N | NI | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Gok Metin 2016** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | Low | I: 17/18 (6%); C: 18/18 (0% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | C group completed the questionnaire via weekly calls. Unclear R group completed the questionnaire via weekly calls or F2F during home visits.  Participants (i.e. outcome assessors) were not blinded. | N | NI | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Goral Turkcu 2021** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, EFMH, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Wanted to leave research (n=3)  I: 2; C: 1  Naïve per protocol  3 deviations (4%) which is <=10% | Y | Y | Y | PY | PY | N | PN |
| 3. Bias due missing outcome data | Low | I: 31/34 (9% missing); C: 31/34 (9% missing)  Analysis method did not correct for bias; no sensitivity analysis  3 participants (4%) were LTFU for reasons unrelated to outcomes (change in treatment; transfer to another centre)  3 participants (4%) had no reason provided for LTFU but patients with worse outcome would have been more likely to attend clinic (anxiety) | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Goral Turkcu 2021** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, EFMH, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Wanted to leave research (n=3)  I: 2; C: 1  Naïve per protocol  3 deviations (4%) which is <=10% | Y | Y | Y | PY | PY | N | PN |
| 3. Bias due missing outcome data | Low | I: 31/34 (9% missing); C: 31/34 (9% missing)  Analysis method did not correct for bias; no sensitivity analysis  3 participants (4%) were LTFU for reasons unrelated to outcomes (change in treatment; transfer to another centre)  3 participants (4%) had no reason provided for LTFU but patients with worse outcome would have been more likely to attend clinic (anxiety) | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Goral Turkcu 2021** | **Outcome domain.** physical function | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, EFMH, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Wanted to leave research (n=3)  I: 2; C: 1  Naïve per protocol  3 deviations (4%) which is <=10% | Y | Y | Y | PY | PY | N | PN |
| 3. Bias due missing outcome data | Low | I: 31/34 (9% missing); C: 31/34 (9% missing)  Analysis method did not correct for bias; no sensitivity analysis  3 participants (4%) were LTFU for reasons unrelated to outcomes (change in treatment; transfer to another centre)  3 participants (4%) had no reason provided for LTFU but patients with worse outcome would have been more likely to attend clinic (anxiety) | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Goral Turkcu 2021** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, EFMH, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Wanted to leave research (n=3)  I: 2; C: 1  Naïve per protocol  3 deviations (4%) which is <=10% | Y | Y | Y | PY | PY | N | PN |
| 3. Bias due missing outcome data | Low | I: 31/34 (9% missing); C: 31/34 (9% missing)  Analysis method did not correct for bias; no sensitivity analysis  3 participants (4%) were LTFU for reasons unrelated to outcomes (change in treatment; transfer to another centre)  3 participants (4%) had no reason provided for LTFU but patients with worse outcome would have been more likely to attend clinic (anxiety) | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hashemzadeh 2019** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hesami 2019** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Block randomisation used, equal sized blocks. No information to determine if the person allocating participants to groups could have predicted the allocation sequence, or if they had motivation to change the allocation (excluding participant or delaying enrolment).  KJ question: differences in fatigue at baseline p=0.054 (control group LOWER fatigue) paper states this is not significant - should this by PY? | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to inactive forms of usual care that were likely to influence the outcome. | N | PN | Y | Y | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hudson 2015** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Allocation was based on dates of surgery and was predictable by the presence of a reflexologist. | PN | N | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. outcome assessors) were not blinded.  Private clinic + R was delivered as part of pre-ops treatment; participants were less likely to notice or expect the intervention. | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hudson 2015** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Allocation was based on dates of surgery and was predictable by the presence of a reflexologist. | PN | N | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. outcome assessors) were not blinded.  Private clinic + R was delivered as part of pre-ops treatment; participants were less likely to notice or expect the intervention. | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hughes 2009** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, fatigue, pain, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – sham was used and effectiveness of blinding was tested.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | N | Y | N | NA | NA | N | N |
| 3. Bias due missing outcome data | High | I: 35/35 (0% missing); C: 31/35 (11% missing)  Analysis method did not correct for bias; no sensitivity analysis  1 participants (1%) were LTFU for reasons related to outcomes (relapse)  2 participants (3%) were LTFU without reasons (withdrew). It is theoretically possible that those with worse outcome (depression) would miss f/u.  1 participants (1%) were LTFU because of death - unclear whether related to MS | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – sham was used and success of blinding was tested. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hughes 2009** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, fatigue, pain, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – sham was used and effectiveness of blinding was tested.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | N | Y | N | NA | NA | N | N |
| 3. Bias due missing outcome data | High | I: 35/35 (0% missing); C: 31/35 (11% missing)  Analysis method did not correct for bias; no sensitivity analysis  1 participants (1%) were LTFU for reasons related to outcomes (relapse)  2 participants (3%) were LTFU without reasons (withdrew). It is theoretically possible that those with worse outcome (fatigue) would miss f/u.  1 participants (1%) were LTFU because of death - unclear whether related to MS | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – sham was used and success of blinding was tested. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hughes 2009** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, fatigue, pain, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – sham was used and effectiveness of blinding was tested.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | N | Y | N | NA | NA | N | N |
| 3. Bias due missing outcome data | Some concerns | I: 35/35 (0% missing); C: 31/35 (11% missing)  Analysis method did not correct for bias; no sensitivity analysis  1 participants (1%) were LTFU for reasons related to outcomes (relapse)  2 participants (3%) were LTFU without reasons (withdrew) but patients with worse outcome (pain) would have been more likely to attend clinic.  1 participants (1%) were LTFU because of death - unclear whether related to MS | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – sham was used and success of blinding was tested. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hughes 2009** | **Outcome domain.** physical function | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, fatigue, pain, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – sham was used and effectiveness of blinding was tested.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | N | Y | N | NA | NA | N | N |
| 3. Bias due missing outcome data | High | I: 35/35 (0% missing); C: 31/35 (11% missing)  Analysis method did not correct for bias; no sensitivity analysis  1 participants (1%) were LTFU for reasons related to outcomes (relapse)  2 participants (3%) were LTFU without reasons (withdrew) - unclear whether patients with worse outcome (physical function) would have been more likely to attend clinic.  1 participants (1%) were LTFU because of death - unclear whether related to MS | N | N | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – sham was used and success of blinding was tested. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Hughes 2009** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, fatigue, pain, physical function, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – sham was used and effectiveness of blinding was tested.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | N | Y | N | NA | NA | N | N |
| 3. Bias due missing outcome data | Some concerns | I: 35/35 (0% missing); C: 31/35 (11% missing)  Analysis method did not correct for bias; no sensitivity analysis  1 participants (1%) were LTFU for reasons related to outcomes (relapse)  2 participants (3%) were LTFU without reasons (withdrew) but patients with worse outcome (QoL) would have been more likely to attend clinic.  1 participants (1%) were LTFU because of death - unclear whether related to MS | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – sham was used and success of blinding was tested. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Icke 2018 S** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff and parents who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | N | NA | NA | N | PN |
| 3. Bias due missing outcome data | Low | I: 33/33 (0% missing), C: 31/33 (6% missing) | PY | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | For R group, last measurement was made after final application of R. No information on when the measurements were made for C group, or the average timing of final application of R for R group.  No info on who completed the questionnaire, but both parents and researchers (i.e. potential outcome assessors) were not blinded. | N | NI | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Imani 2018** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Inkaya 2020** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  1 deviation (1.7%) | N | Y | N | NA | NA | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 30/30 (0% missing); C: 29/30 (3% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded – placebo was used. | N | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Inkaya 2020** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  1 deviation (1.7%) | N | Y | N | NA | NA | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 30/30 (0% missing); C: 29/30 (3% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded – placebo was used. | N | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Jahani 2018** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Block randomisation, fixed block size (6). 14/84 allocations (17%) would be predictable, esp. if convenience sampling | PY | PN | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Unclear how placebo ('sole touching') was delivered, so uncertain whether participants were truly blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | NI | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Unclear how placebo ('sole touching') was delivered, so uncertain whether participants (i.e. outcome assessors) were truly blinded. | N | N | NI | PY | NI |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Jahani 2018** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Block randomisation, fixed block size (6). 14/84 allocations (17%) would be predictable, esp. if convenience sampling | PY | PN | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Unclear how placebo ('sole touching') was delivered, so uncertain whether participants were truly blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | NI | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Unclear how placebo ('sole touching') was delivered, so uncertain whether participants (i.e. outcome assessors) were truly blinded. | N | N | NI | PY | NI |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Jameei-Moghaddam 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation, multiple block sizes (4 and 6) but unclear whether the block size was randomised. This was mitigated by the fact that group assignment was done by someone not involved in sampling. | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  0  ITT | N | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – placebo was used. | PN | N | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Jijimole 2018** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Based on dates of administration | N | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | Y | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. outcome assessors) were not blinded.  R was delivered as part of pre-labour treatment; participants were less likely to notice or expect the intervention. | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Jijimole 2018** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Based on dates of administration | N | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | Y | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. outcome assessors) were not blinded.  R was delivered as part of pre-labour treatment; participants were less likely to notice or expect the intervention. | N | N | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Kabuk 2022** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | "Randomisation table", no details provided.  Allocation described as "simple random allocation", no details provided. | Y | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | High | I:12/15 (20% missing); C: 12/13 (8% missing)  Participant dropout in control group descibed as "discharged", intervention group dropout reasons unclear, descibed as exluded - "evaluated as a pre-intervention" | N | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Kabuk 2022** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | "Randomisation table", no details provided.  Allocation described as "simple random allocation", no details provided. | Y | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | High | I:12/15 (20% missing); C: 12/13 (8% missing)  Participant dropout in control group descibed as "discharged", intervention group dropout reasons unclear, descibed as exluded - "evaluated as a pre-intervention" | N | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Kabuk 2022** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. sleep quality, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | "Randomisation table", no details provided.  Allocation described as "simple random allocation", no details provided. | Y | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | High | I:12/15 (20% missing); C: 12/13 (8% missing)  Participant dropout in control group descibed as "discharged", intervention group dropout reasons unclear, descibed as exluded - "evaluated as a pre-intervention" | N | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Kaplan 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. sleep quality, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Computer generated randomisation decribed. Allocation method not described | Y | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Karatas 2021** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Imbalance in the number of participants were allocated to the intervention (20 participants) and the control (25 participants) groups that is very unlikely to be due to chance and large enough to bias the intervention effect estimate. | PY | PY | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Researcher delivering the intervention were likely aware of the participants’ assigned intervention because the randomised allocation was not concealed.  Intention-to-treat (ITT) analysis | PN | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | High | I: 20/20 (0% missing) C: 20/25 (20% missing)  5 participants in the comparator arm withdrew because they did not come to the sessions (4/5) or they did not want to continue (1/5). A greater proportion of participants were missing from the comparator group and withdrawals were likely to due to outcome worsening in the comparator group. | PN | PN | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Parents (the outcome assessors) were blinded to the intervention received by the infants. | NI | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | There is only one possible way in which the outcome can be measured (and at a single timepoint).  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Kardan 2020** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Block randomisation, fixed block size (4), 25% of allocations were predictable, esp. if convenience sampling | Y | PN | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Not interested in study (n=1)  I: 0; C: 1  Naïve per protocol  1 deviation (0.8%) | Y | Y | Y | PY | N | N | PN |
| 3. Bias due missing outcome data | Low | I: 58/60 (3% missing); C: 58/60 (3% missing) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Khaledifar 2017** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Imbalance in baseline stress score and HR | NI | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Unclear whether the control group was only rest or includes sham massage.  Research staff who delivered the R intervention were not blinded.  Patient dropouts (n=5) but no reasons were provided  Naïve per protocol  5 potential deviations (10%) | NI | Y | NI | NA | NA | N | NI |
| 3. Bias due missing outcome data | High | I: 25/25 (0% missing); C: 20/25 (10% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reasons provided for LTFU | N | N | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Unclear whether participants (i.e. outcome assessors) were blinded - unclear whether control group was only rest or includes sham massage. | N | PN | NI | PY | NI |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Khorsand 2015** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Block randomisation. Unsure whether block size was randomised  Imbalance in baseline distribution of methadone consumption, which is likely to influence outcome (pain) | NI | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | Y | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. Data collector was blinded to allocation. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Koc 2015** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were infants.  Research staff who delivered the R intervention were not blinded.  Mothers changed their mind about getting R treatment (n=2)  I: 2; C: 0  Naïve per protocol  2 deviations (3%) | N | Y | Y | PY | N | N | PN |
| 3. Bias due missing outcome data | Low | I: 28/30 (7% missing); C: 30/30 (0% missing)  Analysis method did not correct for bias; no sensitivity analysis  Mothers decided to withdraw before intervention occured | PN | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Researchers (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Kurt 2018** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, physical function | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Method of randomisation not described.  The allocation ratio was not 1:1 but the assignment ratio at analysis was 1:1.  Male:female ratio at analysis was 1:1 without stratification or block randomisation. | NI | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff and relatives who delivered the R intervention were not blinded.  Declined to continue (n=4); did not do massage regularly (n=6)  I: 0; C: 10  Naïve per protocol  10 participants (10%) were deviations, which is >=10% | Y | Y | Y | PY | N | N | Y |
| 3. Bias due missing outcome data | Some concerns | I: 30/50 (40% missing); C: 30/46 (35% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reason were provided for LTFU but patients with worse outcome (symptoms) would have been more likely to attend clinic | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Kurt 2018** | **Outcome domain.** physical function | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, physical function | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Method of randomisation not described.  The allocation ratio was not 1:1 but the assignment ratio at analysis was 1:1.  Male:female ratio at analysis was 1:1 without stratification or block randomisation. | NI | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff and relatives who delivered the R intervention were not blinded.  Declined to continue (n=4); did not do massage regularly (n=6)  I: 0; C: 10  Naïve per protocol  10 participants (10%) were deviations, which is >=10% | Y | Y | Y | PY | N | N | Y |
| 3. Bias due missing outcome data | High | I: 30/50 (40% missing); C: 30/46 (35% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reason were provided for LTFU. Uncertain whether patients with worse outcome would have been more likely to attend clinic. | N | N | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Levy 2020** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Based on dates of delivery. Predictable allocation. | N | N | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. outcome assessors) were not blinded.  R was delivered as part of pre-labour treatment; participants were less likely to notice or expect the intervention. | N | PN | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Mahdavipour 2019** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Block randomisation. Unsure whether block size was randomised | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Absent in R sessions (n=5)  I: 5; C: 0  5 deviations (5%) | Y | Y | Y | PY | Y | N | PN |
| 3. Bias due missing outcome data | High | I: 45/50 (10%); C: 45/50 (10%)  Analysis method did not correct for bias; no sensitivity analysis  5 participants were LTFU without reasons. It is theoretically possible that those with worse outcome (depression) would miss f/u. | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Mahdavipour 2022** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Block randomisation. Unsure whether block size was randomised | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Patient dropouts but no reasons were provided;  Naïve per protocol  No information on dropouts to determine whether they were deviations | Y | Y | NI | NA | NA | N | NI |
| 3. Bias due missing outcome data | High | I: 45/50 (10% missing); C: 45/50 (10% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reason were provided for LTFU. Uncertain whether patients with worse outcome would have been more likely to attend clinic. | N | N | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Mak 2007** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – placebo was used and effectiveness of blinding was tested.  Research staff who delivered the R intervention were not blinded.  Patient dropouts but no reasons were provided (personal reason n=2; no reason n=1)  Naïve per protocol  3 deviations (3%) which is <=10% | Y | N | NI | NA | NA | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 54/60 (10% missing); C: 43/60 (12% missing)  Analysis method did not correct for bias; no sensitivity analysis  2 participants (2%) were LTFU for reasons potentially related to outcomes (medical reasons)  20 participants (17%) were LTFU for reasons unrelated to outcomes (fear of SARS; personal reasons)  1 participant (1%) had no reason provided for LTFU. Uncertain whether patients with worse outcome (QoL) would have been more likely to attend clinic. | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – placebo was used and effectiveness of placebo was tested. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Miller 2013** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. same RoB all outcomes: EFMH, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Block randomisation used, no further details. The recruiting therapist allocated participants to their intervention group. No information to determine if the person allocating participants to groups could have predicted the allocation sequence, or if they had motivation to change the allocation (excluding participant or delaying enrolment). The first 10 participants were allocated and treated for 8 weeks, then the remaining 10 were allocated and treated to accomodate the reflexologists availability. | PY | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | The same reflexologists were involved in care for both arms and they were aware of the participants’ assigned intervention.  Intention-to-treat (ITT) analysis | PN | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low |  | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Measurement occurred during visits for treatment received by both groups, so the timing and procedure for assessment was likely to be similar. | PN | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Measures eligible for the meta-analysis appear fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Mobini-Bidgoli 2017** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  ITT | N | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded – placebo was used. | N | N | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Molavi Vardanjani 2013** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Imbalance in baseline outcome (statistically significant) but difference is unlikely to be meaningful | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants and data collector (i.e. outcome assessors) were blinded – placebo was used. | N | N | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Murat-Ringot 2021** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms, EFMH, HR-QoL | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | block randomised used, random sized blocks so the person allocating participants to their intervention groups were unlikely to be able to predict the allocation sequence. | PY | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so participants were aware of their assigned intervention.  Reflexologists delivering the intervention were aware of the participants’ assigned intervention because the randomised allocation was not concealed.  Patients in the control group were aware that they have 'missed out' but received two sessions of foot reflexology after completion of the study.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | High | I: 26/40 (35% missing) C: 34/40 (15% missing)  A greater proportion of participants were missing from the reflexology intervention/comparator group and withdrawals were likely to due to outcome worsening and adverse events in the reflexology group. | PN | PN | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | There is evidence that the HADS scale is quicker than other tools however presents more false positives. | PY | NI | NA | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Low | Measures eligible for the meta-analysis appear fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | PY | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Nasiri 2020** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | The sequence for allocating participants to groups may have been based on time. | PN | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so it is likely that participants were aware of their assigned intervention.  Researchers delivering the intervention were likely aware of the participants’ assigned intervention because the randomised allocation was not concealed.  Intention-to-treat (ITT) analysis | Y | Y | PN | NA | NA | PY | NA |
| 3. Bias due missing outcome data | Low | I: 36/36 (0% missing) C: 36/36 (0% missing) | PY | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received reflexology or no intervention.  Participants’ knowledge of the intervention they received could have influenced their response.  Participants were likely to have had a prior belief about the benefits of reflexology compared to no treatment that were likely to influence the outcome. | PN | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | There is only one possible way in which the outcome can be measured (and at a single timepoint).  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Navaee 2020** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | PY | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention | Y | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Nourmohammadi 2019** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Participants were randomised based days of the week "at the beginning of every week, we randomly selected four days and allocated them to reflexology group."  No information provided to determine if the person allocating participants to groups could have predicted the allocation sequence, or if they had motivation to change the allocation (excluding participant or delaying enrolment). | N | PN | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | High | I: 27/30 (10% missing); C: 30/30 (no missing data)  Dropout not decribed | N | N | PY | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Oleson 1993** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – sham intervention was used.  Research staff who delivered the R intervention were not blinded.  Some dropouts but reasons not provided  Naïve per protocol | N | Y | NI | NA | NA | N | NI |
| 3. Bias due missing outcome data | High | I: 18/25 (28% missing); C: 17/25 (32% missing)  Analysis method did not correct for bias; no sensitivity analysis  No reason were provided for LTFU but patients with worse outcome would have been more likely to adhere to recording PMS diary. | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded – placebo was used. | PN | N | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Ozdemir 2013** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Unclear whether placebo was used, but unlikely since there is no description of the control group  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts  No information on dropouts to determine whether they were deviations | PY | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Unclear whether placebo was used, but unlikely since there is no description of the control group. If so, participants (i.e. the outcome assessors) were not blinded. | N | PN | PY | PY | NI |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Ozdemir 2013** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Unclear whether placebo was used, but unlikely since there is no description of the control group  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts  No information on dropouts to determine whether they were deviations | PY | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Unclear whether placebo was used, but unlikely since there is no description of the control group. If so, participants (i.e. the outcome assessors) were not blinded. | N | PN | PY | PY | NI |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Öztürk 2018** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | High | I: 32/50 (36% missing); C: 31/50 (38% missing)  Analysis method did not correct for bias; no sensitivity analysis  32 participants (15%) were LTFU for reasons related to outcomes:  \* Early discharge (n=9)  \* Complications related to PCA use (n=6)  \* Postops complications (n=17)  Imbalance in reasons for LTFU (that are related to outcomes) btw groups  \* Early discharge: I: 4; C: 5  \* Complications related to PCA use: I: 2; C: 4  \* Postops complications: I: 9; C: 8 | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Öztürk 2018** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | High | I: 32/50 (36% missing); C: 31/50 (38% missing)  Analysis method did not correct for bias; no sensitivity analysis  15 participants (15%) were LTFU for reasons related to outcomes:  \* Early discharge (n=9)  \* Complications related to PCA use (n=6)  Imbalance in reasons for LTFU (that are related to outcomes) btw groups  \* Early discharge: I: 4; C: 5  \* Complications related to PCA use: I: 2; C: 4 | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Polat 2017** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | The sequence for allocating participants to groups was based on alternation "following a pattern of experimental-control-experimental-control groups" | N | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or no intervention  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to no intervention that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Poole 2007** | **Outcome domain.** physical function | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. physical function, fatigue, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Withdrawn after randomisation results were revealed (n=8)  Withdrawn during implementation (reasons unknown) (n=30)  Withdrawn after randomisation results were revealed: I: 9; C: 21  Naïve per protocol  Imbalance in no. of withdrawals after randomisation results were revelaed | Y | Y | PY | PY | N | N | PY |
| 3. Bias due missing outcome data | High | I: 65/77 (15% missing); C: 43/75 (43% missing)  Analysis method did not correct for bias; no sensitivity analysis  Measurements were taken on the same day as the last visit so outcome severity is unlikely to affect LTFU | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Poole 2007** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. physical function, fatigue, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Withdrawn after randomisation results were revealed (n=8)  Withdrawn during implementation (reasons unknown) (n=30)  Withdrawn after randomisation results were revealed: I: 9; C: 21  Naïve per protocol  Imbalance in no. of withdrawals after randomisation results were revelaed | Y | Y | PY | PY | N | N | PY |
| 3. Bias due missing outcome data | High | I: 65/77 (15% missing); C: 43/75 (43% missing)  Analysis method did not correct for bias; no sensitivity analysis  Measurements were taken on the same day as the last visit so outcome severity is unlikely to affect LTFU | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Poole 2007** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. physical function, fatigue, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Withdrawn after randomisation results were revealed (n=8)  Withdrawn during implementation (reasons unknown) (n=30)  Withdrawn after randomisation results were revealed: I: 9; C: 21  Naïve per protocol  Imbalance in no. of withdrawals after randomisation results were revelaed | Y | Y | PY | PY | N | N | PY |
| 3. Bias due missing outcome data | High | I: 65/77 (15% missing); C: 43/75 (43% missing)  Analysis method did not correct for bias; no sensitivity analysis  Measurements were taken on the same day as the last visit so outcome severity is unlikely to affect LTFU | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Poole 2007** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. physical function, fatigue, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Withdrawn after randomisation results were revealed (n=8)  Withdrawn during implementation (reasons unknown) (n=30)  Withdrawn after randomisation results were revealed: I: 9; C: 21  Naïve per protocol  Imbalance in no. of withdrawals after randomisation results were revelaed | Y | Y | PY | PY | N | N | PY |
| 3. Bias due missing outcome data | High | I: 65/77 (15% missing); C: 43/75 (43% missing)  Analysis method did not correct for bias; no sensitivity analysis  Measurements were taken on the same day as the last visit so outcome severity is unlikely to affect LTFU | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Quinn 2008** | **Outcome domain.** physical function | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. physical function, fatigue, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Computer generated randomisation performed by an independent researcher. | Y | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded. People delivering the intervention were aware of the assigned intervention.  Full ITT | N | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants were blinded | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Medians (IQR) are reported. Unclear why, but no reason to suspect that the results were selected from multiple analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Quinn 2008** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. physical function, fatigue, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Computer generated randomisation performed by an independent researcher. | Y | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded. People delivering the intervention were aware of the assigned intervention.  Full ITT | N | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants were blinded | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Medians (IQR) are reported. Unclear why, but no reason to suspect that the results were selected from multiple analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Quinn 2008** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. physical function, fatigue, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Computer generated randomisation performed by an independent researcher. | Y | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded. People delivering the intervention were aware of the assigned intervention.  Full ITT | N | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants were blinded | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Medians (IQR) are reported. Unclear why, but no reason to suspect that the results were selected from multiple analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Quinn 2008** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. physical function, fatigue, HR-QoL, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Computer generated randomisation performed by an independent researcher. | Y | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded. People delivering the intervention were aware of the assigned intervention.  Full ITT | N | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants were blinded | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Medians (IQR) are reported. Unclear why, but no reason to suspect that the results were selected from multiple analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Rahmani 2016** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Rahmani Vasokolaei 2019** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation. Block number was unannounced and the person conducting the blocking was blinded. | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded – placebo was used.  ITT | N | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants and data collector (i.e. outcome assessors) were not blinded. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Rambod 2019** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation used, equal sized blocks, block list computer generated and envoloped used to allocate participants. | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Rambod 2019** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation used, equal sized blocks, block list computer generated and envoloped used to allocate participants. | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Rambod 2019** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, pain, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation used, equal sized blocks, block list computer generated and envoloped used to allocate participants. | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Razavi 2022** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Rejeh 2020** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation. Block number was sealed, mitigating risk of predictable allocation. | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Rezaei 2022** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Block randomisation. Unsure whether block size was randomised | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Did not receive allocated intervention (n=7)  I: 4; C: 3  Naïve per protocol  7 deviations (9%)  Imbalance in no. of LTFU btw groups | Y | Y | Y | PY | PN | N | PY |
| 3. Bias due missing outcome data | Some concerns | I: 33/37(10% missing); C: 33/37 (10% missing)  Analysis method did not correct for bias; no sensitivity analysis  Measurements were taken on the same visit so outcome severity is unlikely to affect LTFU | N | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Ross 2002** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | NI |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | N | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | High | Overall: 17/26 (35% missing)  Analysis method did not correct for bias; no sensitivity analysis  LTFU due to death (n=7), which suggests worsening of cancer and thus can be related to outcome | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded – placebo was used. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sajadi 2020a** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Imbalance in baseline measurement of outcome (statistically significant) | Y | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | N | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | High | I: 33/35 (6% missing); C: 30/35 (14% missing)  Analysis method did not correct for bias; no sensitivity analysis | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded – placebo was used. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sajadi 2020a** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Imbalance in baseline measurement of outcome (statistically significant) | Y | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | N | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | High | I: 33/35 (6% missing); C: 30/35 (14% missing)  Analysis method did not correct for bias; no sensitivity analysis | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. outcome assessors) were blinded – placebo was used. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sajadi 2020b** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. same RoB all outcomes: hrqol, physical function, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | "patients randomly using computer program assigned into intervention". No further information to determine allocation concealment. | PY | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | The same people were involved in delivering the intervention for both arms so they were aware of the participants’ assigned intervention.  Analysis excluded both those who did not receive their assigned intervention (naive per protocol analysis), as well as those with missing outcome data (mITT). | PN | PY | N | NA | NA | PN | PN |
| 3. Bias due missing outcome data | Low | I: 33/34 (3% missing); C: 30/34 (12% missing)  LTFU reasons explained, unrelated to true value of outcome. | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low |  | N | N | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Multiple measures eligible for the meta-analysis are fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Samarehfekri 2020** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | PY | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | High | I: 25/26 (8% missing); C: 25/27 (7% missing)  Analysis method did not correct for bias; no sensitivity analysis  LTFU due to transplant rejection and returning to OR, which suggest worsening of conditions and can potentially influence outcome | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Samarehfekri 2020** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | PY | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | PN | NA | NA | N | PN |
| 3. Bias due missing outcome data | High | I: 25/26 (8% missing); C: 25/27 (7% missing)  Analysis method did not correct for bias; no sensitivity analysis  LTFU due to transplant rejection and returning to OR, which suggest worsening of conditions and can potentially influence outcome | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sayari 2021** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | PY | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | KJ: unsure how to assess when we have sham and usucal care controls  Full ITT | PN | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low |  | N | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. Standard error is presented rather than standard deviation, unclear why but but no reason to suspect that the results wer | NI | N | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sayari 2021** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | PY | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | KJ: unsure how to assess when we have sham and usucal care controls  Full ITT | PN | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low |  | N | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. Standard error is presented rather than standard deviation, unclear why but but no reason to suspect that the results wer | NI | N | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sehhatti 2020** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation. Two block sizes (4 & 6); unsure whether block size was randomised. However, randomisation was conducted by an independent person. | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Reluctance to participate (n=2)  I:1; C:1  Naïve per protocol  2 deviations (3%) which is <=10% | Y | Y | Y | PY | Y | N | PN |
| 3. Bias due missing outcome data | Low | I: 36/37 (3%); C: 36/37 (3%) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sehhatti 2020** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation. Two block sizes (4 & 6); unsure whether block size was randomised. However, randomisation was conducted by an independent person. | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Reluctance to participate (n=2)  I:1; C:1  Naïve per protocol  2 deviations (3%) which is <=10% | Y | Y | Y | PY | Y | N | PN |
| 3. Bias due missing outcome data | Low | I: 36/37 (3%); C: 36/37 (3%) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | High | SD was not reported | NI | Y | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Shaermoghadam 2016** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Imbalance in baseline measurement of outcome (statistically significant) | NI | NI | Y |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | C group was not described - unclear whether participants were blinded  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | NI | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | C group was not described - unclear whether participants (i.e. outcome assessors) were blinded | N | PN | NI | PY | NI |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Shaermoghadam 2016** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Imbalance in baseline measurement of outcome (statistically significant) | NI | NI | Y |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | C group was not described - unclear whether participants were blinded  Research staff who delivered the R intervention were not blinded.  Authors did not provide any info on dropouts; no confirmation that all patients completed intervention  No information on dropouts | NI | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not provide any numbers on LTFU  Analysis method did not correct for bias; no sensitivity analysis | NI | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | C group was not described - unclear whether participants (i.e. outcome assessors) were blinded | N | PN | NI | PY | NI |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Shahgholian 2016** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Base characteristics for each group were not reported | Y | Y | NI |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | The researcher (i.e. outcome assessors) was not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sharifi 2022** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation, fixed block size (4) but block size was kept hidden from the research team. | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  Some participants did not receive allocated intervention (I:1; C:3), but they seemed to remain in the original intervention group during analysis. This would correspond to ITT. On the other hand, those LTFU were excluded from analysis and not imputed.  No LTFU that can be considered deviation | N | Y | PN | NA | NA | PN | PN |
| 3. Bias due missing outcome data | High | I: 40/50 (20% missing); C: 40/50 (20% missing)  Analysis method did not correct for bias; no sensitivity analysis  20 participants (20%) were LTFU for reasons related to outcomes (oxytocin/misoprostol admission) | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – placebo was used. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sharifi 2022** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation, fixed block size (4) but block size was kept hidden from the research team. | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  Some participants did not receive allocated intervention (I:1; C:3), but they seemed to remain in the original intervention group during analysis. This would correspond to ITT. On the other hand, those LTFU were excluded from analysis and not imputed.  No LTFU that can be considered deviation | N | Y | PN | NA | NA | PN | PN |
| 3. Bias due missing outcome data | High | I: 40/50 (20% missing); C: 40/50 (20% missing)  Analysis method did not correct for bias; no sensitivity analysis  20 participants (20%) were LTFU for reasons related to outcomes (oxytocin/misoprostol admission) | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – placebo was used. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Sharp 2010** | **Outcome domain.** efmh | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. same RoB all outcomes: efmh, hrqol | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | The same people were involved in delivering the intervention for both arms and so they were aware of the participants’ assigned intervention.  Intention‐to‐treat analysis (ITT), "where data were missing, the mean score for the cohort was imputed as analysis of the reasons for missing data suggested that it was not missing at random" | PN | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low |  | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low |  | N | N | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Measures eligible for the meta-analysis appear fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported for multiple ways of analysing/handling the outcome, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Shobeiri 2017** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | "Participants were randomized by using allocation concealment which prepared a computer generated list (www.randomization.com). An investigator who had not been involved in testing or the delivery of the intervention prepared the  randomization assignments." | PY | PY | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | Y | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Shokrollahi 2022** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. outcome assessors) were not blinded.  R was delivered as part of pre-labour treatment; participants were less likely to notice or expect the intervention. | N | PN | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Shokrollahi 2022** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. outcome assessors) were not blinded.  R was delivered as part of pre-labour treatment; participants were less likely to notice or expect the intervention. | N | PN | Y | PY | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Soheili 2017** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | Y | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Stephenson 2007** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. same RoB all outcomes: EFMH, pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so participants were aware of their assigned intervention.  Intention-to-treat (ITT) analysis | Y | Y | PN | NA | NA | PY | NA |
| 3. Bias due missing outcome data | High | I: 42/45 (7% missing) C: 44/45 (2% missing)  Withdrawals in the reflexology intervention group were due to participants being too ill. This was not the case in the comparator group. | PN | PN | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received reflexology or attention control.  Participants’ knowledge of the intervention they received could have influenced their response.  Participants were likely to have had a prior belief about the benefits of reflexology compared to attention control that were likely to influence the outcome. | PN | NI | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Measures eligible for the meta-analysis appear fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Tan 2014** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Full ITT | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or no intervention  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to no intervention that were likely to influence the outcome. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Topcu 2020** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. HR-QoL, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Randomisation was conducted independent of the research team. | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Withdrew consent (n=1)  Non-compliant (n=4)  Withdrew consent: I: 1, C: 0  Non-compliant: I: 3; C: 1  "Result for the intent-to-treat (ITT) analysis was consistent with that of the per-protocol (PP) analysis."  However, authors did not specify whether the reported results were ITT or PP. The sample size in Results for I group is consistent with ITT (n=32)  5 deviations (8%) | Y | Y | Y | PY | N | NI | PY |
| 3. Bias due missing outcome data | Some concerns | I: 28/32 (13% missing); C: 25/29 (14% missing)  "Result for the intent-to-treat (ITT) analysis was consistent with that of the per-protocol (PP) analysis." | N | PY | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Topcu 2020** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. HR-QoL, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Randomisation was conducted independent of the research team. | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Withdrew consent (n=1)  Non-compliant (n=4)  Withdrew consent: I: 1, C: 0  Non-compliant: I: 3; C: 1  "Result for the intent-to-treat (ITT) analysis was consistent with that of the per-protocol (PP) analysis."  However, authors did not specify whether the reported results were ITT or PP. The sample size in Results for I group is consistent with ITT (n=32)  5 deviations (8%) | Y | Y | Y | PY | N | NI | PY |
| 3. Bias due missing outcome data | Some concerns | I: 28/32 (13% missing); C: 25/29 (14% missing)  "Result for the intent-to-treat (ITT) analysis was consistent with that of the per-protocol (PP) analysis." | N | PY | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | High | The AQLQ sub-component results were reported in a table but not the overall score, which was only reported in a figure. | NI | N | PY |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Toygar 2020** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Randmisation process partially described: "computer-assisted block randomization was used to provide equality of gender between groups" no information provided about allocation concealment | PY | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were blinded. People delivering the intervention were aware of the assigned intervention.  Full ITT | PN | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants were blinded | N | PN | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Tsay 2008** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. pain | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | I: 30/31 (3% mising); C: 31/31 (no missing data) | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | Y | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Uguryol 2022** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | High | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Authors did not clarify how many participants were initially randomised and how many did not complete allocated intervention | Y | Y | NI | NA | NA | NI | NI |
| 3. Bias due missing outcome data | Some concerns | Authors did not clarify how many participants were initially randomised and how many LTFU  Analysis method did not correct for bias; no sensitivity analysis | N | N | NI | NI |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Unal 2016** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Withdrawn from study (reasons not reported) (n=1)  I: 1; C: 0  Naïve per protocol  1 potential deviations (1%) | Y | Y | PY | PY | N | N | PN |
| 3. Bias due missing outcome data | Low | I: 35/36 (4% missing); C: 35/37 (5% missing)  Analysis method did not correct for bias; no sensitivity analysis  2 participants were LTFU for reasons unrelated to outcomes (leaving dialysis centres); 1 participant was LTFU without reasons but patients were unlikely to miss dialysis regardless of outcome. | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Unal 2016** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. fatigue, sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Withdrawn from study (reasons not reported) (n=1)  I: 1; C: 0  Naïve per protocol  1 potential deviations (1%) | Y | Y | PY | PY | N | N | PN |
| 3. Bias due missing outcome data | Low | I: 35/36 (4% missing); C: 35/37 (5% missing)  Analysis method did not correct for bias; no sensitivity analysis  2 participants were LTFU for reasons unrelated to outcomes (leaving dialysis centres); 1 participant was LTFU without reasons but patients were unlikely to miss dialysis regardless of outcome. | N | N | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | N | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Us 2022** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low | Block randomisation, fixed block size (60x5) but only 60 predictable allocations out of 300. | Y | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were infants.  Research staff who delivered the R intervention were not blinded.  ITT | N | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Low | The researcher (outcome assessor) was unaware of allocation and used an objective method (chronometer). | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | High | Median (IQR) not reported for NIPS score | NI | PY | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Uysal 2017** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. HR-QoL, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Imbalance in baseline measurement of outcome (statistically significant) | NI | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | N | NA | NA | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 20/21 (5% missing); C: 20/22 (10% missing)  Analysis method did not correct for bias; no sensitivity analysis  2 participants (7%) were LTFU for reasons related to outcomes (reduced thrombocyte/neutrophil values); 1 for reasons unrelated to outcomes (radiation dermatitis) | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Uysal 2017** | **Outcome domain.** global symptoms | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. HR-QoL, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns |  | NI | NI | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  Naïve per protocol  No LTFU that can be considered deviation | Y | Y | N | NA | NA | N | PN |
| 3. Bias due missing outcome data | Some concerns | I: 20/21 (5% missing); C: 20/22 (10% missing)  Analysis method did not correct for bias; no sensitivity analysis  2 participants (7%) were LTFU for reasons related to outcomes (reduced thrombocyte/neutrophil values); 1 for reasons unrelated to outcomes (radiation dermatitis) | N | N | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. outcome assessors) were not blinded. | N | PN | Y | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
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| **Study ID.  Valizadeh 2015** | **Outcome domain.** sleep quality | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. sleep quality | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | High | Imbalance in baseline measurement of outcome (unclear if statistically significant) | NI | NI | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Participants were not blinded.  Research staff who delivered the R intervention were not blinded.  ITT | Y | Y | N | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | No missing data | Y | NA | NA | NA |  |  |  |
| 4. Bias in the measurement of the outcome | High | The research assistant (i.e. outcome assessor) were blinded – placebo was used. | N | PN | PY | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Williamson 2002** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | Block randomisation, fixed block size (8x10) but only 10 predictable allocations out of 80 (13%)  Imbalance in baseline measurement of outcome | Y | PY | PY |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Some concerns | Participants were blinded – placebo was used.  Research staff who delivered the R intervention were not blinded.  Dropping out of programme (n=3)  I:2; C:1  Naïve per protocol  3 deviations (4%) which is <=10% | N | Y | PY | PY | PY | N | PN |
| 3. Bias due missing outcome data | High | I: 36/42 (14% missing); C: 33/38 (13% missing)  Authors conducted sensitivity analysis to confirm primary analysis but using improper imputation method (last recorded value carried forward), especially when it is theoretically possible that LTFU could be related to outcome (depression). Moreover, autho  6 participants (8%) were LTFU without reasons. It is theoretically possible that those with worse outcome (depression) would miss f/u. | N | PN | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | Low | Participants (i.e. the outcome assessors) were blinded – placebo was used and success of blinding was tested. | N | PN | N | NA | NA |  |  |
| 5. Bias in the selection of the reported results | Some concerns |  | NI | N | N |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
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| **Study ID.  Wyatt 2012** | **Outcome domain.** pain | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. same RoB all outcomes: pain, fatigue, efmh, hrqol, function | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) for summary statistics. | PN | PN | NA | NA | NA | PY | NA |
| 3. Bias due missing outcome data | Some concerns | I: 75/95 (21% missing); C1: 76/96 (21% missing); C2: 71/96 (26% missing)  Main reason for missingness in I and C1 groups reported as "unavailability of women on a scheduled date". No explanation given for C2 group. | PN | N | PY | PN |  |  |  |
| 4. Bias in the measurement of the outcome | Low |  | N | N | PN | NA | NA |  |  |
| 5. Bias in the selection of the reported results | High | Registry record does not report pain, fatigue, physical function or mental distress as outcomes. HR-QoL reported as outcome, however no measures or timepoints specified. Results paper notes that single item of severity of pain at its worst from BPI-SF used in the in the analysis - unclear if other BPI-SF items measured but not reported. Summary statistics only reported for single item of severity of fatigue at its worst from BFI, however fatigue interference with ADL from BFI in LME analysis. SF-36 physical function subscale only reported. FACT-B total, subscale scores and specific symptom items evaluated, however only total scores, nausea and dyspnea reported.  Results are reported for multiple ways of analysing/handling the outcome, and it is unlikely that these were selected from other analyses. | NI | PY | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Wyatt 2017** | **Outcome domain.** HR-QoL | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. same RoB all outcomes: hrqol, physical function, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | Y | Y | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so it is likely that participants were aware of their assigned intervention. Carers delivered the reflexology intervention.  Intention-to-treat (ITT) analysis | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Low | I: 103/128 (20% missing); C: 104/128 (19% missing). Assessed from Figure 1 as sample size in the analysis, however this cannot be verified.  No indication of imputation in analysis methods - possibly missing at random data.  "The characteristics of the drop-outs did not differ by study group". Most frequent reason was inability to reach participants for telephone data collection. | NI | PN | PN | NA |  |  |  |
| 4. Bias in the measurement of the outcome | Some concerns | Participants (i.e. the outcome assessors) were aware that they had received reflexology or no intervention.  Participants’ knowledge of the intervention they received could have influenced their response. However, < reflexology is delivered as a supportive treatment alongside other care (chemotherapy) and there is no reason to assume that participants would have prior beliefs about the effects of reflexology that would be likely to influence the outcome. | N | N | Y | Y | PN |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Measures eligible for the meta-analysis appear fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported for multiple ways of analysing/handling the outcomes, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **Some concerns** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Wyatt 2021** | **Outcome domain.** fatigue | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. same RoB all outcomes: fatigue, global symptoms | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Low |  | PY | PY | PN |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator no intervention (i.e. not a sham/placebo or ‘active’ standard care), so participants were aware of their assigned intervention.  Carers and reflexologists delivering the intervention were aware of the participants’ assigned intervention because the randomised allocation was not concealed.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | PY | NA |
| 3. Bias due missing outcome data | High | I: 126/150 (16% missing) C: 44/47 (6% missing)  A greater proportion of participants were missing from the reflexology intervention group and withdrawals were likely to due to outcome worsening in the reflexology group. | PN | PN | PY | PY |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received reflexology or no intervention.  Participants’ knowledge of the intervention they received could have influenced their response.  Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | PN | NI | PY | PY | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Measures eligible for the meta-analysis appear fully reported in the paper, at multiple time points. It is unlikely that there were other results from which these measures were selected.  Results are reported for multiple ways of analysing/handling the outcome, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

| **Study ID.  Yılar Erkek 2018** | **Outcome domain.** EFMH | | **Comparison.** reflexology versus inactive control | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Assessments**. EFMH | | **Design.** parallel (individually randomised) | | | | | | |
| **Domain** | **Judgment** | **Explanation** (for concerns that lead to high or some concerns about RoB) | **Response to signalling questions** | | | | | | |
| SQ1 | SQ2 | SQ3 | SQ4 | SQ5 | SQ6 | SQ7 |
| 1. Bias arising from the randomisation process | Some concerns | The sequence for allocating participants to groups was based on days of the week "Pregnant women who  applied to the hospital on Mondays, Wednesdays, and Fridays  were included in the experimental group, while the pregnant  women who applied to the hospital on Tuesdays, Thursdays,  and Saturdays were included in the control group. A maximum of three pregnant women were analyzed in one day" | N | NI | N |  |  |  |  |
| 2. Bias due to deviations from the intended intervention | Low | Intervention group received reflexology and comparator usual care, so it is likely that participants and those delivering the intervention were aware of the assigned intervention.  Modified intention-to-treat (mITT) analysis (excluding participants with missing outcome data) | Y | Y | PN | NA | NA | Y | NA |
| 3. Bias due missing outcome data | Some concerns | I:77/95 (19% mising); C: 77/93 (17% missing)  Dropout reasons simalar in broth groups (fetal distress, cesarean, prologned action, complication, leave from study, manual dilation of cervix) | N | N | Y | PN |  |  |  |
| 4. Bias in the measurement of the outcome | High | Participants (i.e. the outcome assessors) were aware that they had received relexology or usual care  Participants' knowledge of the intervention received could have influenced their response. Participants were likely to have had a prior belief about the benefits of reflexology compared to usual care that were likely to influence the outcome. | N | PN | Y | Y | PY |  |  |
| 5. Bias in the selection of the reported results | Some concerns | Results are reported as summary statistics or with minimal analysis, and it is unlikely that these were selected from other analyses. | NI | PN | PN |  |  |  |  |
| **OVERALL risk of bias** | **High** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |