Supplementary material 1

MEDLINE search strategy

1. spinal cord stimulat$.ti,ab,kw.

2. dorsal column stimulat$.ti,ab,kw.

3. epidural stimulat$.ti,ab,kw.

4. or/1-3

5. exp PAIN/

6. pain*.mp.

7. (neuralgi* or myalgi* or neuropath* or arthriti* or osteoarthri* or arthralgi* or sciatica or headache* or migrain*).mp.

8. exp ANALGESIA/

9. analgesi*.mp.

10. exp Tibial Neuropathy/ or exp Femoral Neuropathy/ or exp Radial Neuropathy/ or exp Alcoholic Neuropathy/ or exp Optic Neuropathy, Ischemic/ or exp Median Neuropathy/ or exp Sciatic Neuropathy/

11. Critical limb ischemia.kw.

12. lower limb ischemia.kw.

13. leg ischemia.kw.

14. exp ATHEROSCLEROSIS/

15. exp Vascular Diseases/ or exp Peripheral Vascular Diseases/ or exp Peripheral Arterial Disease/ or exp Arteriosclerosis/ or exp Ischemia/ or exp Arterial Occlusive Diseases/

16. or/5-15

17. randomized controlled trial.pt.

18. controlled clinical trial.pt.

19. randomized.ab.

20. placebo.ab.

21. drug therapy.fs.

22. randomly.ab.

23. trial.ab.

24. groups.ab.

25. or/17-24

26. (animals not (humans and animals)).sh.

27. 25 not 26

28. 4 and 16 and 27

Supplementary material 2

The RoB 2.0 tool (individually randomized, cross-over trials)

Assessor name/initials	RD & SN
Study ID and/or reference(s)	Al-Kaisy 2018

Study design

- ☐ Randomized parallel group trial
- ☐ Cluster-randomized trial
- ☑ Randomized cross-over or other matched design

Specify which outcome is being assessed for risk of bias	Pain intensity

Is your aim for this study…?

- X to assess the effect of *assignment to intervention*
- ☐ to assess the effect of *starting and adhering to intervention*

Which of the following sources have you <u>obtained</u> to help inform your risk of bias judgements (tick as many as apply)?

- X Journal article(s) with results of the trial
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment for a cross-over trial with interest in the effect of assignment to intervention

Domain	Signalling questions	Response options	Description/Support for judgement
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	No information on randomisation. Envelopes used but no additional information on concealment
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	PY	
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	NI	
	1.4 Is a roughly equal proportion of participants allocated to each of the two groups?	Y	
	1.5 If N/PN to 1.4: Are period effects included in the analysis?	NA	
	Risk of bias judgement	Low	
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during each period of the trial?	PN	
	2.2. Were carers and trial personnel aware of participants' assigned intervention during each period of the trial?	PN	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	NA	
	2.4. If Y/PY to 2.3: Were these deviations from intended interventions unbalanced between the two interventions *and* likely to have affected the outcome?	NA	
	2.5 Was there sufficient time for any carry-over effects to have disappeared before outcome assessment in the second period?	PY	Only outcome data from the last 3 days used to minimise carryover effect. Carryover effect, was tested and removed from the final model as not being statistically significant (numerical results not presented).
	Risk of bias judgement	Low	

Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	N	24 participants out of 30 randomised (20%)
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across interventions?	NI	Reasons presented but not by intervention arm
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NI	
	Risk of bias judgement	Some concerns	
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	PN	
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	Low	
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from…		Statistical analyses well described. Numerical results provided only for statistically significant results
	5.1. … multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	
	5.2 … multiple analyses of the data?	N	
	5.3 … the outcome of a statistical test for carry-over?	PN	Carryover effect, was tested and removed from the final model as not being statistically significant. Numerical results to support this not presented
	Risk of bias judgement	Some concerns	
Overall bias	**Risk of bias judgement**	Some concerns	

Assessor name/initials	RD & SN
Study ID and/or reference(s)	De Ridder 2013

Study design

- ☐ Randomized parallel group trial
- ☐ Cluster-randomized trial
- ☑ Randomized cross-over or other matched design

Specify which outcome is being assessed for risk of bias	Pain (back pain, limb pain and general pain)

Is your aim for this study…?

- X to assess the effect of *assignment to intervention*
- ☐ to assess the effect of *starting and adhering to intervention*

Which of the following sources have you <u>obtained</u> to help inform your risk of bias judgements (tick as many as apply)?

- X Journal article(s) with results of the trial
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment for a cross-over trial with interest in the effect of assignment to intervention

Domain	Signalling questions	Response options	Description/Support for judgement
Bias arising from the randomization process	1.1 Was the allocation sequence random?	NI	Described as 'random' but no further information given
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	NI	
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	NI	
	1.4 Is a roughly equal proportion of participants allocated to each of the two groups?	Y	
	1.5 If N/PN to 1.4: Are period effects included in the analysis?	NA	
	Risk of bias judgement	Some concerns	
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during each period of the trial?	PY	At least during tonic stimulation, patients would have paraesthesia sensations and therefore would be aware of the intervention
	2.2. Were carers and trial personnel aware of participants' assigned intervention during each period of the trial?	PN	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	N	
	2.4. If Y/PY to 2.3: Were these deviations from intended interventions unbalanced between the two interventions *and* likely to have affected the outcome?	NA	
	2.5 Was there sufficient time for any carry-over effects to have disappeared before outcome assessment in the second period?	PY	There was no washout period, no significant effect was found including order in the analysis (no numerical results provided to support this).
	Risk of bias judgement	Low	

Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	PY	15 consecutive patients randomised, not clear if any patients rejected participation
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across interventions?	NA	
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NA	
	Risk of bias judgement	Low	
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	PY	At least during tonic stimulation, patients would have paraesthesia sensations and therefore would be aware of the intervention
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NI	
	Risk of bias judgement	Some concerns	
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from…		Limited information provided the statistical analysis methods and the numerical results (only significant or non-significant).
	5.1. … multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	NI	
	5.2 … multiple analyses of the data?	NI	
	5.3 … the outcome of a statistical test for carry-over?	NI	No significant effect was found including order in the analysis (no numerical results provided to support this).
	Risk of bias judgement	Some concerns	
Overall bias	**Risk of bias judgement**	Some concerns	

Assessor name/initials	RD & SN
Study ID and/or reference(s)	Kriek 2017

Study design

- ☐ Randomized parallel group trial
- ☐ Cluster-randomized trial
- ☑ Randomized cross-over or other matched design

Specify which outcome is being assessed for risk of bias	Pain reduction

Is your aim for this study…?

- X to assess the effect of *assignment to intervention*
- ☐ to assess the effect of *starting and adhering to intervention*

Which of the following sources have you <u>obtained</u> to help inform your risk of bias judgements (tick as many as apply)?

- X Journal article(s) with results of the trial
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment for a cross-over trial with interest in the effect of assignment to intervention

Domain	Signalling questions	Response options	Description/Support for judgement
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	The stimulation programming order was generated at the beginning of the trial using a computer-based list without any restrictions. The stimulation setting to be programmed was revealed to the SCS programming assistant at the start of each of the five crossover periods, by opening the appropriate envelope. The patients were blinded with a mask during programming. Treatment allocation was concealed for the statistician who performed the analyses.
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	Y	
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	NI	
	1.4 Is a roughly equal proportion of participants allocated to each of the two groups?	Y	
	1.5 If N/PN to 1.4: Are period effects included in the analysis?	NA	
	Risk of bias judgement	Low	
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during each period of the trial?	PY	Study was designed to be double-blinded but where patients felt paraesthesia within the intervention arm
	2.2. Were carers and trial personnel aware of participants' assigned intervention during each period of the trial?	PN	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	N	

	2.4. If Y/PY to 2.3: Were these deviations from intended interventions unbalanced between the two interventions *and* likely to have affected the outcome?	NA	
	2.5 Was there sufficient time for any carry-over effects to have disappeared before outcome assessment in the second period?	PY	A 2-day washout period was incorporated between the periods to reduce the carryover effect. "Significantly increased NRS pain scores found during the washout periods indicate that there was no carryover effect in terms of lingering pain reduction or a metaplasticity effect."
	Risk of bias judgement	Low	
Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	PY	33 patients randomised and 29 patients who completed the study were included in analysis (12% of randomised patients excluded)
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across interventions?	NI	
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NI	
	Risk of bias judgement	Some concerns	
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	PY	Intervention arm where patients felt paraesthesia
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NI	
	Risk of bias judgement	Some concerns	
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from... 5.1. ... multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	Statistical analyses well described. Numerical results provided only for statistically significant results
	5.2 ... multiple analyses of the data?	N	

	5.3 … the outcome of a statistical test for carry-over?	N	
	Risk of bias judgement	Some concerns	
Overall bias	**Risk of bias judgement**	Some concerns	

Assessor name/initials	RD & SN
Study ID and/or reference(s)	Meier 2015

Study design

- ☐ Randomized parallel group trial
- ☐ Cluster-randomized trial
- ☑ Randomized cross-over or other matched design

Specify which outcome is being assessed for risk of bias	Pain Intensity

Is your aim for this study…?

- X to assess the effect of *assignment to intervention*
- ☐ to assess the effect of *starting and adhering to intervention*

Which of the following sources have you <u>obtained</u> to help inform your risk of bias judgements (tick as many as apply)?

- X Journal article(s) with results of the trial
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment for a cross-over trial with interest in the effect of assignment to intervention

Domain	Signalling questions	Response options	Description/Support for judgement
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	automated number generator (blocks of 4)
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	NI	
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	NI	
	1.4 Is a roughly equal proportion of participants allocated to each of the two groups?	Y	
	1.5 If N/PN to 1.4: Are period effects included in the analysis?	NA	
	Risk of bias judgement	Some concerns	
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during each period of the trial?	Y	When the replies to the question about stimulator setting at various stage of the examination sequence were compared with the records, it showed that all patients, except 1 (ID 9), were able to identify during the study if their stimulator was turned ON or OFF, indicating that the study de facto was a single-blinded study.
	2.2. Were carers and trial personnel aware of participants' assigned intervention during each period of the trial?	PN	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	PN	
	2.4. If Y/PY to 2.3: Were these deviations from intended interventions unbalanced between the two interventions *and* likely to have affected the outcome?	NA	
	2.5 Was there sufficient time for any carry-over effects to have disappeared before outcome assessment in the second period?	PN	12 hours, authors suggest that carry-over effect may have impacted on their results
	Risk of bias judgement	High	

Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	NI	Unclear how many randomised
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across interventions?	NI	
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NI	
	Risk of bias judgement	Some concerns	
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	Y	
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NI	
	Risk of bias judgement	Some concerns	
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from…		Statistical analyses well described and all relevant numerical results presented
	5.1. … multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	
	5.2 … multiple analyses of the data?	PN	
	5.3 … the outcome of a statistical test for carry-over?	PN	
	Risk of bias judgement	Low	
Overall bias	**Risk of bias judgement**	High	
	Optional: What is the overall predicted direction of bias for this outcome?	Favours experimental / Favours comparator / Towards null /Away from null / Unpredictable	

Assessor name/initials	RD & SN
Study ID and/or reference(s)	Perruchoud 2013

Study design

- ☐ Randomized parallel group trial
- ☐ Cluster-randomized trial
- ☑ Randomized cross-over or other matched design

Specify which outcome is being assessed for risk of bias	Pain

Is your aim for this study…?

- X to assess the effect of *assignment to intervention*
- ☐ to assess the effect of *starting and adhering to intervention*

Which of the following sources have you <u>obtained</u> to help inform your risk of bias judgements (tick as many as apply)?

- X Journal article(s) with results of the trial
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment for a cross-over trial with interest in the effect of assignment to intervention

Domain	Signalling questions	Response options	Description/Support for judgement
Bias arising from the randomization process	1.1 Was the allocation sequence random?	PY	Central randomization service
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	PY	
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	NI	
	1.4 Is a roughly equal proportion of participants allocated to each of the two groups?	Y	
	1.5 If N/PN to 1.4: Are period effects included in the analysis?	NA	
	Risk of bias judgement	Low	
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during each period of the trial?	PN	Study double blinded, patients asked to guess which groups they were in and the percentage guessing correctly is what can be expected from chance
	2.2. Were carers and trial personnel aware of participants' assigned intervention during each period of the trial?	PN	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	NA	
	2.4. If Y/PY to 2.3: Were these deviations from intended interventions unbalanced between the two interventions *and* likely to have affected the outcome?	NA	
	2.5 Was there sufficient time for any carry-over effects to have disappeared before outcome assessment in the second period?	PY	Two week washout period with conventional stimulation.
	Risk of bias judgement	Low	

Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	N	Complete data were available from 33 patients out of 40 randomised (17.5% of randomised patients not included in analysis).
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across interventions?	NI	No information provided on the 7 patients with missing data excluded from analysis and whether results were robust to this missing data
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NI	
	Risk of bias judgement	Some concerns	
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	PN	
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	Low	
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from…		
	5.1. … multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Statistical analyses well described and all relevant numerical results presented
	5.2 … multiple analyses of the data?	PN	
	5.3 … the outcome of a statistical test for carry-over?	PN	
	Risk of bias judgement	Low	
Overall bias	**Risk of bias judgement**	Some concerns	

Assessor name/initials	RD & SN
Study ID and/or reference(s)	Schu 2014

Study design

- ☐ Randomized parallel group trial
- ☐ Cluster-randomized trial
- ☑ Randomized cross-over or other matched design

Specify which outcome is being assessed for risk of bias	Pain Intensity

Is your aim for this study…?

- X to assess the effect of *assignment to intervention*
- ☐ to assess the effect of *starting and adhering to intervention*

Which of the following sources have you <u>obtained</u> to help inform your risk of bias judgements (tick as many as apply)?

- X Journal article(s) with results of the trial
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment for a cross-over trial with interest in the effect of assignment to intervention

Domain	Signalling questions	Response options	Description/Support for judgement
Bias arising from the randomization process	1.1 Was the allocation sequence random?	Y	An independent pain nurse allocated a colored ballot to each of the six possible treatment sequences and drew lots in order to prepare the randomization table. Sealed envelopes containing colored ballots were then prepared by the independent pain nurse according to the randomization table and subsequently stored by the independent pain nurse in a secure location to ensure that the randomization envelopes remained concealed until treatment assignment. The independent pain nurse had no contact with the patient prior to randomization.
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	Y	
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	NI	
	1.4 Is a roughly equal proportion of participants allocated to each of the two groups?	Y	
	1.5 If N/PN to 1.4: Are period effects included in the analysis?	NA	
	Risk of bias judgement	Low	
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during each period of the trial?	PN	The patients were not given a programming device to take home in order to ensure that they remained blinded. All patients were advised to recharge on a daily basis to prevent unblinding. A study nurse who was blinded to the treatment allocation recorded data at each follow-up. Independent time slots were used to ensure that the investigator and study nurse remained blinded.
	2.2. Were carers and trial personnel aware of participants' assigned intervention during each period of the trial?	PN	

	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	NA	
	2.4. If Y/PY to 2.3: Were these deviations from intended interventions unbalanced between the two interventions *and* likely to have affected the outcome?	NA	
	2.5 Was there sufficient time for any carry-over effects to have disappeared before outcome assessment in the second period?	PN	Mentions that carry-over effects cannot be eliminated.
	Risk of bias judgement	High	
Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	PY	All randomised patients included in analysis
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across interventions?	NA	
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NA	
	Risk of bias judgement	Low	
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	N	
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	Low	
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from…		Statistical analyses well described and all relevant numerical results presented
	5.1. … multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	
	5.2 … multiple analyses of the data?	PN	
	5.3 … the outcome of a statistical test for carry-over?	PN	
	Risk of bias judgement	Low	
Overall bias	**Risk of bias judgement**	High	

Assessor name/initials	RD & SN
Study ID and/or reference(s)	Tjepkema-Cloostermans 2016

Study design

- ☐ Randomized parallel group trial
- ☐ Cluster-randomized trial
- ☑ Randomized cross-over or other matched design

Specify which outcome is being assessed for risk of bias	Pain

Is your aim for this study…?

- X to assess the effect of *assignment to intervention*
- ☐ to assess the effect of *starting and adhering to intervention*

Which of the following sources have you <u>obtained</u> to help inform your risk of bias judgements (tick as many as apply)?

- X Journal article(s) with results of the trial
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment for a cross-over trial with interest in the effect of assignment to intervention

Domain	Signalling questions	Response options	Description/Support for judgement
Bias arising from the randomization process	1.1 Was the allocation sequence random?	NI	Described as randomized, no further information provided
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	NI	
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	NI	
	1.4 Is a roughly equal proportion of participants allocated to each of the two groups?	Y	
	1.5 If N/PN to 1.4: Are period effects included in the analysis?	NA	
	Risk of bias judgement	Some concerns	
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during each period of the trial?	NI	Labelled as double-blind but no information on who was blinded
	2.2. Were carers and trial personnel aware of participants' assigned intervention during each period of the trial?	NI	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	NI	
	2.4. If Y/PY to 2.3: Were these deviations from intended interventions unbalanced between the two interventions *and* likely to have affected the outcome?	NA	
	2.5 Was there sufficient time for any carry-over effects to have disappeared before outcome assessment in the second period?	Y	
	Risk of bias judgement	Some concerns	

Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	Y	40 out of 41 randomised patients (98%) who completed the study included in analysis
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across interventions?	NA	
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NA	
	Risk of bias judgement	Low	
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	NI	
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NI	
	Risk of bias judgement	Some concerns	
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from…		
	5.1. … multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	PN	Limited information provided on statistical analysis but numerical results well presented
	5.2 … multiple analyses of the data?	PN	
	5.3 … the outcome of a statistical test for carry-over?	PN	
	Risk of bias judgement	Low	
Overall bias	**Risk of bias judgement**	Some concerns	

Assessor name/initials	RD & SN
Study ID and/or reference(s)	Wolter 2012

Study design

- ☐ Randomized parallel group trial
- ☐ Cluster-randomized trial
- ☑ Randomized cross-over or other matched design

Specify which outcome is being assessed for risk of bias	Pain

Is your aim for this study…?

- X to assess the effect of *assignment to intervention*
- ☐ to assess the effect of *starting and adhering to intervention*

Which of the following sources have you <u>obtained</u> to help inform your risk of bias judgements (tick as many as apply)?

- X Journal article(s) with results of the trial
- ☐ Trial protocol
- ☐ Statistical analysis plan (SAP)
- ☐ Non-commercial trial registry record (e.g. ClinicalTrials.gov record)
- ☐ Company-owned trial registry record (e.g. GSK Clinical Study Register record)
- ☐ "Grey literature" (e.g. unpublished thesis)
- ☐ Conference abstract(s) about the trial
- ☐ Regulatory document (e.g. Clinical Study Report, Drug Approval Package)
- ☐ Research ethics application
- ☐ Grant database summary (e.g. NIH RePORTER, Research Councils UK Gateway to Research)
- ☐ Personal communication with trialist
- ☐ Personal communication with the sponsor

Risk of bias assessment for a cross-over trial with interest in the effect of assignment to intervention

Domain	Signalling questions	Response options	Description/Support for judgement
Bias arising from the randomization process	1.1 Was the allocation sequence random?	NI	Described as randomized, no further information provided
	1.2 Was the allocation sequence concealed until participants were recruited and assigned to interventions?	NI	
	1.3 Were there baseline imbalances that suggest a problem with the randomization process?	NI	
	1.4 Is a roughly equal proportion of participants allocated to each of the two groups?	Y	
	1.5 If N/PN to 1.4: Are period effects included in the analysis?	NA	
	Risk of bias judgement	Some concerns	
Bias due to deviations from intended interventions	2.1. Were participants aware of their assigned intervention during each period of the trial?	PN	Patients were asked to walk and make trunk movements in order not to miss any kind of stimulation paraesthesia which would have led to unblinding
	2.2. Were carers and trial personnel aware of participants' assigned intervention during each period of the trial?	NI	
	2.3. If Y/PY/NI to 2.1 or 2.2: Were there deviations from the intended intervention beyond what would be expected in usual practice?	NI	
	2.4. If Y/PY to 2.3: Were these deviations from intended interventions unbalanced between the two interventions *and* likely to have affected the outcome?	NA	
	2.5 Was there sufficient time for any carry-over effects to have disappeared before outcome assessment in the second period?	PN	No washout period mentioned and unclear if potential carry-over has been considered at all
	Risk of bias judgement	High	

Bias due to missing outcome data	3.1 Were outcome data available for all, or nearly all, participants randomized?	NI	No information on how many patients randomised, unclear if only those 10
	3.2 If N/PN/NI to 3.1: Are the proportions of missing outcome data and reasons for missing outcome data similar across interventions?	NI	
	3.3 If N/PN/NI to 3.1: Is there evidence that results were robust to the presence of missing outcome data?	NI	
	Risk of bias judgement	Some concerns	
Bias in measurement of the outcome	4.1 Were outcome assessors aware of the intervention received by study participants?	PN	
	4.2 If Y/PY/NI to 4.1: Was the assessment of the outcome likely to be influenced by knowledge of intervention received?	NA	
	Risk of bias judgement	Low	
Bias in selection of the reported result	Are the reported outcome data likely to have been selected, on the basis of the results, from…		Statistical analyses well described and all relevant numerical results presented
	5.1. … multiple outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	N	
	5.2 … multiple analyses of the data?	N	
	5.3 … the outcome of a statistical test for carry-over?	N	
	Risk of bias judgement	Low	
Overall bias	**Risk of bias judgement**	High	