

Supplementary file

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Appendix 1 Search strategies

Embase

#1 'osteoarthritis'/exp

#2 'osteoarthritides' OR 'osteoarthrosis' OR 'osteoarthroses' OR 'degenerative arthritides' OR 'degenerative arthritis' OR 'osteoarthrosis deformans'

#3 #1 OR #2

#4 'mesenchymal stem cell'/exp

#5 'mesenchymal stem cells' OR 'wharton jelly cells' OR 'whartons jelly cells' OR 'mesenchymal stromal cells' OR 'mesenchymal stromal cell' OR 'multipotent bone marrow stromal cells' OR 'bone marrow stromal stem cells' OR 'multipotent mesenchymal stromal cells' OR 'mesenchymal progenitor cell' OR 'mesenchymal progenitor cells' OR 'bone marrow mesenchymal stem cells' OR 'bone marrow stromal cells' OR 'bone marrow stromal cell' OR 'adipose-derived mesenchymal stem cells' OR 'adipose derived mesenchymal stem cells' OR 'adipose tissue derived mesenchymal stem cells' OR 'adipose-derived mesenchymal stromal cells' OR 'adipose derived mesenchymal stromal cells' OR 'adipose tissue-derived mesenchymal stromal cells' OR 'adipose tissue derived mesenchymal stromal cells' OR 'stromal cells' OR 'stromal cell' OR 'stem cells' OR 'stem cell'

#6 #4 OR #5

#7 'randomized controlled trial'/exp

#8 ('randomized controlled trial' OR 'controlled clinical trial' OR 'random allocation' OR 'double blind method' OR 'double-blind' OR 'single blind method' OR 'triple blind method' OR 'triple-blind' OR 'clinical trial' OR 'comparative study' OR 'follow up studies' OR 'follow-up studies' OR 'prospective studies') NOT 'evaluation studies'

#9 #7 OR #8

#10 #3 AND #6 AND #9

Cells[Title/Abstract]) OR Bone Marrow Stromal Cells[Title/Abstract]) OR Bone Marrow Stromal Cell[Title/Abstract]) OR Adipose-Derived Mesenchymal Stem Cells[Title/Abstract]) OR Adipose Derived Mesenchymal Stem Cells[Title/Abstract]) OR Adipose Tissue-Derived Mesenchymal Stem Cells[Title/Abstract]) OR Adipose Tissue Derived Mesenchymal Stem Cells[Title/Abstract]) OR Adipose-Derived Mesenchymal Stromal Cells[Title/Abstract]) OR Adipose Derived Mesenchymal Stromal Cells[Title/Abstract]) OR Adipose Tissue-Derived Mesenchymal Stromal Cells[Title/Abstract]) OR Adipose Tissue Derived Mesenchymal Stromal Cells[Title/Abstract]) OR Stromal Cells[Title/Abstract]) OR Stromal Cell[Title/Abstract]) OR Stem Cells[Title/Abstract]) OR Stem Cell[Title/Abstract]) OR MSC[Title/Abstract]))

#8 Search "Randomized Controlled Trials as Topic"[Mesh]

#9 Search (((((((((((((randomized controlled trial) OR controlled clinical trial) OR random allocation) OR double blind method) OR double-blind) OR single blind method) OR triple blind method) OR triple-blind) OR clinical trial) OR comparative study) OR follow up studies) OR follow-up studies) OR prospective studies) NOT evaluation studies

#10 Search ("Randomized Controlled Trials as Topic"[Mesh]) OR (((((((((((((randomized controlled trial) OR controlled clinical trial) OR random allocation) OR double blind method) OR double-blind) OR single blind method) OR triple blind method) OR triple-blind) OR clinical trial) OR comparative study) OR follow up studies) OR follow-up studies) OR prospective studies) NOT evaluation studies)

#11 Search (((("Osteoarthritis"[Mesh]) OR (((((((Osteoarthritis[Title/Abstract]) OR Osteoarthrosis[Title/Abstract]) OR Osteoarthroses[Title/Abstract]) OR Degenerative Arthritides[Title/Abstract]) OR Degenerative Arthritis[Title/Abstract]) OR Osteoarthrosis Deformans[Title/Abstract]) OR OA[Title/Abstract]))) AND ("Mesenchymal Stem Cells"[Mesh]) OR (((((((((((((((((((Wharton Jelly Cells[Title/Abstract]) OR Whartons Jelly Cells[Title/Abstract]) OR Mesenchymal Stromal Cells[Title/Abstract]) OR Mesenchymal Stromal Cell[Title/Abstract]) OR

Multipotent Bone Marrow Stromal Cells[Title/Abstract]) OR Bone Marrow Stromal Stem Cells[Title/Abstract]) OR Multipotent Mesenchymal Stromal Cells[Title/Abstract]) OR Mesenchymal Progenitor Cell[Title/Abstract]) OR Mesenchymal Progenitor Cells[Title/Abstract]) OR Bone Marrow Mesenchymal Stem Cells[Title/Abstract]) OR Bone Marrow Stromal Cells[Title/Abstract]) OR Bone Marrow Stromal Cell[Title/Abstract]) OR Adipose-Derived Mesenchymal Stem Cells[Title/Abstract]) OR Adipose Derived Mesenchymal Stem Cells[Title/Abstract]) OR Adipose Tissue-Derived Mesenchymal Stem Cells[Title/Abstract]) OR Adipose Tissue Derived Mesenchymal Stem Cells[Title/Abstract]) OR Adipose-Derived Mesenchymal Stromal Cells[Title/Abstract]) OR Adipose Derived Mesenchymal Stromal Cells[Title/Abstract]) OR Adipose Tissue-Derived Mesenchymal Stromal Cells[Title/Abstract]) OR Adipose Tissue Derived Mesenchymal Stromal Cells[Title/Abstract]) OR Stromal Cells[Title/Abstract]) OR Stromal Cell[Title/Abstract]) OR Stem Cells[Title/Abstract]) OR Stem Cell[Title/Abstract]) OR MSC[Title/Abstract]) AND (("Randomized Controlled Trials as Topic"[Mesh] OR (((((((((((randomized controlled trial) OR controlled clinical trial) OR random allocation) OR double blind method) OR double-blind) OR single blind method) OR triple blind method) OR triple-blind) OR clinical trial) OR comparative study) OR follow up studies) OR follow-up studies) OR prospective studies) NOT evaluation studies))

Cochrane Library

#1 MeSH descriptor Osteoarthritis explode all trees

#2 osteoarthriti* OR osteoarthro* OR arthros* OR arthrot* OR degenerative:ti,ab,kw

#3 #1 OR #2

#4 MeSH descriptor Mesenchymal Stem Cell explode all trees

#5 Wharton Jelly Cells OR Whartons Jelly Cells OR Mesenchymal Stromal Cells OR Mesenchymal Stromal Cell OR Multipotent Bone Marrow Stromal Cells OR Bone Marrow Stromal Stem Cells OR Multipotent Mesenchymal Stromal Cells OR

Mesenchymal Progenitor Cell OR Mesenchymal Progenitor Cells OR Bone Marrow
Mesenchymal Stem Cells OR Bone Marrow Stromal Cells OR Bone Marrow Stromal
Cell OR Adipose-Derived Mesenchymal Stem Cells OR Adipose Derived
Mesenchymal Stem Cells OR Adipose Tissue-Derived Mesenchymal Stem Cells OR
Adipose Tissue Derived Mesenchymal Stem Cells OR Adipose-Derived
Mesenchymal Stromal Cells OR Adipose Derived Mesenchymal Stromal Cells OR
Adipose Tissue-Derived Mesenchymal Stromal Cells OR Adipose Tissue Derived
Mesenchymal Stromal Cells OR Stromal Cells OR Stromal Cell OR Stem Cells OR
Stem Cell OR MSC:ti,ab,kw

#6 #4 OR #5

#7 #3 AND #6

Appendix 2 Methodological quality of the included studies

	Random sequence generation (selective bias)	Allocation concealment (selective bias)	Binding of participant and personal (performance bias)	Binding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Emadedin 2018	?	+	+	+	-	+
Gupta 2016	+	+	+	+	?	+
Kuah 2018	+	+	+	+	-	+
Lamo-Espinosa 2016, 2018	+	+	+	+	+	+
Lee 2019	?	+	+	+	+	+
Matas 2019	+	+	+	+	+	+
Vega 2015	?	+	+	?	+	+

Figure S1 Risk of bias summary: review authors' judgements for each risk of bias item for the included randomized controlled trials.

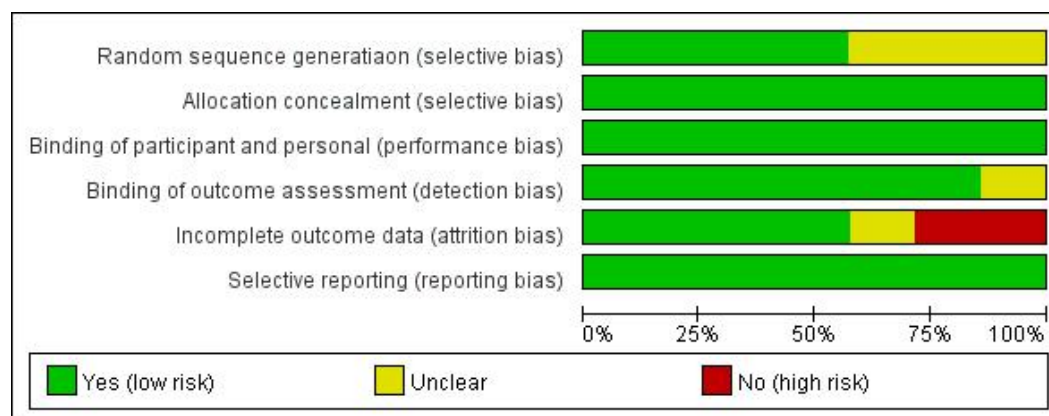


Figure S2 Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included randomized controlled studies.

Appendix 3 funnel plot

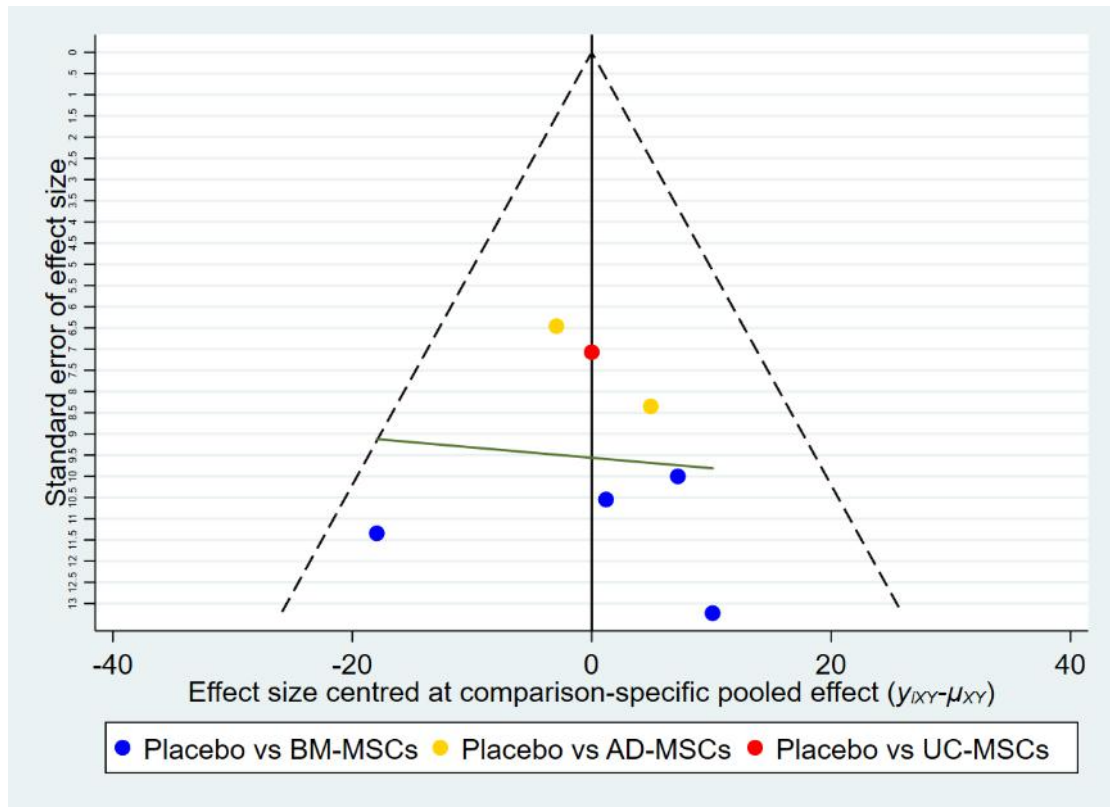


Figure S1 Pain relief.

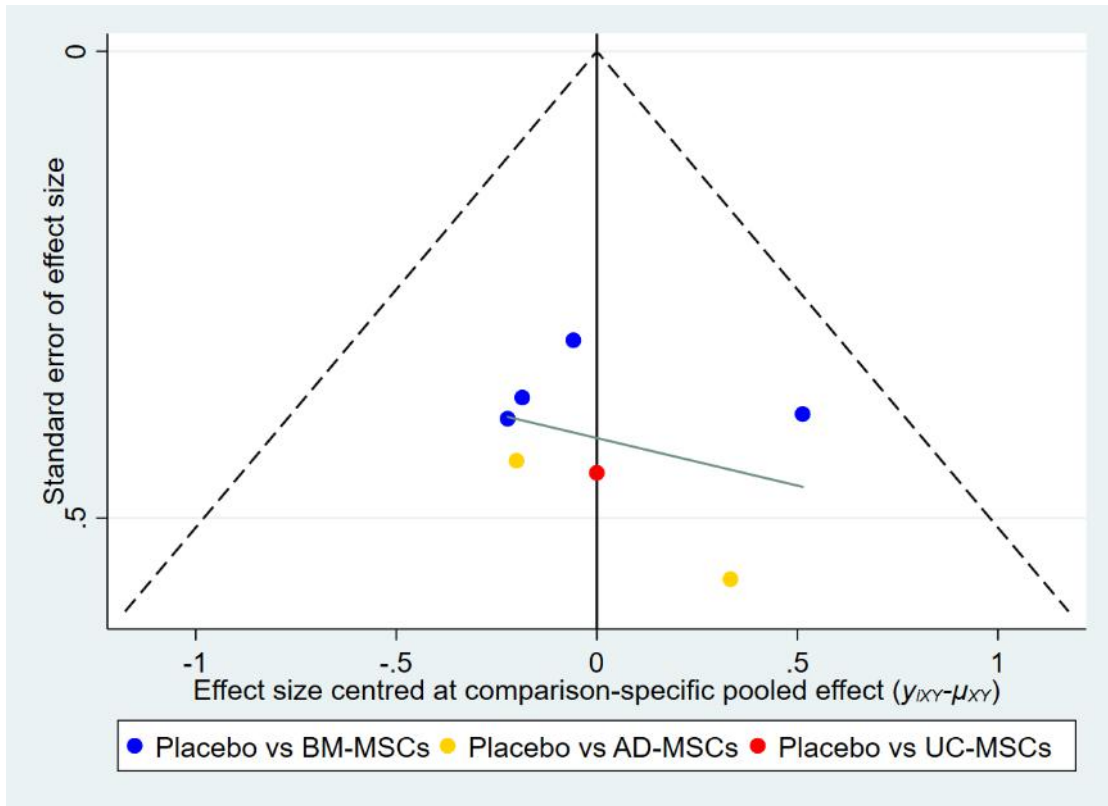


Figure S2 Functional improvement.

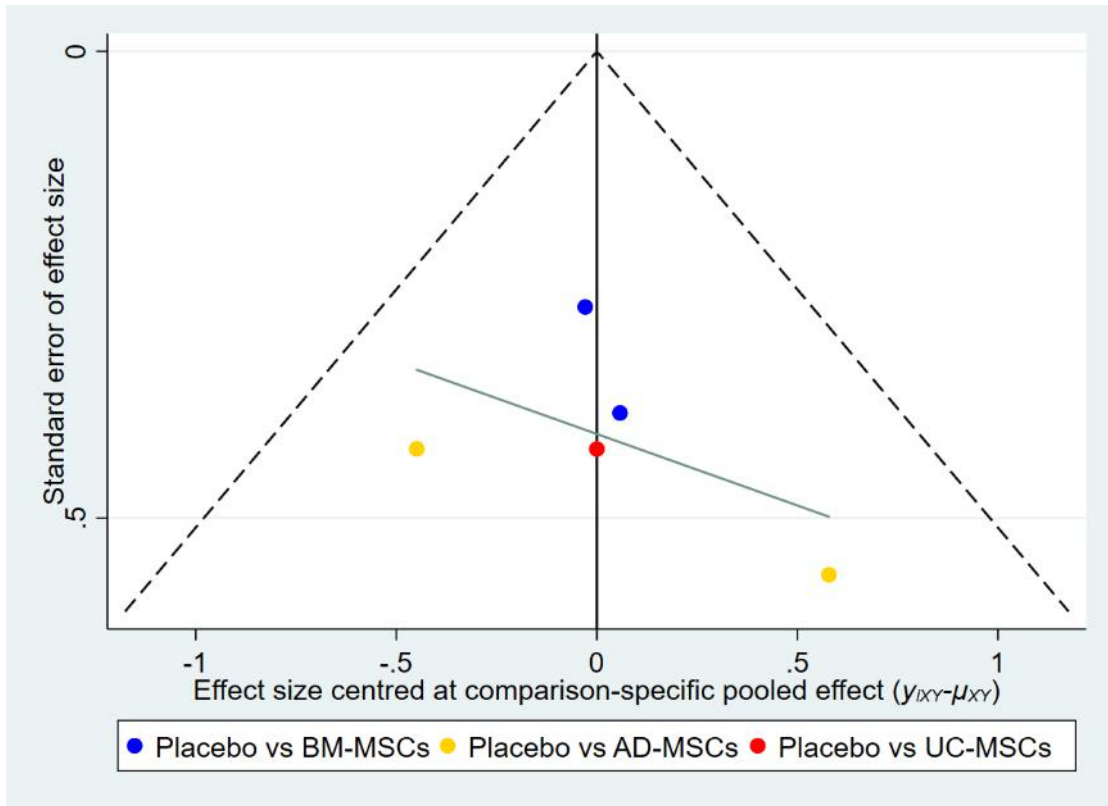


Figure S3 structural assessment.

Appendix 4 Results of SUCRA

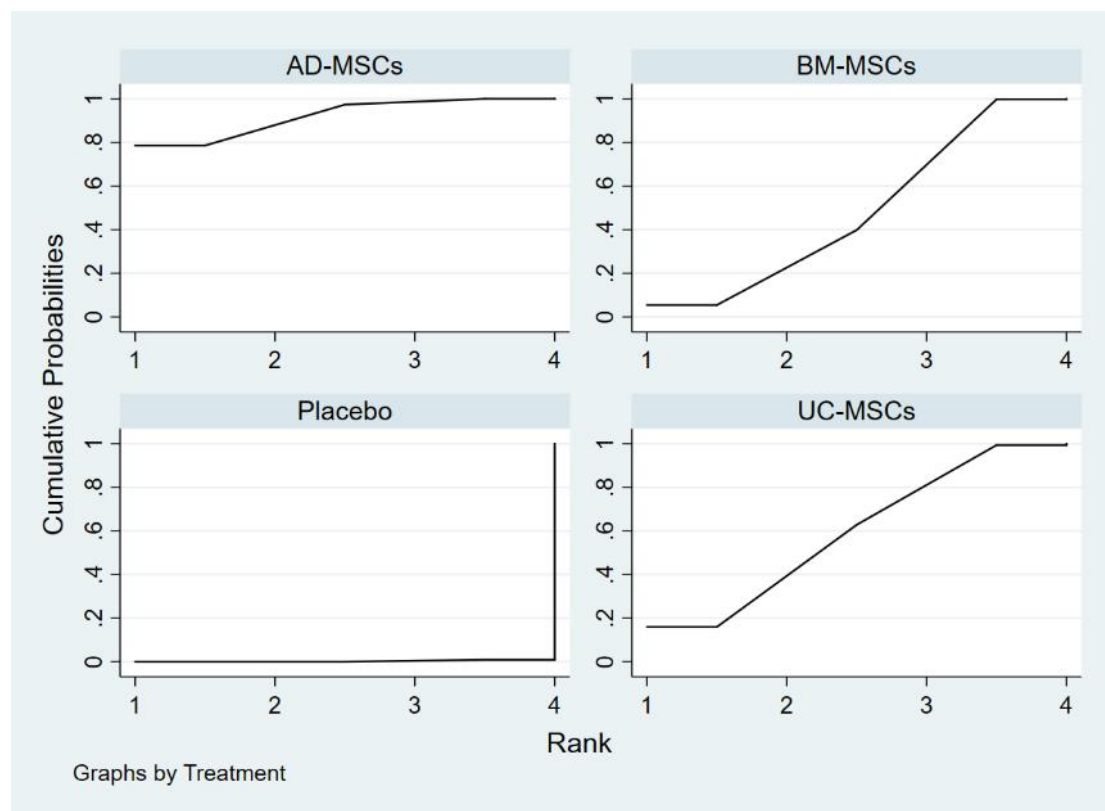


Figure S1 Rankings for effects on pain relief. Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
AD-MSCs	92.0
UC-MSCs	59.4
BM-MSCs	48.4
Placebo	0.3

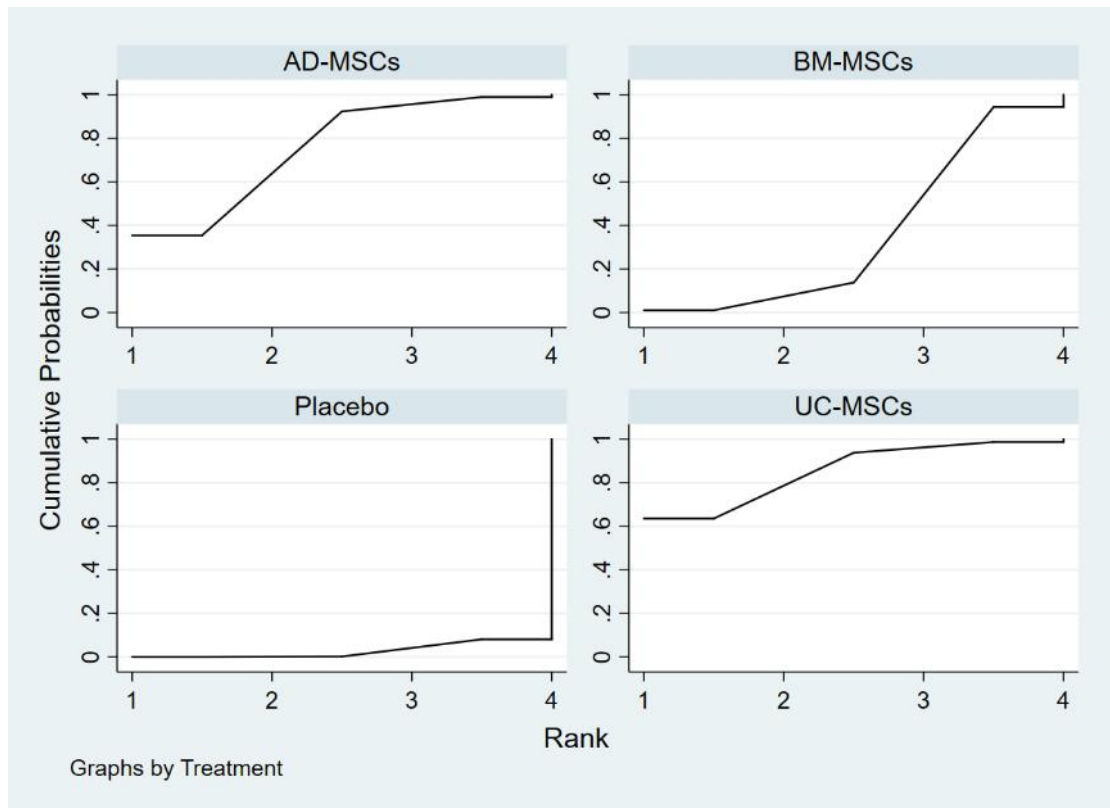


Figure S2 Rankings for effects of function improvement. Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
UC-MSCs	85.3
AD-MSCs	75.6
BM-MSCs	36.4
Placebo	2.8

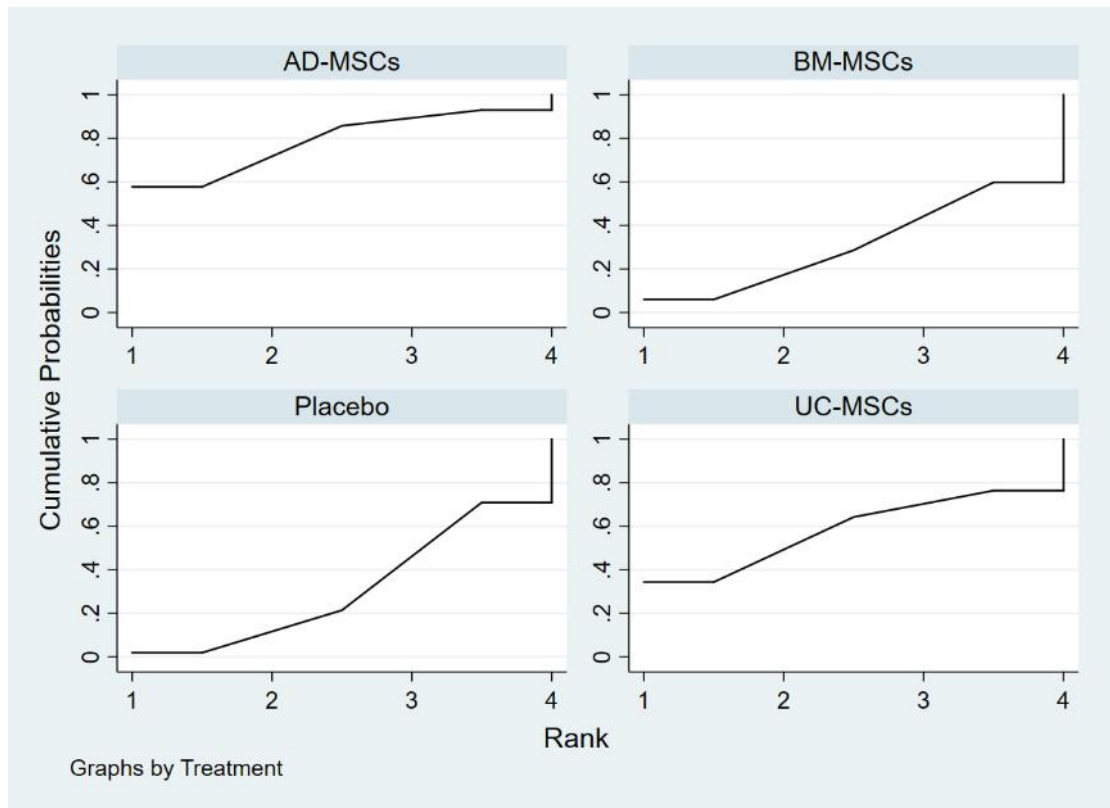


Figure S3 Rankings for effects on structural assessment. Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
UC-MSCs	57.6
AD-MSCs	78.2
BM-MSCs	32.4
Placebo	31.8

Appendix 5 Network meta-analyses results

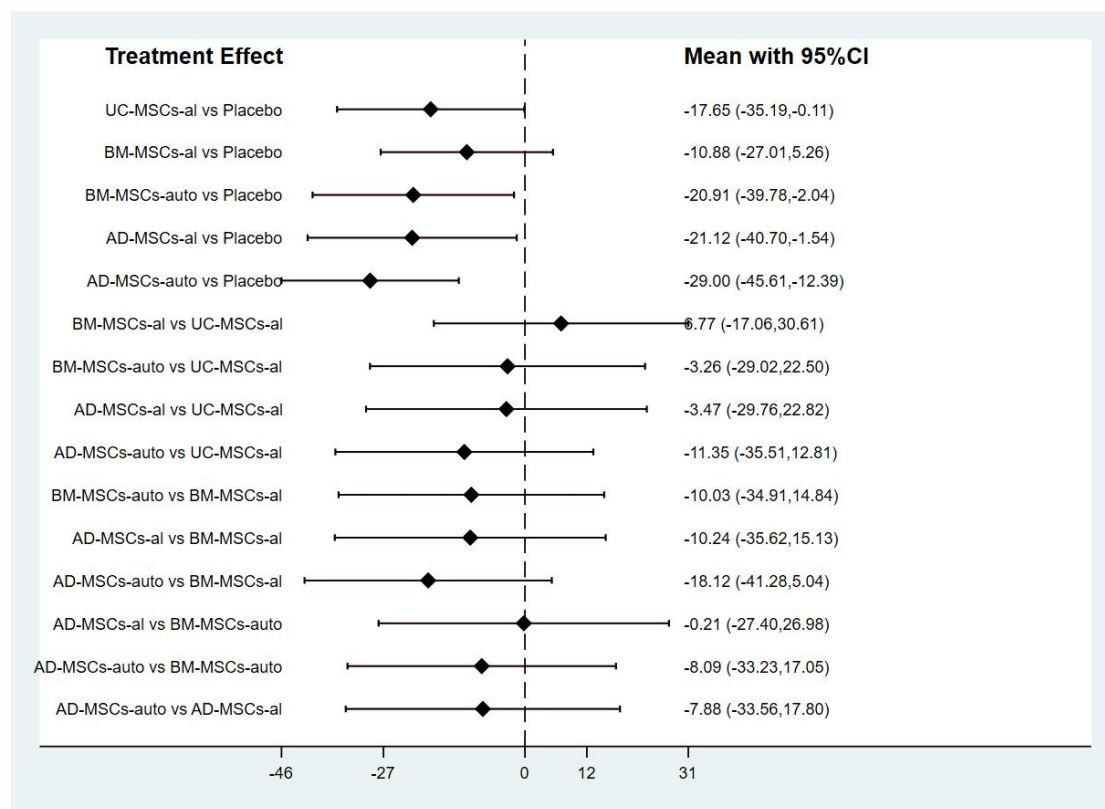


Figure S1 Subgroup analysis (different sources) of pain relief for MSCs overall compared with placebo in RCTs.

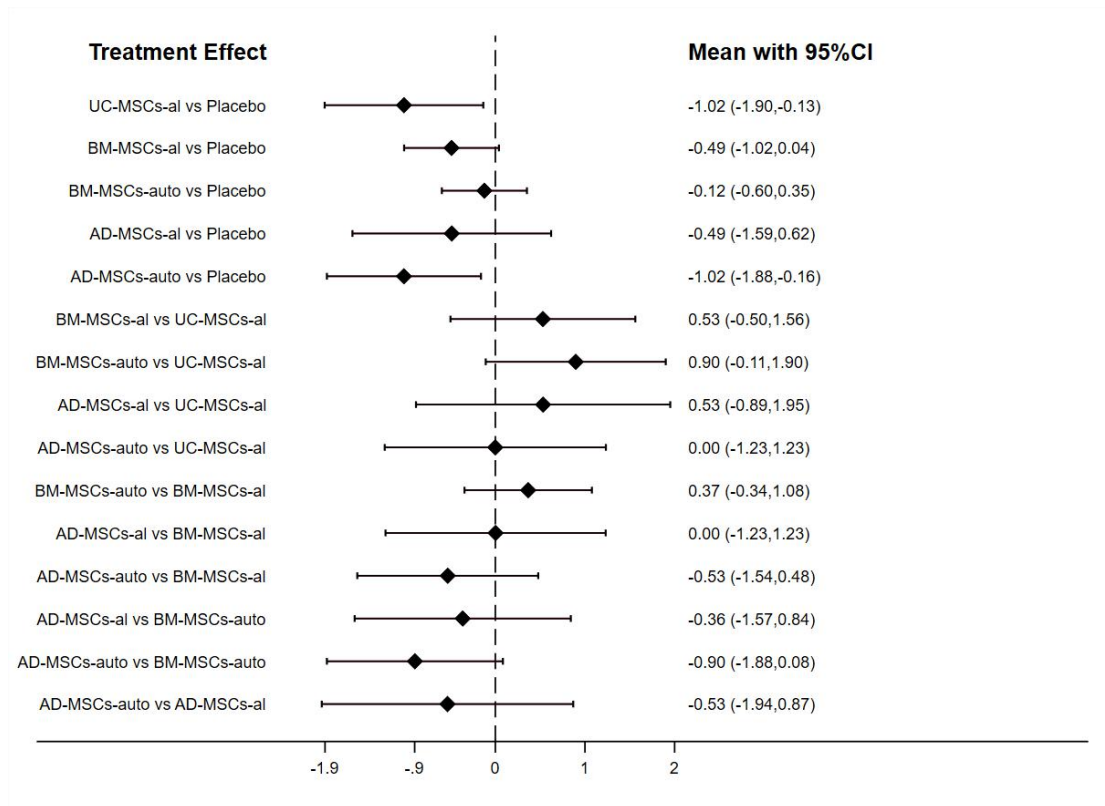


Figure S2 Subgroup analysis (different sources) of functional improvement for MSCs overall compared with placebo in RCTs.

Appendix 6 Results of SUCRA (subgroup analysis)

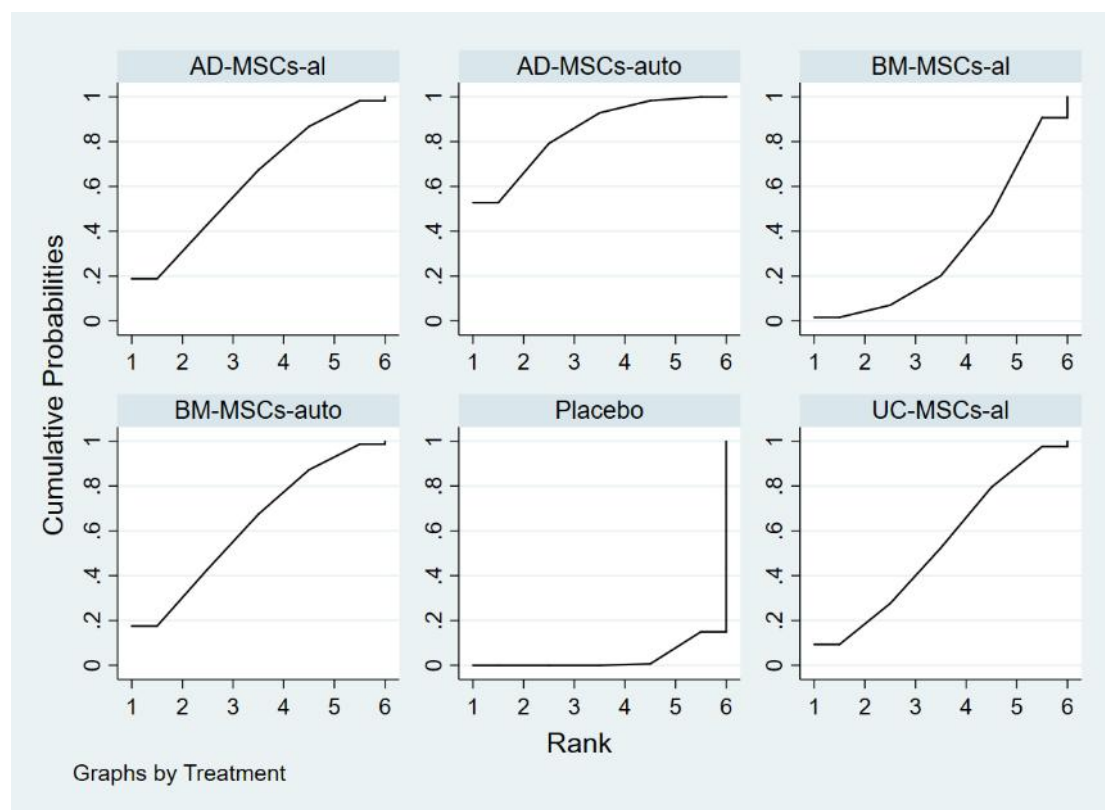


Figure S1 Rankings for effects on pain relief. Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
AD-MSCs-Auto	84.8
AD-MSCs-Al	63.0
BM-MSCs-Auto	62.4
UC-MSCs-Al	53.1
BM-MSCs-Al	33.7
Placebo	3.0

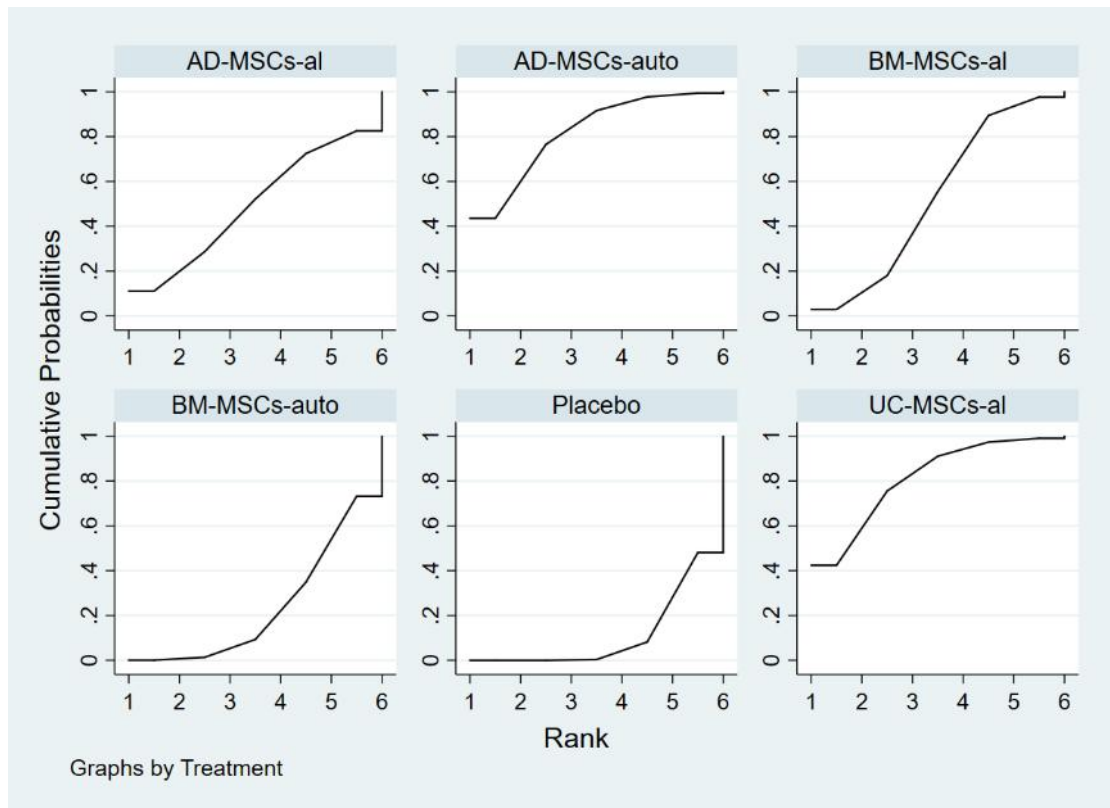


Figure S2 Rankings for effects of function improvement. Graph displays distribution of probabilities for each treatment. X-axis represents the possible rank of each treatment (from the best to worst according to the outcomes), Y-axis represents the cumulative probability for each treatment to be the best option, among the best two options, among the best three options, and so on.

The SUCRA values were as followed:

Treatment	SUCRA (%)
AD-MSCs-Auto	81.8
UC-MSCs-AI	81.1
BM-MSCs-AI	52.7
AD-MSCs-AI	49.4
BM-MSCs-Auto	23.8
Placebo	11.3

Appendix 7 Subgroup analysis of conventional meta-analysis

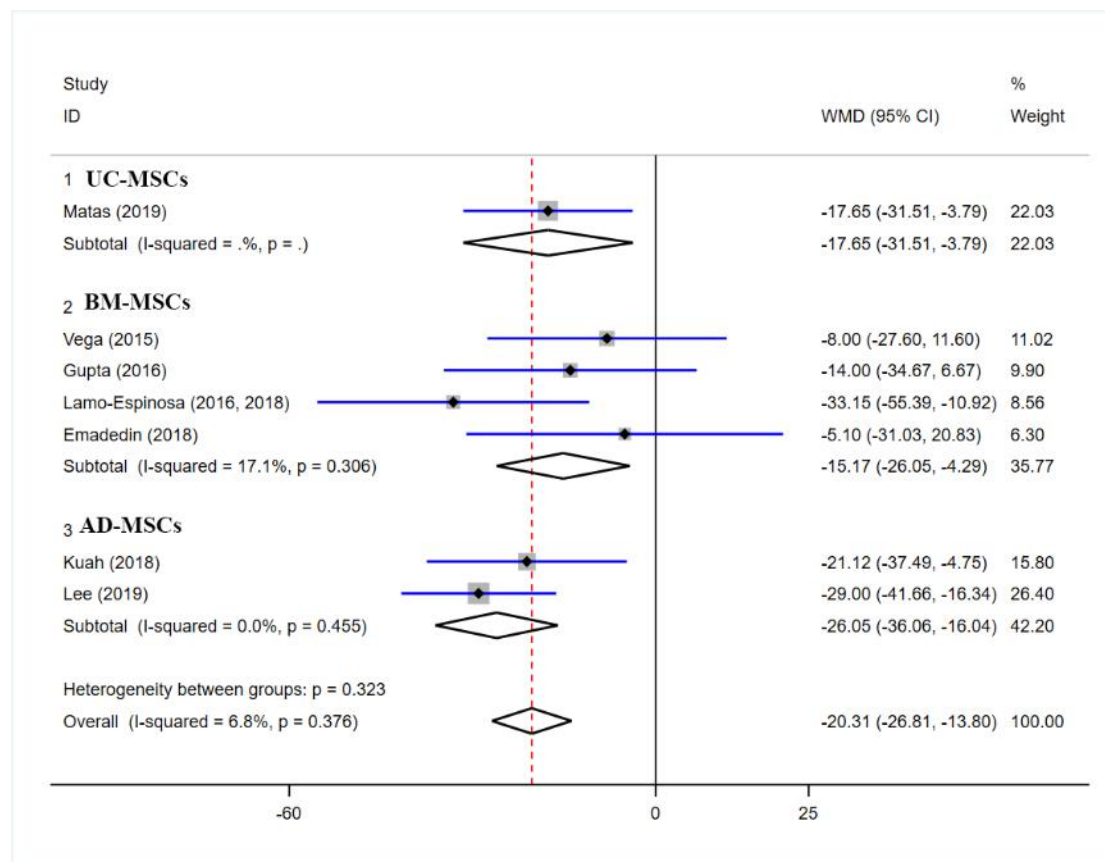


Figure S1 Subgroup A analysis of conventional meta-analysis for pain relief.

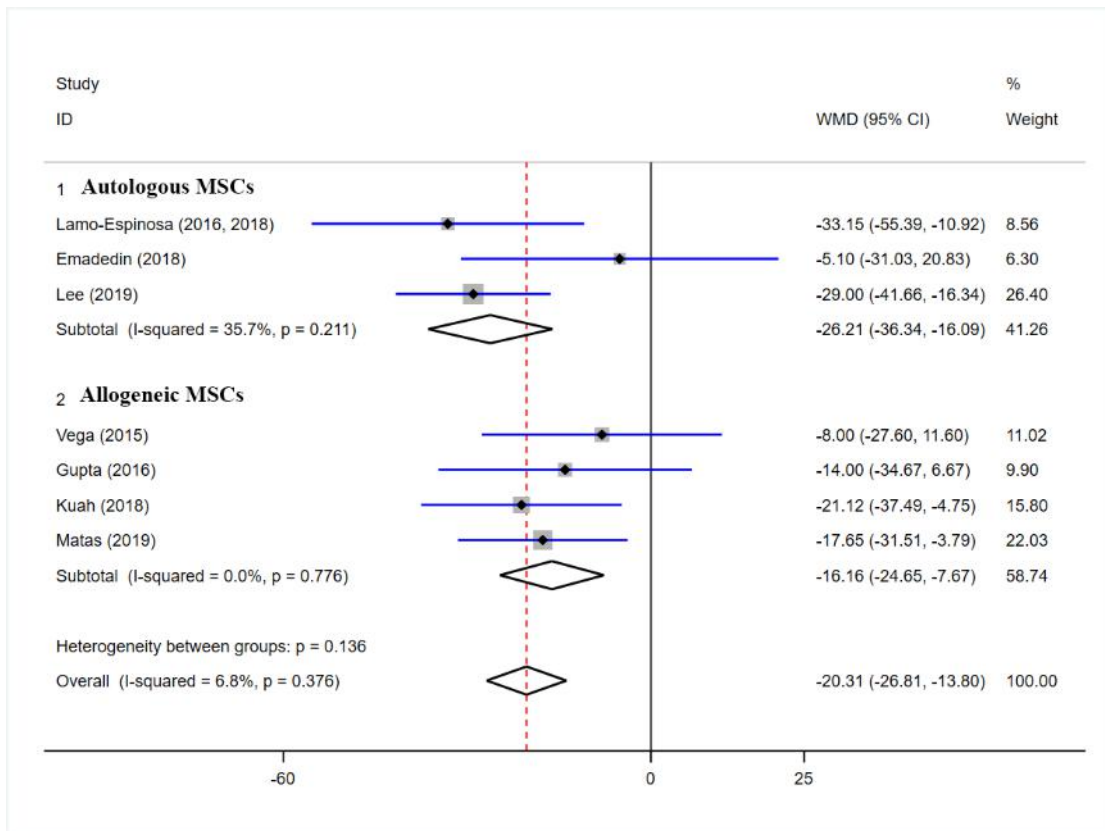


Figure S2 Subgroup B analysis of conventional meta-analysis for pain relief.

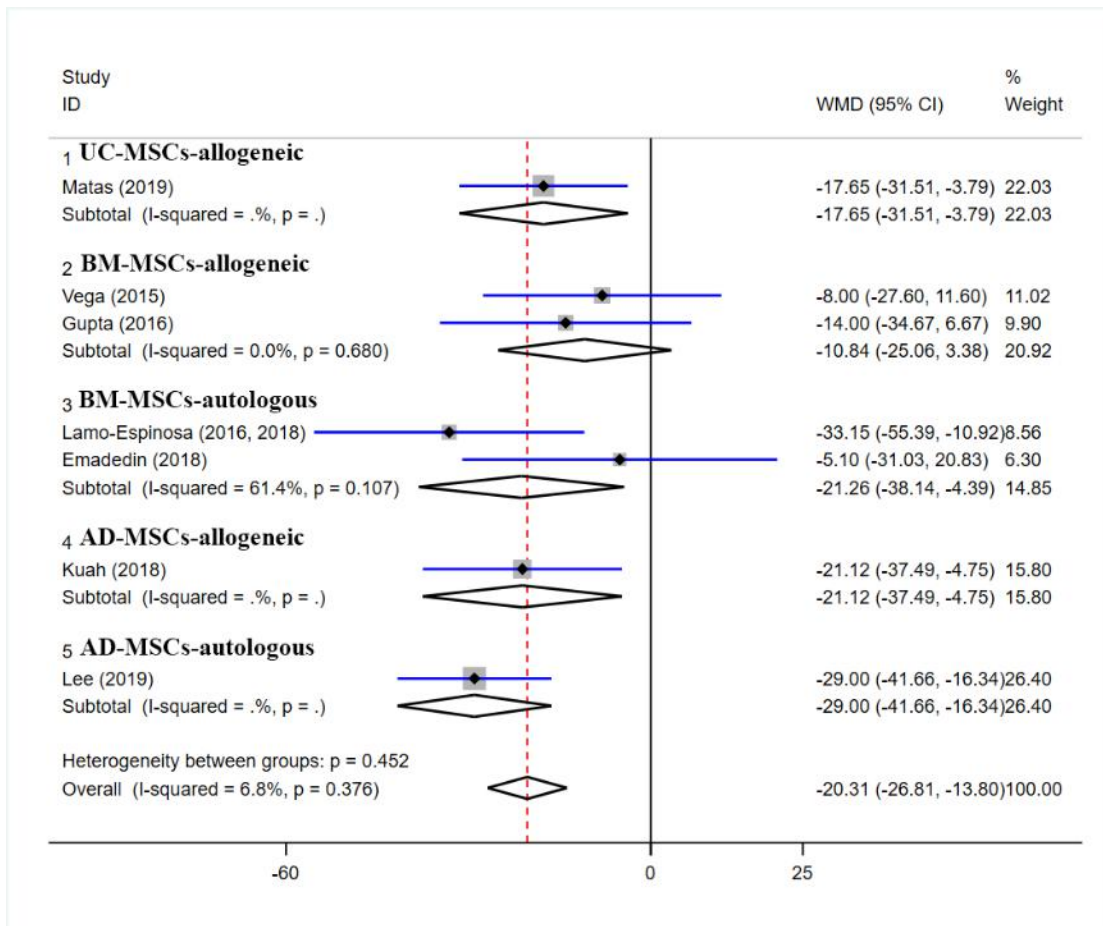


Figure S3 Subgroup C analysis of conventional meta-analysis for pain relief.

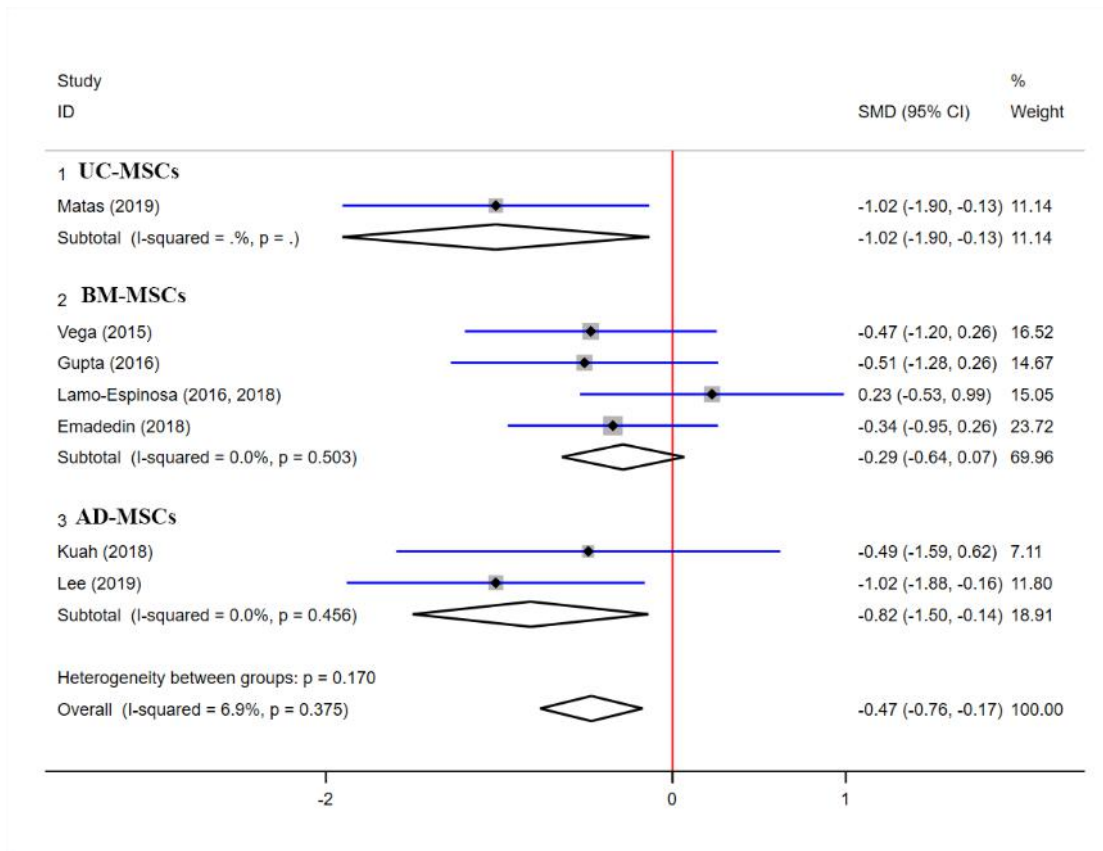


Figure S4 Subgroup A analysis of conventional meta-analysis for function improvement.

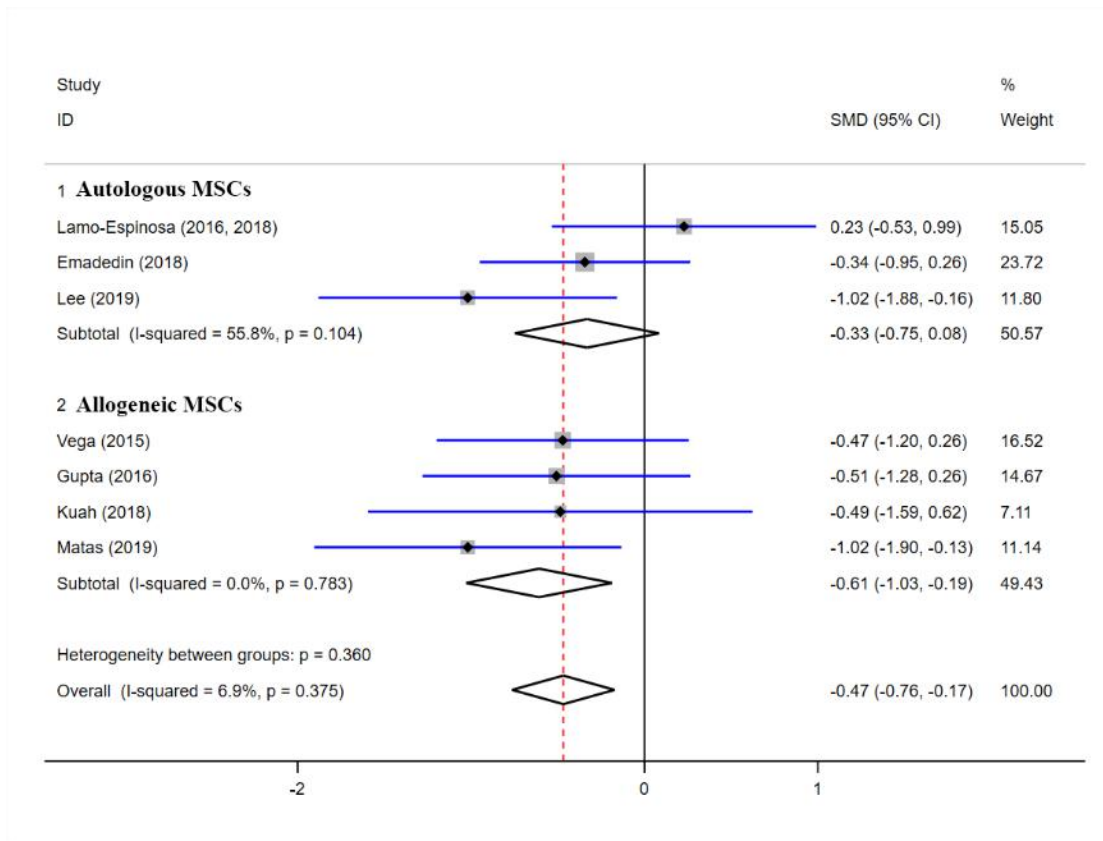


Figure S5 Subgroup B analysis of conventional meta-analysis for function improvement.

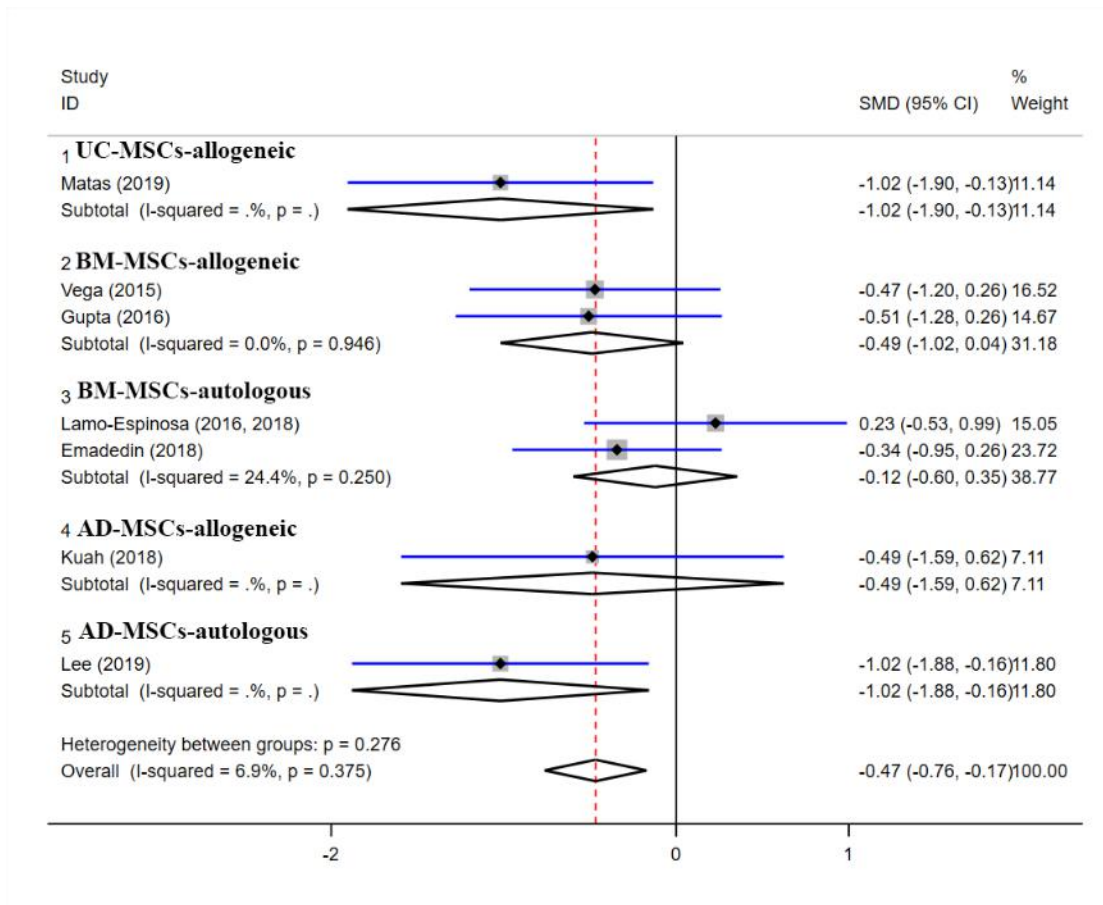


Figure S6 Subgroup C analysis of conventional meta-analysis for function improvement.

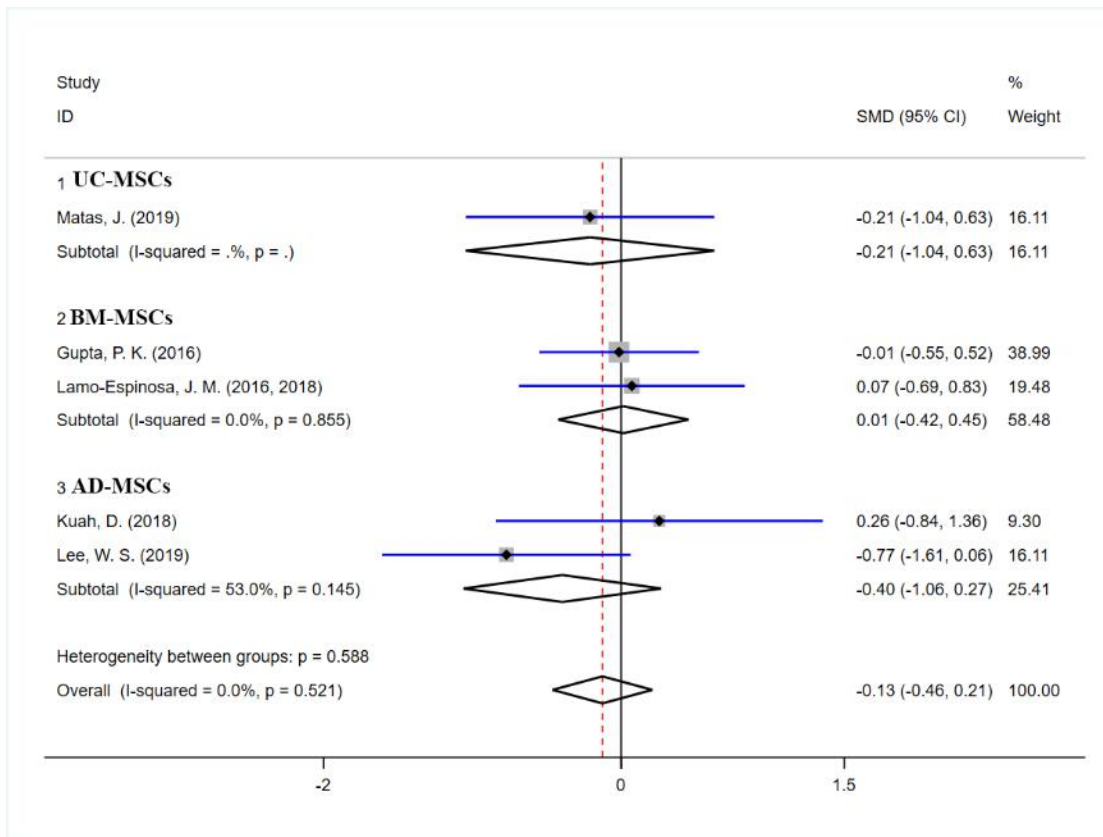


Figure S7 Subgroup A analysis of conventional meta-analysis for structural assessment.

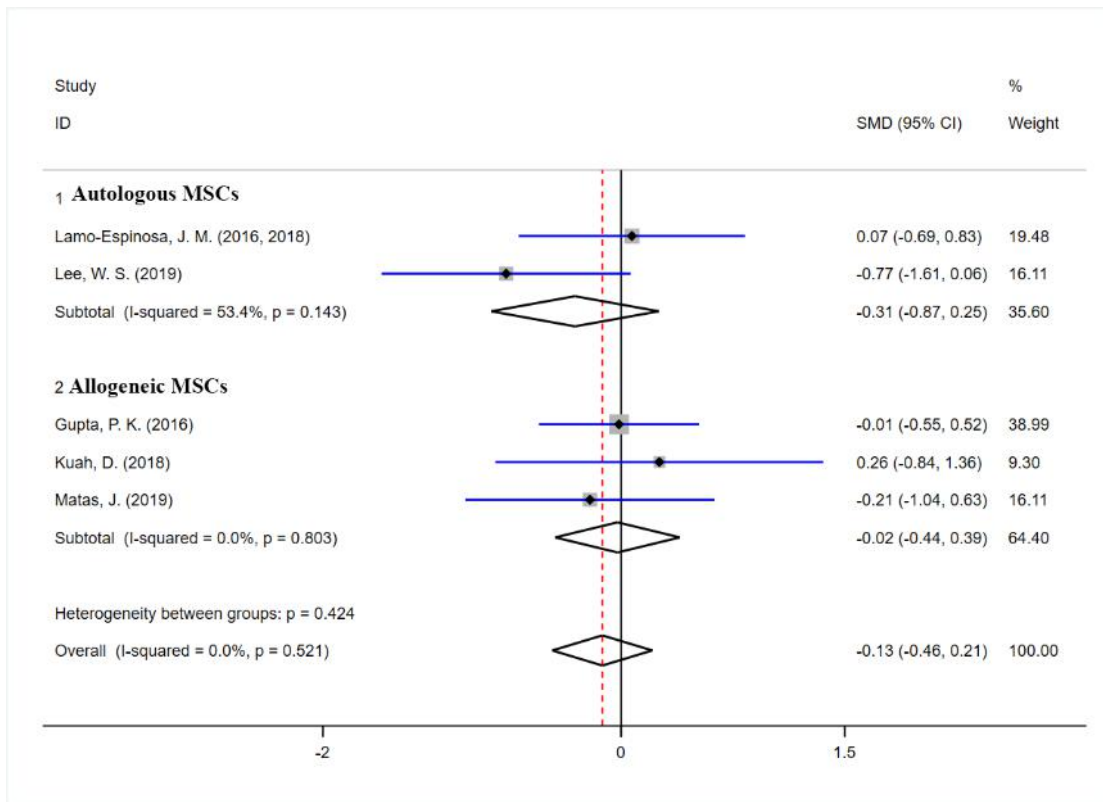


Figure S8 Subgroup B analysis of conventional meta-analysis for structural assessment.

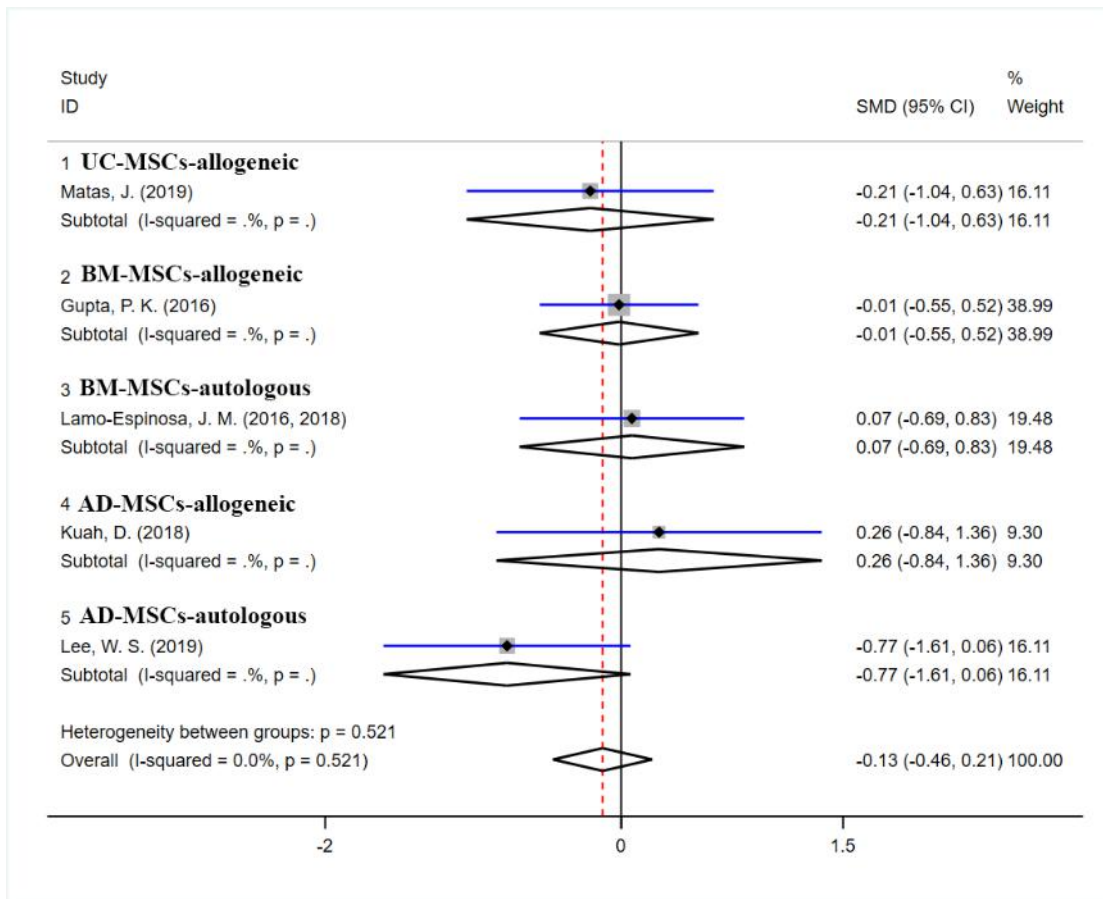


Figure S9 Subgroup C analysis of conventional meta-analysis for structural assessment.