Entering the Era of Living Biopharmaceuticals for Treating Knee Osteoarthritis:
Systematic Review and Network Meta-analysis to Compare
Allogenic and Autologous MSCs

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Supplementary Materials

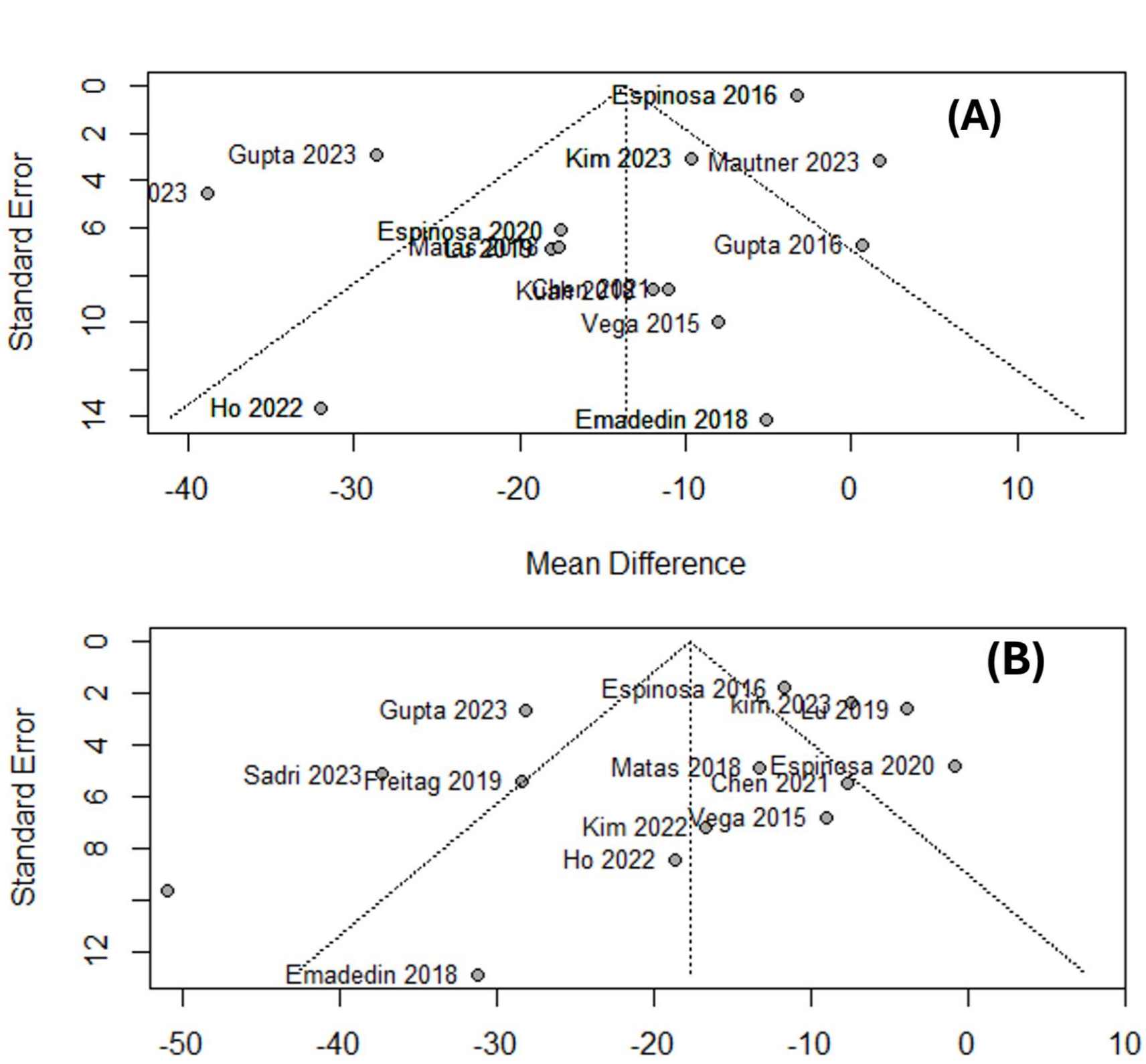
Supplementary Table 1 Quality assessment of the included studies based on Cochrane collaboration tool for bias assessment

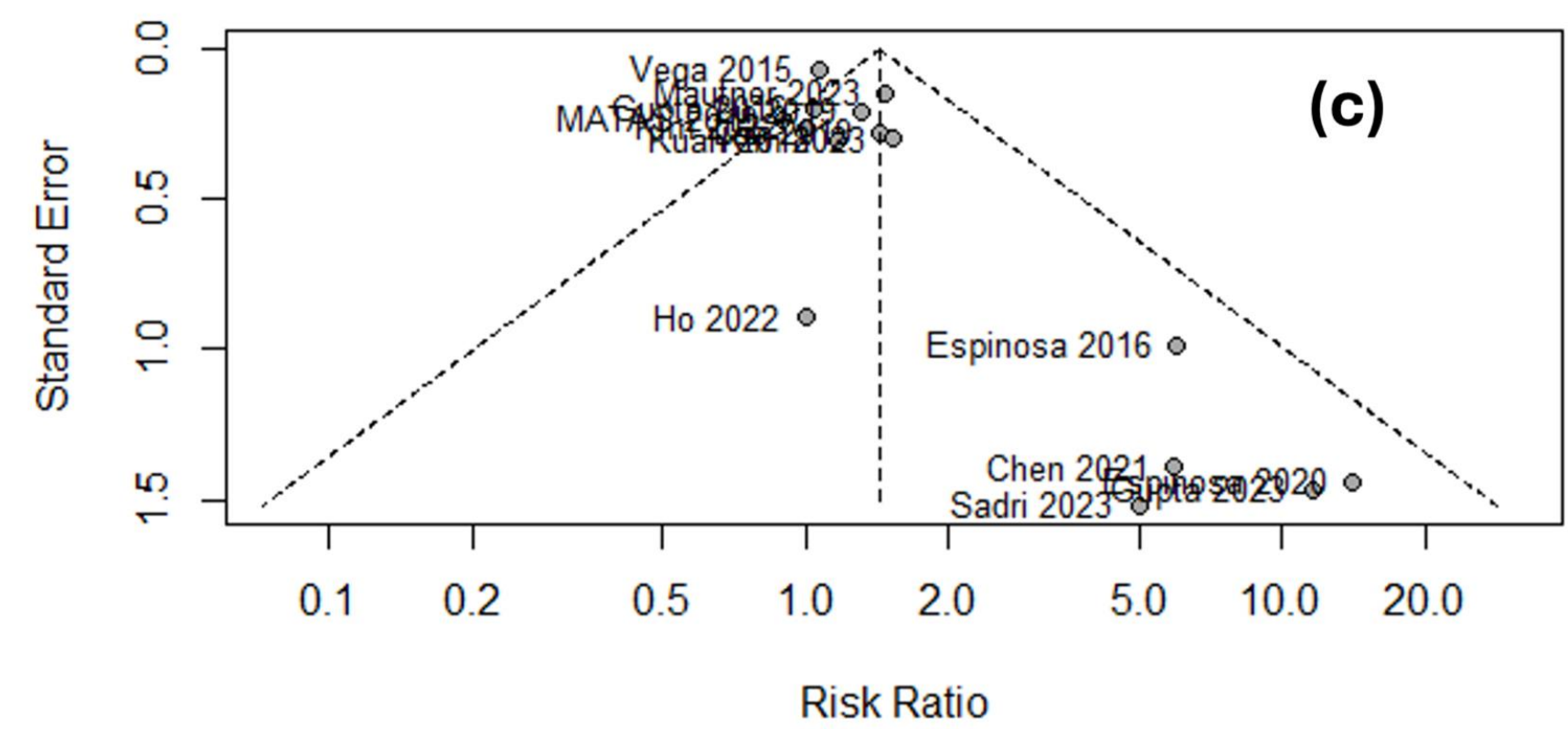
Study	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Lee et al., 2019	Low	Low	Low	Low	Low	Low	Low
Chen et al., 2021	Low	Low	Low	High	Low	Low	Low
Espinosa et al., 2020	Low	Low	High	Low	High	Low	Low
Ho et al., 2022	Low	Low	High	Low	Low	Low	Low
Kauh et al., 2018	Low	Low	Low	Low	Low	Low	Low
Mautner et al., 2023	Low	Low	Low	High	Low	Low	Low
Kim et al., 2022	Low	Low	Unclear	Low	Low	Low	Low
Gupta et al., 2023	Low	Unclear	Low	Low	Low	Low	Low
Kim et al., 2023	Low	Low	Low	Low	High	Low	Low
Matas et al., 2018	Low	Low	Low	Low	High	Low	Low
Emadedin et al., 2018	Low	Low	Low	Low	High	Low	Low
Bastos et al., 2019	Low	Unclear	Low	Low	Low	Low	Low
Freitag et al., 2019	Low	Low	High	Low	Low	Low	Low
Lu et al., 2019	Low	Low	Low	Low	High	Low	Low
Sadri et al., 2023	Low	Low	Low	Low	Unclear	Low	Low
Vega et al., 2015	Low	Low	Low	Low	Unclear	Low	Low
Gupta et al., 2016	Low	Low	Low	Low	Low	Low	Low
Wang et al., 2016	Low	Unclear	Unclear	Unclear	Low	Low	Low
Espinosa et al., 2016	Low	Low	High	High	Low	Low	Low

Supplementary Table 2 Reasons for reports exclusion during full text screening

Author	Study title	Reason for exclusion
Song et al., 2018	Human Adipose-Derived Mesenchymal Stem Cells for Osteoarthritis: A Pilot Study with Long-Term Follow-Up and Repeated Injections	No control group.
Espinosa et al., 2021	Long-term efficacy of autologous bone marrow mesenchymal stromal cells for the treatment of knee osteoarthritis	Not RCT.
Koh et al., 2013	Infrapatellar fat pad-derived mesenchymal stem cell therapy for knee osteoarthritis	Not RCT.
Pers et al., 2016	Adipose Mesenchymal Stromal Cell-Based Therapy for Severe Osteoarthritis of the Knee: A Phase I Dose-Escalation Trial	No control group.
Hernigou et al., 2018	Subchondral stem cell therapy versus contralateral total knee arthroplasty for osteoarthritis following secondary osteonecrosis of the knee	No control group.
Alnajar et al., 2017	Intra-articular injection of expanded autologous bone marrow mesenchymal cells in moderate and severe knee osteoarthritis is safe: a phase I/II study.	No control group.
Jo et al., 2014	Intra-Articular Injection of Mesenchymal Stem Cells for the Treatment of Osteoarthritis of the Knee: A Proof-of-Concept Clinical Trial	Not RCT.
Hernigou et al., 2021	Human bone marrow mesenchymal stem cell injection in subchondral lesions of knee osteoarthritis: a prospective randomized study versus contralateral arthroplasty at a mean fifteen-year follow-up	No control group.
Matas et al., 2024	A Phase I Dose-Escalation Clinical Trial to Assess the Safety and Efficacy of Umbilical Cord-Derived Mesenchymal Stromal Cells in Knee Osteoarthritis	No control group.
Chahal et al., 2019	Bone Marrow Mesenchymal Stromal Cell Treatment in Patients with Osteoarthritis Results in Overall Improvement in Pain and Symptoms and Reduces Synovial Inflammation	Not RCT.
Park et al., 2016	Cartilage Regeneration in Osteoarthritic Patients by a Composite of Allogeneic Umbilical Cord Blood-Derived Mesenchymal Stem Cells and Hyaluronate Hydrogel: Results from a Clinical Trial for Safety and Proof-of-Concept with 7 Years of Extended Follow-Up	Not RCT.
Verma et al., 2010	The new avenues in the management of osteo-arthritis of the knee--stem cells	Not available in full text.
Lu et al., 2020	Intra-Articular Injections of Allogeneic Human Adipose-Derived Mesenchymal Progenitor Cells in Patients with Symptomatic Bilateral Knee Osteoarthritis: A Phase I pilot study	No control group.
Pintore et al., 2023	Intra-articular injection of bone marrow aspirate concentrate (BMAC) or adipose-derived stem cells (ADSCs) for knee osteoarthritis: a prospective comparative clinical trial	No control group.
Davatchi et al., 2015	Mesenchymal stem cell therapy for knee osteoarthritis: 5-year follow-up of three patients	No control group.
Diogo et al., 2020	Umbilical cord-derived mesenchymal stem cells for treating osteoarthritis of the knee: a single-arm, open-label study	Not RCT.
Hernigou et al., 2021	Subchondral bone or intra-articular injection of bone marrow concentrate mesenchymal stem cells in bilateral knee osteoarthritis: can it postpone knee arthroplasty for fifteen years? A randomized study	No control group.

Vangsness et al., 2014	Adult human mesenchymal stem cells delivered via intra-articular injection to the knee following partial medial meniscectomy: a randomized, double-blind, controlled study	It was not an RCT and included patients not diagnosed with KOA.
Orozco et al., 2013	Treatment of Knee Osteoarthritis With Autologous Mesenchymal Stem Cells: A Pilot Study	No control group.
Fodor et al., 2016	Adipose-Derived Stromal Cell (ADSC) Injections for Pain Management of Osteoarthritis in the Human Knee Joint	Not RCT.
Zhao et al., 2019	Multi-compositional MRI evaluation of repair cartilage in knee osteoarthritis with treatment of allogeneic human adipose-derived mesenchymal progenitor cells	No control group.
Peretti et al., 2018	Evaluation of the use of autologous micro-fragmented adipose tissue in the treatment of knee osteoarthritis: preliminary results of a randomized controlled trial	Mixed interventions with MSCs.
Mendoza et al., 2018	The effect of intra-articular injection of autologous bone marrow stem cells on pain and knee function in patients with osteoarthritis.	The intervention group consisted of hematopoietic stem cells.
Wong et al., 2013	Injectable cultured bone marrow-derived mesenchymal stem cells in varus knees with cartilage defects undergoing high tibial osteotomy: a prospective, randomized controlled clinical trial with 2 years' follow-up.	Did not report any of the specified outcomes.
Soltani et al., 2019	Safety and efficacy of allogenic placental mesenchymal stem cells for treating knee osteoarthritis: a pilot study	Did not provide enough data for the meta-analysis.





Supplementary Figure 1 Publication bias assessment by funnel plots. A: VAS score; B: WOMAC index; C: Adverse events.

Allogenic.MSCs		
-1.96 [-16.92 , 13.00]	Autologous.MSCs	
-14.91 [-24.52 , -5.30]	-12.95 [-24.42 , -1.48]	Control

(A)

Allogenic.MSCs		
-10.67 [-21.23 , -0.11]	Autologous.MSCs	
-23.12 [-31.15 , -15.10]	-12.45 [-19.32 ,-5.59]	Control

(B)

Allogenic.MSCs		
0.81 [0.62 , 1.07]	Autologous.MSCs	
1.12 [1.01, 1.25]	1.39 (1.07,1.79)	Control

(C)

Supplementary Figure 2 Net league tables for the study outcomes. A: VAS score; B: WOMAC index; C: Adverse events.