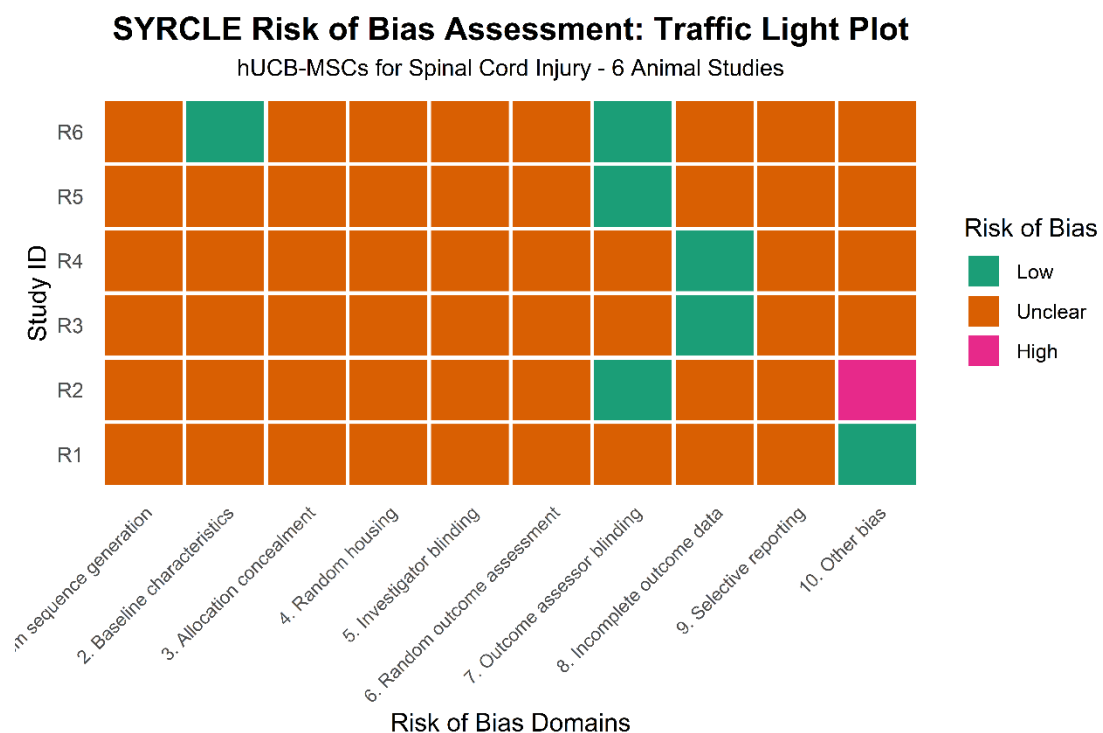
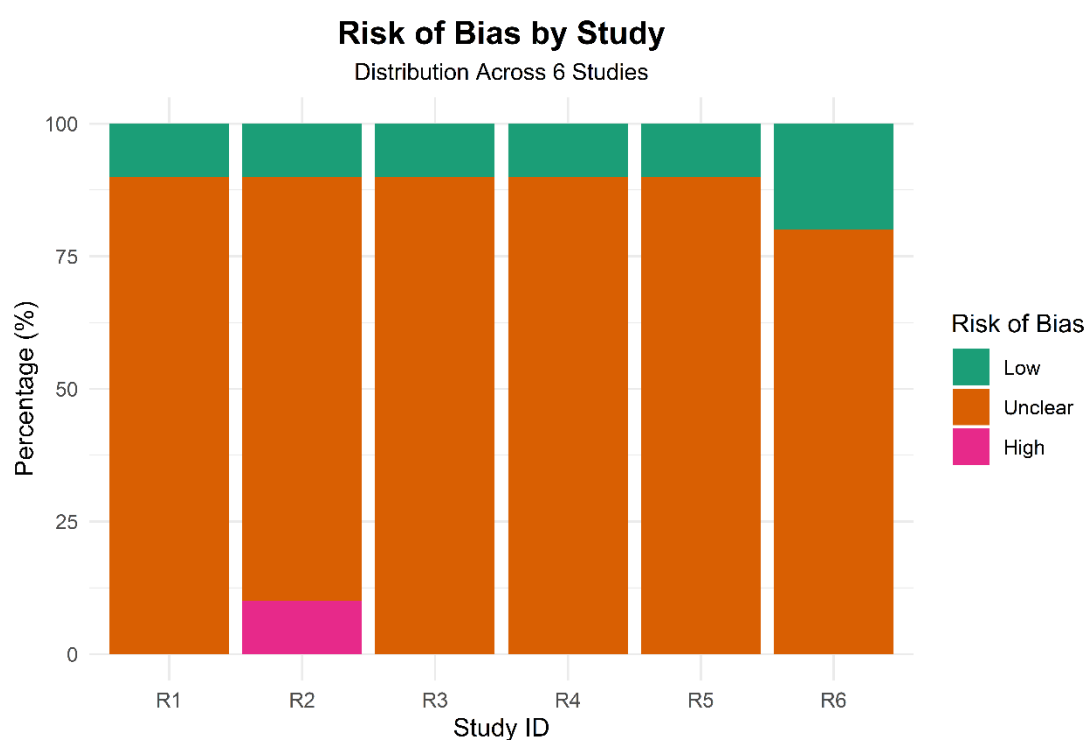
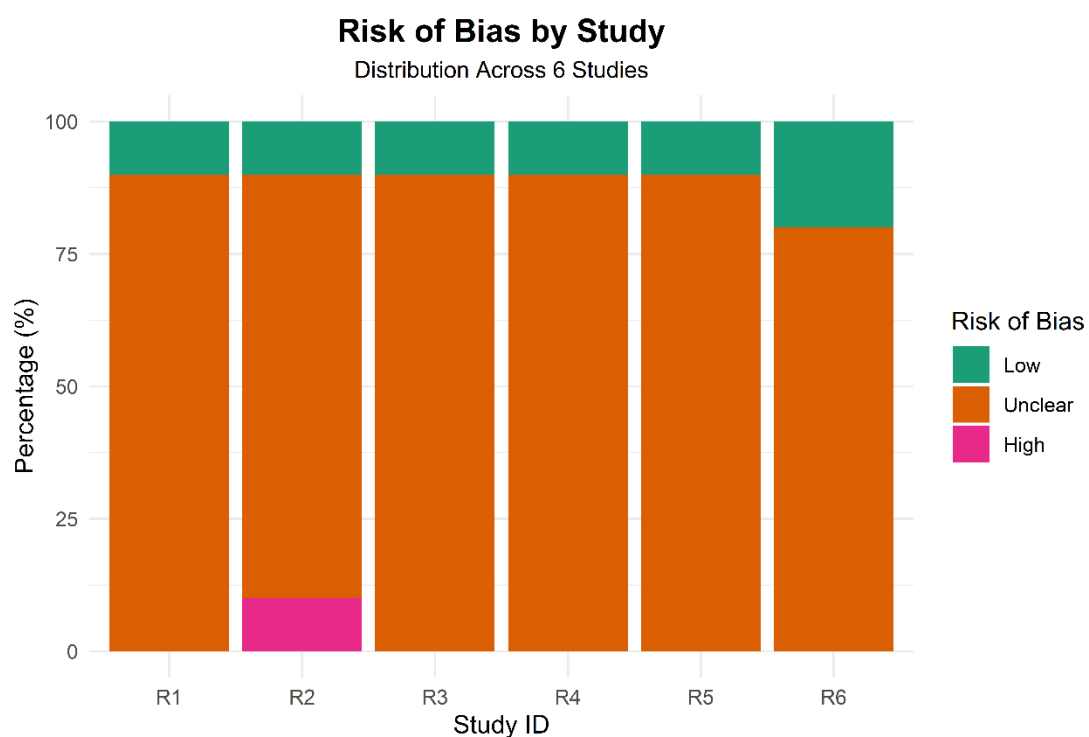




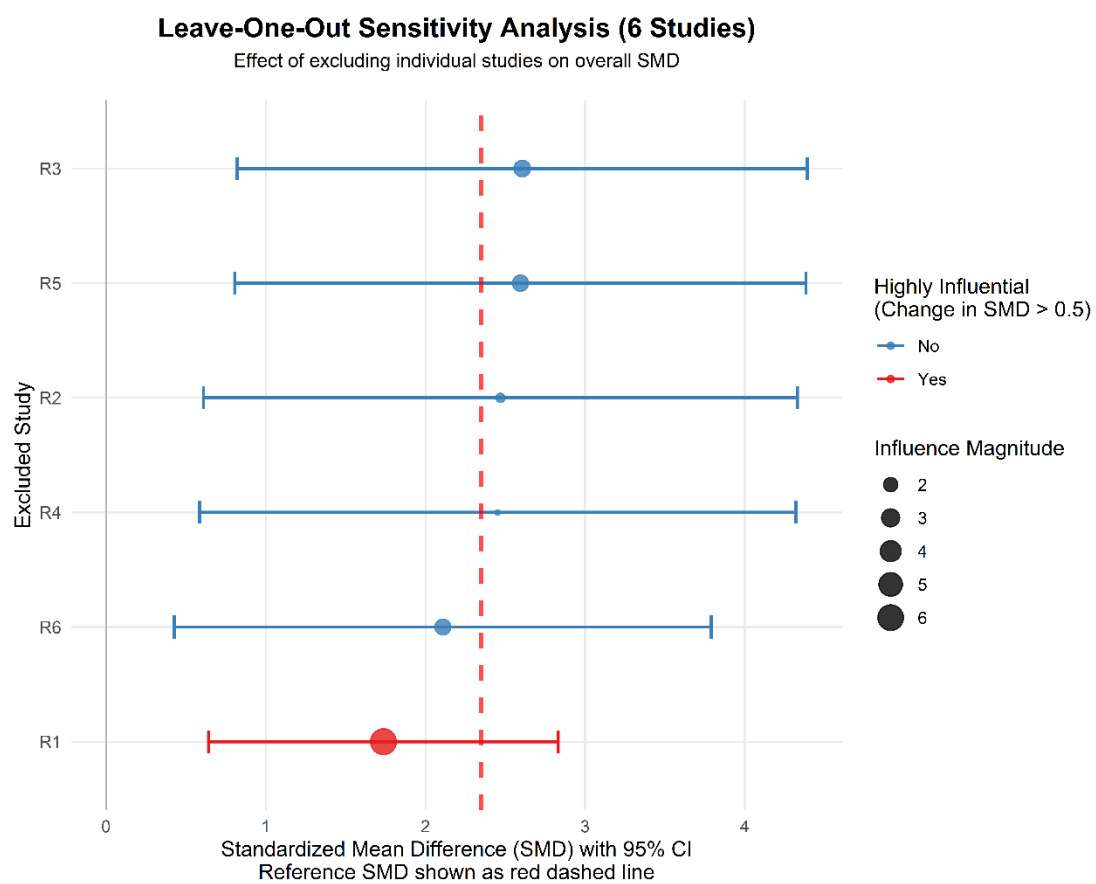
Supplementary Figure 1 Risk-of-bias assessment traffic light plot (SYRCLE tool).



Supplementary Figure 2 Risk-of-bias assessment summary plot (SYRCLE tool).

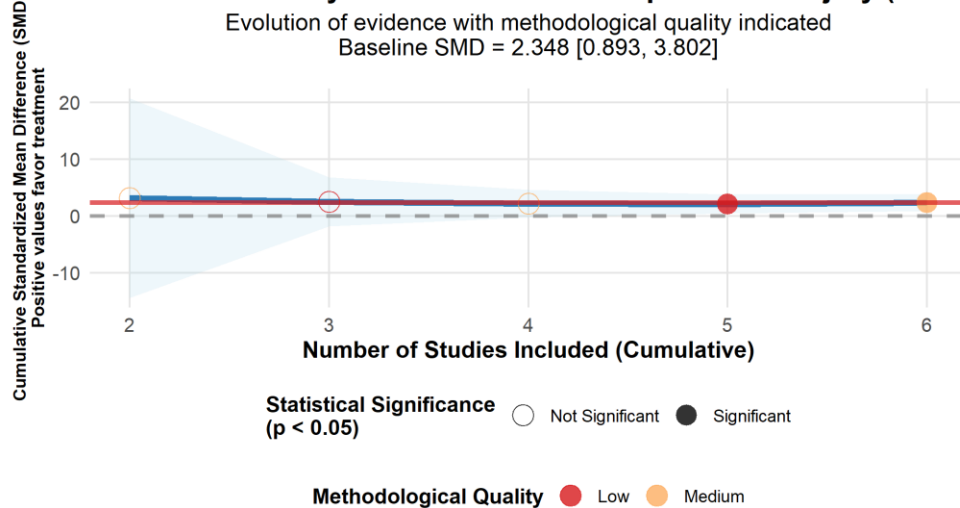


Supplementary Figure 3 Meta-regression summary plot illustrating the association between potential moderators and treatment effect.



Supplementary Figure 4 Leave-one-out sensitivity analysis plot.

Cumulative Meta-Analysis: hUCB-MSCs for Spinal Cord Injury (7 Studies)



Supplementary Figure 5 Cumulative meta-analysis plot of functional recovery outcomes ordered by publication year.

Supplementary Table 1 Detailed results of subgroup analyses for functional recovery

Subgroup _Type	Subgroup_L evel	Stud ies	SM D	CI_Lo wer	CI_U pper	P_Va lue	I2	Tau2	Q_Stat istic	Q_P_V alue	Significa nce	Interpretation
Species	Dog	2	1.746	1.2119	2.2814	0.015	0	0	0.0050	0.94356	Significan	Favors
			72	49	92	336			12	1	t	Treatment
Species	Rat	3	2.319	-	6.7787	0.154	91.37	2.193	23.185	9.23E-	Non-	No Significant
			007	2.1407	36	71	404	559	82	06	significan	Difference
				2							t	
Timing	Acute (<=24 hours)	2	2.876	-	22.846	0.318	94.47	4.669	18.114	2.08E-	Non-	No Significant
			165	17.094	88	391	953	058	39	05	significan	Difference
				5							t	
Timing	Subacute (>24 hours)	4	1.983	0.3032	3.6629	0.032	54.56	0.575	6.6028	0.08569	Significan	Favors
			12	91	49	957	507	429	49	3	t	Treatment
Cell_Dose	Low (<=1e6 cells)	4	1.397	1.0930	1.7022	6.96E	0	0	0.4271	0.93457	Significan	Favors
			647	77	17	-04			62	6	t	Treatment
Route	Local injection	3	2.731	-	6.7137	0.098	81.07	2.416	10.567	0.00507	Non-	No Significant
			187	1.2513	31	223	443	158	72	3	significan	Difference

			6								t		
Route	Systemic injection	3	1.856	-	4.9515	0.122	71.21	0.630	6.9474	0.03100	Non-significant	No Significant Difference	
			8								t		
Injury_Mo del	Compression	4	1.983	0.3032	3.6629	0.032	54.56	0.575	6.6028	0.08569	Significant	Favors Treatment	
Cell_Type	Native	6	2.347	0.8934	3.8022	0.008	81.84	1.534	27.538	4.48E-	Significant	Favors Treatment	
	hUCB-MSC		859	35	82	913	356	77	44	05	t		
Native_M SC	Native	6	2.347	0.8934	3.8022	0.008	81.84	1.534	27.538	4.48E-	Significant	Favors Treatment	
	hUCB-MSC		859	35	82	913	356	77	44	05	t		

Supplementary Table 2 Detailed results of meta-regression analyses

Moderator	Category	Type	Studies	Coefficient	P_Value	R2	QM_Statistic	QM_P_Value	Interpretation
Study_Design	Other	Categorical	6	NA	0.0033	10.0	66.774	0.0033	Significant (p < 0.05)
Cell_dose_per_injection	Intervention	Continuous	5	0	0.0064	10.0	46.525	0.0064	Significant (p < 0.05)
Total_cell_dose	Intervention	Continuous	5	0	0.0064	10.0	46.525	0.0064	Significant (p < 0.05)
Sex	Demographic	Categorical	6	NA	0.0324	10.0	30.07	0.0324	Significant (p < 0.05)
Exclusion_Criteria_clean	Methodological	Categorical	6	NA	0.0413	83.7	8.802	0.0413	Significant (p < 0.05)
Injury_model	Injury_Characteristics	Categorical	6	NA	0.1777	62.5	3.245	0.1777	Trend (0.1 ≤ p < 0.2)
Country	Other	Categorical	6	NA	0.2124	0	2.197	0.2124	Not significant (p ≥ 0.2)

Number_of_doses	Intervention	Continuous	6	0.839	0.3575	4.9	1.079	0.3575	Not significant (p ≥0.2)
Cell_passage	Intervention	Continuous	6	-0.122	0.4832	0	0.596	0.4832	Not significant (p ≥0.2)
Route	Intervention	Categorical	6	NA	0.5223	22.7	0.49	0.5223	Not significant (p ≥0.2)
Injury_level	Injury_Characteristics	Categorical	6	NA	0.5437	0	0.439	0.5437	Not significant (p ≥0.2)
Timing_category	Timing	Categorical	6	NA	0.5772	0	0.367	0.5772	Not significant (p ≥0.2)
Species	Demographic	Categorical	6	NA	0.6422	0	0.515	0.6422	Not significant (p ≥0.2)
Time_first_dose_hours	Timing	Continuous	6	-0.003	0.6586	0	0.227	0.6586	Not significant (p ≥0.2)
Animal_Housing_clean	Methodological	Categorical	6	NA	0.6774	0	0.445	0.6774	Not significant (p ≥0.2)

Year	Other	Continuous	6	0.078	0.7179	0	0.15	0.7179	Not significant (p ≥0.2)
Blinding_clean	Methodological	Categorical	6	NA	0.8093	0	0.066	0.8093	Not significant (p ≥0.2)
Control_Group_clean	Methodological	Categorical	6	NA	0.8427	0	0.274	0.8427	Not significant (p ≥0.2)

EmBase:

#1: fetal blood'/exp or 'cord blood stem cell transplantation'/exp or ("umbilical blood" or "hucb" or "ucb" or "hcb" or "cb"):ab,ti or ("cord blood" not "Spinal Cord Blood"):ab,ti or (cord NEAR/2 blood):ab,ti or (umbilic* NEAR/2 blood):ab,ti or "umbilical cord blood-derived":ab,ti or "cord blood-derived":ab,ti or "hucb-derived":ab,ti or "ucb-derived":ab,ti or "cb-derived":ab,ti or "hcb-derived":ab,ti OR "Umbilical Cord Blood":ab,ti

#2: "mesenchymal stem cell"/exp OR 'stromal cell'/exp OR (MSC OR MSCs OR ""mesenchymal stem cell*"" OR ""mesenchymal stromal cell*"" OR ""multipotent stromal cell*"" OR ""mesenchymal progenitor cell*"" OR ""mesenchymal cell*"" OR ""stromal cell*"" OR ""multipotent cell*"):ab,ti OR (mesenchym* AND stem cell*):ab,ti OR (mesenchym* AND cell*):ab,ti OR (multipoten* AND cell*):ab,ti OR (multipoten* AND stem cell*):ab,ti OR (stromata* AND cell*):ab,ti OR (stromata* AND stem cell*):ab,ti OR (""interstitial substance*"" AND cell*):ab,ti OR (""interstitial substance*"" AND stem cell*):ab,ti OR 'Mesenchymal Stromal Cells'/exp OR ""mesenchymal NEAR/1 cell*"":ab,ti OR ""multipotent NEAR/1 cell*"":ab,ti OR ""multipotent NEAR/1 stem cell*"":ab,ti OR ""stromal NEAR/1 cell*"":ab,ti OR ""stromal NEAR/1 stem cell*"":ab,ti"

#3: ("umbilical cord blood stem cell*" OR "cord blood stem cell*" OR "umbilical cord blood derived stem cell*" OR "cord blood derived stem cell*" OR "umbilical cord blood-derived stem cell*" OR "cord blood-derived stem cell*" OR "hucb stem cell*" OR "ucb stem cell*" OR "cb stem cell*" OR "hucb derived stem cell*" OR "ucb

derived stem cell*" OR "cb derived stem cell*" OR "hucb-derived stem cell*" OR "ucb-derived stem cell*" OR "cb-derived stem cell*"):ab,ti OR "hCB-derived stem cell*":ab,ti

#4: "spinal cord injury"/exp OR 'paraplegia'/exp OR 'quadriplegia'/exp OR ("Spinal Cord Trauma*" OR "Spinal Cord Contusion*" OR "Spinal Cord Transection*" OR "Spinal Cord Laceration*" OR "Spinal Cord Compression*" OR "traumatic myelopath*" OR "SCI*" OR "SCIs*" OR paraplegi* OR tetraplegi* OR quadriplegi*):ab,ti OR (("Spinal Cord*" OR "medulla spinal*" OR "spinal marrow*") NEAR/2 (injur* OR trauma* OR contusion* OR compress* OR transect* OR lacerat* OR hemisection*)):ab,ti OR (spinal NEAR/2 (injur* OR trauma* OR contusion* OR compress* OR transect* OR lacerat* OR hemisection*)):ab,ti OR (cord NEAR/2 (injur* OR trauma* OR contusion* OR compress* OR transect* OR lacerat* OR hemisection*)):ab,ti OR 'Tetraplegia'/exp"

The search strategy and results for September 12, 2025 are as follows:

#1 = 107,888

#2 = 335,957

#3 = 1,720

#4 = 215,407

#5 = #1 AND #2 = 6,091

#6 = #3 OR #5 = 7,531

#7 = #4 AND #6 = 258

OR (unchanged: #1, #2, #3, #4, #5):

#6 = #3 AND #4 = 43

#7 = #5 AND #4 = 228

#8 = #6 OR #7 = 258

WOS:

#1: TS=("fetal blood" OR "cord blood stem cell transplantation" OR "umbilical blood" OR "hucb" OR "ucb" OR "hcb" OR "cb" OR "umbilical cord blood-derived" OR "cord blood-derived" OR "hucb-derived" OR "ucb-derived" OR "cb-derived" OR "hcb-derived" OR "Umbilical Cord Blood") OR TS=(cord NEAR/2 blood) OR TS=(umbilic* NEAR/2 blood) NOT TS=("Spinal Cord Blood")

#2: TS=("mesenchymal stem cell*" OR "mesenchymal stromal cell*" OR "multipotent stromal cell*" OR "mesenchymal progenitor cell*" OR "mesenchymal cell*" OR "stromal cell*" OR "multipotent cell*" OR MSC OR MSCs) OR TS=(mesenchym* AND "stem cell*") OR TS=(mesenchym* AND cell*) OR TS=(multipoten* AND cell*) OR TS=(multipoten* AND "stem cell*") OR TS=(stromata* AND cell*) OR TS=(stromata* AND "stem cell*") OR TS=("interstitial substance*" AND cell*) OR TS=("interstitial substance*" AND "stem cell*") OR TS=("mesenchymal NEAR/1 cell*") OR TS=("multipotent NEAR/1 cell*") OR TS=("multipotent NEAR/1 stem cell*") OR TS=("stromal NEAR/1 cell*") OR TS=("stromal NEAR/1 stem cell*")

#3: TS=("umbilical cord blood stem cell*" OR "cord blood stem cell*" OR "umbilical cord blood derived stem cell*" OR "cord blood derived stem cell*" OR "umbilical cord blood-derived stem cell*" OR "cord blood-derived stem cell*" OR "hucb stem cell*" OR "ucb stem cell*" OR "cb stem cell*" OR "hucb derived stem cell*" OR "ucb derived stem cell*" OR "cb derived stem cell*" OR "hucb-derived stem cell*" OR "ucb-derived stem cell*" OR "cb-derived stem cell*" OR "hcb-derived stem cell*")

#4: TS=("spinal cord injury" OR paraplegia OR quadriplegia OR tetraplegia OR "Spinal Cord Trauma*" OR "Spinal Cord Contusion*" OR "Spinal Cord Transection*" OR "Spinal Cord Laceration*" OR "Spinal Cord Compression*" OR "traumatic myelopath*" OR "SCI" OR "SCIs" OR paraplegi* OR tetraplegi* OR quadriplegi*) OR TS=((("Spinal Cord*" OR "medulla spinal*" OR "spinal marrow*") NEAR/2 (injur* OR trauma* OR contusion* OR compress* OR transect* OR lacerat* OR hemisection*))) OR TS=((spinal NEAR/2 (injur* OR trauma* OR contusion* OR compress* OR

transect* OR lacerat* OR hemisection*)) OR TS=((cord NEAR/2 (injur* OR trauma* OR contusion* OR compress* OR transect* OR lacerat* OR hemisection*)))

The search strategy and results for September 12, 2025 are as follows:

#1 = 103265

#2 = 324618

#3 = 1299

#4 = 195885

#5 = #1 AND #2 = 6247

#6 = #3 OR #5 = 7331

#7 = #4 AND #6 = 171

PubMed:

#1: ("Fetal Blood"[Mesh] OR "umbilical blood"[tiab] OR ("cord blood"[tiab] NOT "Spinal Cord Blood"[tiab]) OR "hUCB"[tiab] OR "UCB"[tiab] OR "hCB"[tiab] OR "CB"[tiab] OR (cord[tiab] ADJ/2 blood[tiab]) OR (umbilic*[tiab] ADJ/2 blood[tiab]) OR "Cord Blood Stem Cell Transplantation"[Mesh] OR "umbilical cord blood-derived"[tiab] OR "cord blood-derived"[tiab] OR "hUCB-derived"[tiab] OR "UCB-derived"[tiab] OR "CB-derived"[tiab] OR "hCB-derived"[tiab])

#2: ("Mesenchymal Stem Cells"[Mesh] OR "Stromal Cells"[Mesh] OR MSC[tiab] OR MSCs[tiab] OR "mesenchymal stem cell*" [tiab] OR "mesenchymal stromal cell*" [tiab] OR "multipotent stromal cell*" [tiab] OR "mesenchymal progenitor cell*" [tiab] OR "mesenchymal cell*" [tiab] OR "stromal cell*" [tiab] OR "multipotent cell*" [tiab] OR (mesenchym*[tiab] AND stem cell*[tiab]) OR (mesenchym*[tiab] AND cell*[tiab]) OR (mesenchym*[tiab] AND stem cell*[tiab]) OR (multipoten*[tiab] AND cell*[tiab]) OR (multipoten*[tiab] AND stem cell*[tiab]) OR (stromata*[tiab] AND cell*[tiab]) OR (stromata*[tiab] AND stem cell*[tiab]) OR (interstitial substance*[tiab] AND cell*[tiab]) OR (interstitial substance*[tiab] AND stem cell*[tiab]))

#3: "umbilical cord blood stem cell*" [tiab] OR "cord blood stem cell*" [tiab] OR "umbilical cord blood derived stem cell*" [tiab] OR "cord blood derived stem cell*" [tiab]

OR "umbilical cord blood-derived stem cell*" [tiab] OR "cord blood-derived stem cell*" [tiab] OR "hUCB stem cell*" [tiab] OR "UCB stem cell*" [tiab] OR "CB stem cell*" [tiab] OR "hUCB derived stem cell*" [tiab] OR "UCB derived stem cell*" [tiab] OR "CB derived stem cell*" [tiab] OR "hUCB-derived stem cell*" [tiab] OR "UCB-derived stem cell*" [tiab] OR "CB-derived stem cell*" [tiab]

#4: ("Spinal Cord Injuries" [Mesh] OR "Spinal Cord Trauma*" [tiab] OR "Spinal Cord Contusion*" [tiab] OR "Spinal Cord Transection*" [tiab] OR "Spinal Cord Laceration*" [tiab] OR "Spinal Cord Compression*" [tiab] OR "traumatic myelopath*" [tiab] OR "SCI" [tiab] OR "SCIs" [tiab] OR (((Spinal Cord* [tiab] OR (medulla spinal* [tiab]) OR (spinal marrow* [tiab])) OR (spinal [tiab] OR cord [tiab])) ADJ/2 (injur* [tiab] OR trauma* [tiab] OR contusion* [tiab] OR compress* [tiab] OR transect* [tiab] OR lacerat* [tiab] OR hemisection* [tiab]))) OR "Paraplegia" [Mesh] OR "Quadriplegia" [Mesh] OR paraplegi* [tiab] OR tetraplegi* [tiab] OR quadriplegi* [tiab]

The search strategy and results for September 16, 2025 are as follows:

#1 = 79,504

#2 = 238,887

#3 = 1,061

#4 = 119,824

#5 = #1 AND #2 = 3,493

#6 = #3 AND #4 = 16

#7 = #5 AND #4 = 51

#8 = #6 OR #7 = 62

Supplementary Method 2: Data Extraction and Quality Assessment Codebook

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Section1: Preamble & General Rules

1.1 Purpose of this Codebook

This codebook provides the detailed *a priori* protocol and criteria for data extraction and methodological quality assessment in the systematic review titled “Efficacy and Safety of Umbilical Cord Blood-Derived Mesenchymal Stem Cell Therapy in Experimental Spinal Cord Injury: A Systematic Review and Meta- Analysis.” It was developed prior to data extraction to ensure objectivity, consistency, and reproducibility throughout the review process. All extraction and assessment procedures were performed independently by two reviewers (L.L. and R.L.) following the rules stipulated herein. Any discrepancies were resolved through consensus or by consultation with a third reviewer (Y.L.).

1.2 Scope and Application

All rules and definitions specified in this codebook were strictly and uniformly applied to the seven (7) included studies. Any deviation from these rules, or any inference made during extraction, was explicitly documented in the General_notes field of the master data sheet to ensure transparency and auditability.

1.3 General Data Extraction Rules

The following overarching principles guided the data extraction process:

(1) Source Fidelity: Data were extracted verbatim from the main text, tables, figures, legends, or supplementary materials of the included publications. Textual data (e.g., author names, strain, model descriptions) preserved original spelling and capitalization. Numerical data retained their original units.

(2) Handling of Graphical Data: For outcomes presented only in graphical form, numerical data (e.g., mean, standard error of the mean) were extracted using validated digital extraction software (Engauge Digitizer, version 11.3, and Fiji/ImageJ, version 1.54p). The source of such extracted data was documented in the General_notes field.

(3) Handling of Missing or Unclear Data: If a parameter was not reported or was ambiguously described, it was recorded as “Not Reported” (or the equivalent categorical option Not_reported/Unclear). No data imputation was performed at the extraction stage.

(4) Categorical Variables: For parameters with predefined categorical options, extractors

selected one and only one option based on explicit criteria defined in Section 2. The selection was based solely on information reported in the source publication.

(5) Derived Variables: Some analysis-ready variables (e.g., Timing_category derived from Time_first_dose_hrs) were defined in the codebook. Their derivation logic is specified in Section 2 to ensure consistent application during data cleaning.

(6) Data Integrity and Version Control: To preserve data integrity, the structure of the master extraction file (columns, sheets, defined names) was not modified after finalization. All data entry and subsequent verification were performed within the established framework.

1.4 Excel Data Management Protocol

The extracted data were managed in a structured Microsoft Excel workbook (DataExtraction AND Quality Assessment 20260130.xlsx), which contained the following key worksheets:

- Readme: Project overview, workbook guide, and important operational notes.
- Codebook (**This document**): The comprehensive data dictionary defining all variables and assessment criteria.
- Master_Data: The primary data extraction sheet, with one row per included study, containing all methodological characteristics, interventions, outcomes, and results.
- Quality_Assessment: Risk of bias and methodological quality assessments using the SYRCLE, CAMARADES, and ARRIVE 2.0 tools.
- QUANT_DATA_POOL: A faithful repository of raw quantitative data as extracted from source publications, preserving original layout for record-keeping.
- QUANT_Data_For_Analysis: A structured, 'tidy data' transformation of the pool sheet, optimized for statistical analysis in R.

1.5 How to Use This Codebook

Reviewers were instructed to adhere to the following workflow:

(1) Consult this Preamble & General Rules section to understand the overall principles and data management structure.

(2) For extracting a specific study characteristic (e.g., species, dose), refer to Section 1 for the parameter's definition and data type, then follow the precise corresponding Section 2 rules for extraction and coding.

(3) When performing methodological quality assessments, use the dedicated protocols in Sections 3 (SYRCLE), 4 (CAMARADES), and 5 (ARRIVE 2.0). All extraction decisions and quality judgments, along with any necessary justifications or notes, were documented in the corresponding columns of the Master_Data and Quality_Assessment sheets.

Section 2: Data Dictionary – Variable Definitions and Types

This section defines all variables extracted for this systematic review. Variables are grouped into four categories, corresponding to the extraction framework outlined in the main manuscript. The Data Type indicates the nature of the variable (Categorical, Text, Integer, Numeric). Format/Note provides key instructions; full and detailed extraction and coding rules for each variable are provided in Section 3.

2.1 Study Characteristics

Variable Name	Description	Data Type	Format / Note
Study_ID	A unique identifier assigned to each included study.	Text	Assigned sequentially as R1-R9 based on publication year.
First_author	Surname and initials of the first author as listed in the publication.	Text	Transcribed verbatim from the source.
Year	The year of publication.	Integer	Four-digit year (YYYY). Extract the numerical year only.
Journal	The full, official name of the journal in which the study was published.	Text	Transcribed verbatim.
Country	The country of the primary institution of the first author.	Text	Copied directly from the article. A single spelling standard per country was enforced.
Funding	The specific funding source(s) declared in the article.	Text	Funding statement transcribed verbatim. Blank if no information provided.
Conflict_of_Interest	A statement regarding any potential conflicts of interest declared by the study authors.	Categorical	Must be selected from a predefined list (see Section 3).
Ethical_Approval	A statement indicating approval from an institutional animal ethics committee or equivalent review body.	Categorical	Must be selected from a predefined list (see Section 3).
Study_Design	The overall methodological design of the experimental study, defined by the presence of a control group and the method of allocation.	Categorical	Must be selected from a predefined list (see Section 3).
Randomization_Method	Verbatim description of the method used to randomly allocate animals to experimental groups.	Text	Free-text. Transcribe only if a specific method is described.
Blinding_Outcome_Assessment	Whether the individuals assessing the primary outcomes were reported to be blinded to group allocation.	Categorical	Must be selected from a predefined list (see Section 3).

Exclusion_Criteria_Stated	Whether the study explicitly stated pre-defined criteria for excluding animals from the analysis.	Categorical	Must be selected from a predefined list (see Section 3).
Sample_Size_Justification	Whether the study provided a rationale for the sample size used (e.g., power calculation).	Categorical	Must be selected from a predefined list (see Section 3).
Statistical_Methods_Described	Whether the statistical methods used to compare groups were explicitly described.	Categorical	Must be selected from a predefined list (see Section 3).
Control_Group_Type	The nature of the active intervention in the primary control group used for efficacy comparison.	Categorical	Must be selected from a predefined list (see Section 3).
Control_Group	The description of the control group(s) as named or described in the source publication.	Text	Free-text. Transcribe group name(s) directly (e.g., "Sham", "Vehicle").

2.2 Animal Model Details

Variable Name	Description	Data Type	Format / Note
Species	The species of animals used in the experiment.	Categorical	Must be selected from a predefined list (e.g., Rat, Mouse, Dog). "Other" must be specified in notes.
Strain	The strain or breed of the animals used.	Text	Free-text. Transcribe the strain name directly and consistently from the source.
Sex	The sex of the animals used in the experiment.	Categorical	Must be selected from: Male, Female, Mixed, Not_reported. Inference documented in notes.
Age_weeks	Age of the animals at the time of SCI induction (experiment start) in weeks.	Numeric	Convert all ages to weeks, rounded to two decimal places.
Animal_Housing_Des c	Key descriptive details about the housing and husbandry conditions.	Text	Free-text. Record concisely (e.g., "Group housed (4/cage); 12-h light/dark; food/water ad libitum").
Anesthesia_Analgesia _Desc	Description of agents, doses, and routes used for anesthesia and/or analgesia.	Text	Free-text. Transcribe key details as concisely as possible from the source.
Number_of_animals	The total number of animals used in the experiment across all groups.	Integer	Plain integer. Sum all reported group sizes.
Injury_model	The method used to induce spinal cord injury.	Categorical	Must be selected from a predefined list (e.g., Contusion, Compression, Transection).
Injury_level	The vertebral level of the induced spinal cord injury.	Categorical	Must be selected from: Cervical, Thoracic, Lumbar, Sacral, Not_specified.
Injury_severity	Objective parameters defining the intensity and extent of the SCI.	Text	Free-text. Record key parameters verbatim with units (e.g., "200 kDyn impact force", "35g compression for 5 min").

2.3 Intervention and Control Details

Variable Name	Description	Data Type	Format / Note
UCB_donors	Number of individual umbilical cord blood donors from which the MSCs were derived.	Categorical	Must be selected from a predefined list (e.g., Single_donor, Pooled_donors).
Cell_source_consistency	Whether all transplanted cells were derived from the same source or donor across the experiment.	Categorical	Must be selected from a predefined list (e.g., Same_source, Different_sources).
Cell_Type_Detailed	Detailed classification of the cellular intervention based on cell type and combination status.	Categorical	Must be selected from a predefined list (e.g., native_hUCB-MSC, native_hUCB-MSC_plus, engineered_hUCB-MSC, engineered_hUCB-MSC_plus, hUCB-MSC_derivative, hUCB-MSC_derivative_plus, combination_unseparable, non_hUCB-MSC).
Is_Native_hUCB_MSC	Binary indicator specifying whether the intervention meets the strict definition of native (unmodified) hUCB-MSC monotherapy.	Categorical	Must be selected from a predefined list (e.g., Yes, No).
Cell_passage	The passage number of the MSCs at the time of intervention.	Numeric	Enter as a plain number. If a range was used, calculate and enter the midpoint.
Cell_viability	The percentage of live cells immediately prior to injection, as determined by a specific assay.	Numeric	Enter as a plain number without the "%" symbol.
Cell_dose_per_injection	The total number of cells administered to each animal in a single injection event.	Numeric	Convert to a plain number (e.g., 5×10^6 becomes 5000000).
Total_cell_dose	The cumulative total number of cells administered to each animal over the entire study.	Numeric	Enter as a plain number. For single-dose studies, equals Cell_dose_per_injection.
Route	The anatomical route of cell administration.	Categorical	Must be selected from a predefined list (e.g., Intravenous, Intralesional, Intrathecal).
Time_first_dose_hrs	Time from SCI induction to the first dose, in hours.	Numeric	Convert all time units to hours. Time zero is the completion of the injury model.
Timing_category	A derived category for the intervention timing relative to injury.	Categorical	Automatically derived from Time_first_dose_hrs (Acute_≤24h, Subacute, Chronic).
Number_of_doses	The total number of cell doses administered per animal.	Integer	Plain integer.
Dosing_schedule_desc	A description of the dosing schedule per animal.	Text	Free-text. Transcribe the schedule from the source text.
Immunosuppression	Whether immunosuppressive drugs were used in the study.	Categorical	Must be selected from a predefined list (Yes, No, Not_reported).
Immunosuppression_regimen	The specific immunosuppressive protocol or drug(s) used.	Text	Free-text. Copy drug names and doses directly from the source text.

2.4 Outcome Data

Variable Name	Description	Data Type	Format / Note
Functional_outcome_scale	The specific scale used to assess locomotor functional recovery (e.g., BBB, Tarlov).	Categorical	Must be selected from a predefined list. Primary scale selected if multiple reported.
Outcome_direction	Indicates whether higher scores represent better, worse, or non-directional outcomes.	Categorical	Must be selected from: Higher_better, Lower_better, Continuous_outcome, Dichotomous_outcome.
Func_mean_Tx	Functional score mean for the Treatment group at the final assessment time point.	Numeric	Plain number. Extracted from text, table, or digitized from figure.
Func_SD_Tx	Functional score standard deviation for the Treatment group.	Numeric	Plain number. Calculated from SEM or CI if necessary; method documented.
Func_n_Tx	Functional score sample size (number of animals) for the Treatment group.	Integer	Plain integer.
Func_mean_Ctrl	Functional score mean for the Control group at the final assessment time point.	Numeric	Plain number. Rules identical to Func_mean_Tx.
Func_SD_Ctrl	Functional score standard deviation for the Control group.	Numeric	Plain number. Rules identical to Func_SD_Tx.
Func_n_Ctrl	Functional score sample size for the Control group.	Integer	Plain integer.
LesionVol_mean_Tx	Lesion volume mean for the Treatment group, typically from histology.	Numeric	Plain number (e.g., mm ³). Leave blank if only qualitative descriptions exist.
LesionVol_SD_Tx	Lesion volume standard deviation for the Treatment group.	Numeric	Plain number.
LesionVol_n_Tx	Lesion volume sample size for the Treatment group.	Integer	Plain integer.
LesionVol_mean_Ctrl	Lesion volume mean for the Control group.	Numeric	Plain number.
LesionVol_SD_Ctrl	Lesion volume standard deviation for the Control group.	Numeric	Plain number.
LesionVol_n_Ctrl	Lesion volume sample size for the Control group.	Integer	Plain integer.
Mortality_events_Tx	Number of animals that died during the observation period in the Treatment group.	Integer	Plain integer. Used for calculating mortality rates.
Mortality_total_n_Tx	Initial total number of animals in the Treatment group at the start of the experiment.	Integer	Plain integer. Must be consistent with other sample size fields.
Mortality_events_Ctrl	Number of animals that died during the observation period in the Control group.	Integer	Plain integer.
Mortality_total_n_Ctrl	Initial total number of animals in the Control group at the start.	Integer	Plain integer.
Adverse_Events_Occurred	Occurrence of any treatment-related adverse events explicitly reported or denied.	Categorical	Must be selected from: Yes, No, Not_reported.
Exploratory_outcomes_notes	Free-text field for recording significant findings from histology, molecular assays, etc.	Text	Used for qualitative synthesis.
Dosing_notes	Free-text field for recording typical or complex dosing details.	Text	Record faithfully, retaining original units and symbols.
Meets_PICOS_Inclusion	Overall eligibility flag indicating whether the study met all pre-specified PICOS criteria after full-text review.	Categorical	Must be selected from a predefined list (e.g., Yes, No). Only studies with "Yes" are included in the final synthesis.
General_notes	Master field for all extraction inferences, clarifications, and methodological notes.	Text	Use strict format: [Field_name]: Note content. Separate entries with a line break.

Section 3: Detailed Data Extraction and Coding Rules

This section provides the precise, step-by-step rules for extracting and coding each variable defined in Section 2. Rules must be applied strictly to ensure consistency between independent reviewers. The variables are organized into the same four thematic groups for ease of reference.

3.1 Rules for Study Characteristics Variables

■ Study_ID

- **Rule:** Assign a unique identifier in the format “R” followed by a sequential number (R1, R2,... R7). Numbering is based on the chronological order of the study’s publication year (ascending). This ID is used for all subsequent referencing.

■ First_author

- **Rule:** Transcribe the “first author” field exactly as it appears in the original publication (e.g., “Smith, J.A.”, “Li, X.”). Preserve punctuation, spacing, and capitalization. Do not expand initials unless they are expanded in the source.

■ Year

- **Rule:** Extract and enter only the numerical year of publication as a 4-digit number. If the text states “published online in 2024”, enter 2024. Ignore month or season.

■ Journal

- **Rule:** Record the full, official name of the journal as listed on the publication (e.g., “Journal of Neurotrauma”, not “J Neurotrauma”).

■ Country

- **Rule:** Copy the country of the first author’s primary institution directly from the article. Standardize spelling across all studies: the spelling from the study with the lowest Study_ID is adopted as the standard for that country.

■ Funding

- **Rule:** Transcribe the entire funding statement verbatim from the acknowledgments or methods section. If the article states there was no external funding, transcribe that statement (e.g., “This research received no specific grant from any funding agency”). Leave the cell blank only if absolutely no funding information is provided.

■ Conflict_of_Interest

- **Rule:** Select one and only one option based on explicit statements in the publication.
- **Disclosed_none:** The article states: “The authors declare no conflict of interest” or equivalent.

- Disclosed_specific: The article discloses specific conflicts (e.g., financial, patent, affiliation).
- Not_reported: No statement regarding conflicts of interest is provided in the manuscript.

■ **Ethical Approval**

- **Rule:** Select one and only one option.
- Yes: The article mentions approval (e.g., IACUC approval number) or compliance with guidelines (e.g., NIH, ARRIVE).
- No: The article explicitly states ethical approval was not obtained. (This is rare).
- Not_reported: No statement regarding ethical approval is provided.

■ **Study Design**

- **Rule:** Classify the study based solely on the reported presence of a control group and allocation method.
- Randomized_Controlled_Trial: MUST have a concurrent control group AND explicitly describe a truly random method (e.g., random number table, computer-generated sequence).
- QuasiRandomized_Controlled_Experiment: MUST have a concurrent control group BUT uses a systematic, non-random method (e.g., alternation, allocation by body weight order).
- NonRandomized_Controlled_Experiment: MUST have a concurrent control group, but the allocation method is neither random nor systematic (e.g., only states “randomly divided” without describing the method).
- Uncontrolled_Experiment_WithRandomization: Does NOT have a concurrent control group, BUT a random method was used for allocation within the group.
- Uncontrolled_Experiment_WithoutRandomization: Does NOT have a concurrent control group AND no randomization was used or reported.
- Other_Design: For designs not covered above (e.g., crossover). Must be specified in General_notes.
- Not_Reported: No description of design or allocation is provided.

■ **Randomization Method**

- **Rule:** Free-text field. Transcribe only the specific description of the randomization method if provided (e.g., “using a random number table”, “computer-generated sequence”). If the article only states “animals were randomly assigned” without describing the method, leave this cell blank.

■ **Blinding Outcome Assessment**

- **Rule:** Select one and only one option.

- Yes: The article explicitly states that outcome assessors were blinded to group allocation.
- No: The article explicitly states that outcome assessors were not blinded.
- Not_reported: No information on blinding of outcome assessors is provided.
- **Exclusion_Criteria_Stated**
 - **Rule:** Select one and only one option.
 - Yes: Pre-defined exclusion criteria are described (e.g., death unrelated to treatment, surgical model failure).
 - No: The article explicitly states no animals were excluded.
 - Not_reported: No information on exclusion criteria is provided.
- **Sample_Size_Justification**
 - **Rule:** Select one and only one option.
 - Yes: A rationale is provided (e.g., power analysis, reference to a pilot study or prior literature).
 - No: The article explicitly states no sample size calculation was performed.
 - Not_reported: No rationale for sample size is provided.
- **Statistical_Methods_Described**
 - **Rule: Select one and only one** option.
 - Yes: Specific statistical tests are named (e.g., “Student’s t-test”, “two-way ANOVA with Tukey’s post-hoc test”).
 - No: The article states no statistical comparisons were made. (Rare).
 - Not_reported: The statistical methods are not described.
- **Control_Group_Type**
 - **Rule:** Categorize the nature of the primary control intervention.
 - No_active_treatment: Tests the cell transplantation procedure against a baseline of no therapy. Includes: ‘Sham operation’, ‘Vehicle injection’, ‘Sham+Vehicle’, ‘No treatment’ after SCI. Key: absence of any putative therapeutic agent.
 - Any_active_control: The control group received a different, active intervention. Includes: ‘Scaffold/Carrier only’, ‘Other cell type’, ‘Other active drug/molecule’. Key: presence of a therapeutic intervention that is not UCB-MSC.
 - Not_reported: Nature of the control intervention is not described.
 - Not_applicable: Must be selected for studies classified as any ‘Uncontrolled_Experiment...’ in the Study_Design field.
- **Control_Group**
 - **Rule:** Free-text field. Transcribe the control group name(s) directly as they appear in the

source (e.g., “Sham”, “Vehicle”, “SCI only”). For multiple groups, list separated by commas. Preserve original capitalization.

3.2 Rules for Animal Model Details Variables

■ Species

- **Rule:** Select from the predefined
 - list: Rat, Mouse, Rabbit, Dog, Pig, Primate, Other.
 - If Other is selected, the specific species name (e.g., “Cat”) must be consistently transcribed from the source text and documented in the General_notes column using the format: [Species]: [transcribed name].

■ Strain

- **Rule:** Free-text field. Transcribe the strain or breed name directly and exactly as reported in the source text (e.g., “Sprague-Dawley”, “Beagle”). If ‘Other’ is selected for Species, the strain (if provided) must still be transcribed here.

■ Sex

- **Rule:** Select one and only one option based on explicit statements.
 - Male: The study explicitly states that only male animals were used.
 - Female: The study explicitly states that only female animals were used.
 - Mixed: The study explicitly states that animals of both sexes were used. Do NOT infer ‘Mixed’ from unreported sex.
 - Not_reported: The sex of the animals is not explicitly stated in the manuscript. If a reasonable inference is made (document in General_notes), select the inferred sex.

■ Age_weeks

- **Rule:** Enter the age at injury in weeks as a numeric value with two decimal places.
 - Convert from days: [days]/7.
 - Convert from months using the standard: 1 month = 4.34524 weeks.
 - Example: “8 weeks” → 8.00; “10 days” → 1.43; “2 months” → 8.69.

■ Animal_Housing_Desc

- **Rule:** Free-text field. Record concise information in the suggested format: [Housing type]; [Light cycle]; [Diet]. Omit missing parts.
 - Example: Group housed (4/cage); 12-h light/dark; food/water ad libitum.

■ Anesthesia_Analgesia_Desc

- **Rule:** Free-text field. Transcribe key details about the agents, doses, and routes used for anesthesia during surgery and/or post-operative analgesia. Be concise.

- Example: Isoflurane inhalation (2-3%) for surgery; Buprenorphine (0.05 mg/kg, s.c.) every 12h for 48h post-op.

■ **Number_of_animals**

- **Rule:** Enter as a plain integer. Extract from an explicit statement or sum all group sizes reported in the methods. After entry, verify consistency with Mortality_total_n_* fields.

■ **Injury_model**

- **Rule:** Select from the predefined
- list: Contusion, Compression, Transection, Hemisection, Chemical, Ischemic, Other, Not_specified.
- Classification is based on the primary method described.

■ **Injury_level**

- **Rule:** Select based on the spinal anatomy of the reported vertebral level.
- Cervical: Injuries at levels C1-C8.
- Thoracic: Injuries at levels T1-T13. Also select if only the spinal region (e.g., "thoracic") is specified without a vertebral level.
- Lumbar: Injuries at levels L1-L6.
- Sacral: Injuries at levels S1-S3.
- Not_specified: The injury level is not reported.

■ **Injury_severity**

- **Rule:** Free-text field. Record the key objective parameter(s) that define the injury severity, as reported verbatim.
- For contusion: Record impact force (e.g., "200 kDyn"), drop height (mm), rod weight/diameter.
- For compression: Record force (e.g., "35 g"), duration (e.g., "5 min"), aneurysm clip type/force (e.g., "50-g closing force").
- For transection/hemisection: Record the nature (e.g., "complete transection at T10", "left hemisection").
- For other models: Record the agent, concentration, and duration (e.g., "4% agarose, applied for 10 min").
- Preserve original units and symbols.

3.3 Rules for Intervention and Control Details Variables

■ **UCB_donors**

- **Rule:** Select from the predefined list to categorize the source of
- MSCs: Single_donor, Pooled_donors, Not_specified. This variable is used to assess potential batch effects.
- **Cell_source_consistency**
 - **Rule:** Select from the predefined
 - list: Same_source, Different_sources, Not_specified. This variable assesses whether all animals received cells from the same donor(s) or batch, which may affect outcome consistency.
- **Cell_Type_Detailed**
 - **Rule:** Select from the predefined
 - list: native_hUCB-MSC, native_hUCB-MSC_plus, engineered_hUCB-MSC, engineered_hUCB-MSC_plus, hUCB-MSC_derivative, hUCB-MSC_derivative_plus, combination_unseparable, non_hUCB-MSC
 - Classification must be based on the experimental group being considered for this systematic review. For studies with multiple experimental groups, select the category that best represents the group that could potentially meet inclusion criteria. Describe the specific nature of "plus" interventions in the General_notes column.
- **Is_Native_hUCB_MSC**
 - **Rule:** Select from the predefined
 - list: Yes, No.
- **Cell_passage**
 - **Rule:** Enter as a plain number. This refers to the passage number at the time of intervention.
 - Do not use designations like 'P4'. Enter 4.
 - If a range of passages was used (e.g., P3 to P5), calculate and enter the midpoint (e.g., 4). The original range must be documented in
 - the General_notes column (e.g., [Cell_passage]: Reported as P3-P5; midpoint 4 entered.).
- **Cell_viability**
 - **Rule:** Enter as a plain number, without the "%" symbol. Viability refers to the percentage of live cells assessed immediately prior to injection (e.g., by trypan blue exclusion).
 - If viability is reported at preparation/pre-freezing but not pre-injection, enter the value and document the timing in General_notes (e.g., [Cell_viability]: Viability (95%) reported at time of freezing, not pre-injection.).
- **Cell_dose_per_injection**
 - **Rule:** The number of cells administered per animal in a single injection event.

- Convert to a plain number.
- Example: 5×10^6 becomes 5000000.
- If multiple injection sites are used in a single administration, sum the cells across all sites.
- For studies with multiple administrations, record the dose of the first injection here.
- If dose cannot be calculated due to missing information (e.g., concentration given but not volume), leave blank. Document the available information and reason for omission in both Dosing_notes and General_notes.
- **Total_cell_dose**
 - **Rule:** The cumulative number of cells administered per animal over the entire study. Enter as a plain number.
 - For single-administration studies, this equals Cell_dose_per_injection.
 - For multiple administrations, it is the sum of all doses.
 - If dose cannot be calculated, leave blank and document as per Cell_dose_per_injection.
- **Route**
 - **Rule:** Select from the predefined
 - list: Intravenous, Intrathecal, Intralesional, Intramedullary, Intraperitoneal, Subarachnoid, Other, Not_specified.
 - If Other is selected (e.g., nasal), specify the route in Dosing_notes.
- **Time_first_dose_hrs**
 - **Rule:** Enter the time to the first dose in hours post-injury as a numeric value.
 - Time zero is defined as the moment when SCI modeling is complete.
 - Conversions: 1 day = 24 hours; 1 week = 168 hours; 1 month = 4.34524 weeks.
 - Operation: If stated as “injected on day 3”, enter 72. If vaguely described as “post-operative day 3”, assume time zero is at injury and enter 72, adding a note:
[Time_first_dose_hrs]: Reported as '3 days post-operation'; assumed from time of injury.
- **Timing_category**
 - **Rule:** This analysis variable is derived from Time_first_dose_hrs but must be verified during extraction. Select one option:
 - Acute_leq_24h: First dose $\leq$ 24 hours post-injury.
 - Subacute_gt_24h: First dose $>$ 24 hours and $\leq$ 168 hours (1 week) post-injury.
 - Chronic_gt_1wk: First dose $>$ 168 hours post-injury.
 - Not_applicable: For studies where timing is not relevant (e.g., no defined injury timepoint).
- **Number_of_doses**

- **Rule:** Enter the total number of cell doses administered per animal as a plain integer, without units.
- **Dosing_schedule_desc**
 - **Rule:** Free-text field. Transcribe the schedule description from the source text verbatim.
 - Example: “once daily for 3 days”, “on post-injury days 1 and 7”.
- **Immunosuppression**
 - **Rule:** A key variable for subgroup analysis. Select one option:
 - Yes: The study explicitly states that immunosuppressive drugs were administered.
 - No: The study explicitly states that no immunosuppression was used.
 - Not_reported: No information on immunosuppression is provided.
- **Immunosuppression_regimen**
 - **Rule:** Free-text field. If immunosuppression was used, copy the drug names and doses directly from the source text.
 - Example: Cyclosporine A (10 mg/kg/day, s.c.), FK506 (1 mg/kg/day) and Mycophenolate mofetil (20 mg/kg/day).

3.4 Rules for Outcome Data Variables

- **Functional_outcome_scale**
 - **Rule:** Select the primary locomotor function scale from a predefined
 - list: BBB, Tarlov, Basso Mouse Scale (BMS), Combined Behavioral Score (CBS), Reuter, Other, Not measured.
 - If multiple scales are reported, select the primary one based on this hierarchy:
 - 1) Pre-validated continuous scales (BBB for rats, BMS for mice), 2) Other ordinal scales (Tarlov), 3) Instrumented tests if sole functional endpoint. Document the choice in General_notes.
 - but results are only presented graphically without numerical data in text/tables, still select the scale name (e.g., BBB), but leave all Func_* data columns blank.
 - Document this explicitly in General_notes using the
 - format: [Functional_outcome_scale]: Data presented only graphically; quantitative mean/SD could not be extracted.If Other is selected, specify the scale in General_notes.
 - If Not measured is selected, leave all subsequent Func_* columns blank.
 - Critical: If a scale was used
- **Outcome_direction**
 - **Rule:** Select one and only one option based on the nature of the scale. This determines

how scores are harmonized for analysis.

- Higher_better: Higher scores indicate better outcomes. Applies to: BBB, Tarlov, BMS, inclined plane test.
- Lower_better: Lower scores indicate better outcomes (deficit scores). Applies to: Reuter, Neurological Severity Score (NSS), mNSS.
- Continuous_outcome: Continuous variable without inherent direction (e.g., lesion volume, molecular marker levels).
- Dichotomous_outcome: Binary yes/no outcomes (e.g., survival, complication occurrence).
- Not_applicable: Use sparingly; provide detailed justification in Exploratory_outcomes_notes.
- **Func_mean_Tx, Func_SD_Tx, Func_n_Tx, Func_mean_Ctrl, Func_SD_Ctrl, Func_n_Ctrl**
 - **Rule:** These six fields contain the functional outcome data for the Treatment (Tx) and Control (Ctrl) groups at the final reported assessment time point.
 - Mean/SD: Enter as plain numbers. If SD is not reported, it may be calculated from Standard Error of the Mean (SEM) or Confidence Interval (CI) using standard formulas (document method in General_notes, e.g., [BBB_score]: SD calculated from SEM ($n=6$)).
 - n: Enter as a plain integer (sample size).
 - If data were extracted from figures, note the software and method in General_notes.
 - If a functional scale was used but no quantitative data could be obtained (see rule for Functional_outcome_scale), leave all six cells blank.
- **LesionVol_mean_Tx, LesionVol_SD_Tx, LesionVol_n_Tx, LesionVol_mean_Ctrl, LesionVol_SD_Ctrl, LesionVol_n_Ctrl**
 - **Rule:** These six fields contain quantitative lesion volume data, typically from histological analysis.
 - Enter means and standard deviations as plain numbers (e.g., mm³).
 - Enter sample size (n) as a plain integer.
 - If only qualitative descriptions exist (e.g., “reduced cyst size”), leave all six cells blank. Describe qualitative findings in Exploratory_outcomes_notes.
- **Mortality_events_Tx, Mortality_total_n_Tx, Mortality_events_Ctrl, Mortality_total_n_Ctrl**
 - **Rule:** Used for calculating mortality rates.
 - Mortality_events_*: Number of animals that died during the observation period from any

cause in that group. Plain integer.

- Mortality_total_n_*: The initial total number of animals in that group at the start of the experiment. Must be consistent with other sample size fields (e.g., Number_of_animals, Func_n_*). Plain integer.

■ Adverse_Events_Occurred

- **Rule:** Assessment is independent of other quality scores. Select based on explicit reporting of treatment-related adverse events.
- Yes: The study explicitly reported the occurrence of one or more adverse events deemed related to cell therapy (e.g., tumor formation, abnormal proliferation, infection).
- No: The study explicitly stated that no treatment-related adverse events were observed.
- Not_reported: The study did not mention or assess treatment-related adverse events.

■ Exploratory_outcomes_notes

- **Rule:** Free text field. Used to record positive findings from histology, significant changes in specific factors (e.g., BDNF, IL-10), etc. This information will be used for qualitative synthesis, not meta-analysis.

■ Dosing_notes

- **Rule:** Free text field. Used to record any atypical or complex dosing details (e.g., "Second dose was halved compared to the first", "Dosing interval was adjusted based on animal body weight").
- Remain faithful to the original description and retain the original units and symbols.

■ Meets_PICOS_Inclusion

- **Rule:** Final determination of study eligibility for the systematic review and meta-analysis.
- Must be selected from: Yes | No
- A study receives 'Yes' ONLY when ALL the following criteria are satisfied:
 - Is_Native_hUCB_MSC = Yes OR Cell_Type_Detailed = native_hUCB-MSC_plus.
 - Reports extractable quantitative data for at least one pre-specified primary outcome (functional recovery, histopathology like lesion volume, or safety) for both treatment and control groups.
 - Appropriate control group present (e.g., vehicle, sham, injury-only).
 - Sufficient cell characterization reported (at least one positive MSC marker and one negative hematopoietic marker).
 - Experimental traumatic spinal cord injury model used.
 - Study design is a controlled animal experiment.
- A study receives No if ANY of the above criteria are not met.

- This decision should be made independently by two reviewers, with disagreements resolved by consensus or third reviewer consultation.
- All studies with Yes in this field will be included in the final analysis.
- **General notes**
 - **Rule:** The master field for documenting any inference, assumption, clarification, or data handling decision related to extraction. Use a strict, standardized format.
 - Format: [Field_name]: Note content. Every entry must end with a period. Separate different entries with a line break.
 - Examples:
 - [Sex]: Not explicitly stated; inferred as male based on common use for this strain.
 - [Cell_dose]: Reported as 'approximately 1 million cells'; entered as 1000000.
 - [Time_first_dose_hrs]: Reported as '1 week post-injury'; entered as 168 hours.
 - [BBB_score]: Data extracted from Figure 3 using Engauge Digitizer v11.3. SD calculated from SEM.

Section 4: SYRCLE Risk of Bias Tool – Assessment Protocol

This section details the protocol for assessing the internal validity (risk of bias) of the included animal studies using the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) risk of bias (RoB) tool.

4.1 Tool Overview

The SYRCLE RoB tool evaluates ten domains of methodological quality that are critical for minimizing bias in animal intervention studies. Each domain is assessed based solely on information explicitly reported in the study publication.

4.2 Assessment Items and Judgment Criteria

Two reviewers independently judged each domain as “Low”, “High”, or “Unclear” risk of bias according to the criteria below. The default judgment was “Unclear”; reviewers did not assume that methods were used but not reported.

Domain (Parameter)	Assessment Item (Question)	Judgment Criteria
SYRCLE_RoB_Q1	Was the allocation sequence adequately generated and applied?	Low: The study describes an adequate random sequence generation method (e.g., computer-generated, random number table). High: The study describes a non-random or systematic allocation method (e.g., alternation, allocation by date). Unclear: The method of

		sequence generation is not described.
SYRCLE_RoB_Q2	Were the groups similar at baseline or were they adjusted for confounders in the analysis?	Low: Baseline characteristics are reported and show no significant differences, OR statistical adjustment for baseline differences is used. High: Important baseline differences are reported and not adjusted for. Unclear: Baseline characteristics are not reported or information is insufficient to assess similarity.
SYRCLE_RoB_Q3	Was the allocation to the different groups adequately concealed during the allocation sequence?	Low: The study describes adequate allocation concealment (e.g., sequentially numbered, sealed, opaque envelopes). High: The allocation was not concealed or a method prone to bias was used. Unclear: Allocation concealment is not described.
SYRCLE_RoB_Q4	Were the animals randomly housed during the experiment?	Low: The study describes random or stratified random housing of animals from different intervention groups. High: Housing was not randomized and could systematically differ between groups. Unclear: Random housing is not mentioned.
SYRCLE_RoB_Q5	Were the caregivers and/or investigators blinded from knowledge which intervention each animal received during the experiment?	Low: The study explicitly states that caregivers/investigators were blinded to group allocation during the intervention period. High: The study states blinding was not performed for caregivers/investigators, or describes situations where blinding was broken. Unclear: No information on blinding of caregivers/investigators is provided.
SYRCLE_RoB_Q6	Were animals selected at random for outcome assessment?	Low: The study describes random selection of animals for outcome assessment (e.g., histological analysis). High: A non-random selection method is described or implied. Unclear: The method of selecting animals for outcome assessment is not described.
SYRCLE_RoB_Q7	Was the outcome assessor blinded?	Low: The study explicitly states that outcome assessors were blinded to group allocation, especially for subjective outcomes. High: The study explicitly states that outcome assessors were not blinded for subjective outcomes. Unclear: No information on blinding of outcome assessors is provided.
SYRCLE_RoB_Q8	Were incomplete outcome data adequately addressed?	Low: The number of and reasons for animal exclusions are clearly reported, OR intention-to-treat analysis is used. High: Evidence of incomplete outcome data without adequate explanation, OR exclusion rates differ substantially between groups. Unclear: Insufficient information is provided about animal exclusions or missing data.
SYRCLE_RoB_Q9	Are reports of the study free of selective outcome reporting?	Low: All pre-specified outcomes from the methods are reported in the results, OR a study protocol is available and followed. High: Clearly important pre-specified outcomes are missing from results. Unclear: Insufficient information to assess selective reporting (e.g., no protocol available).
SYRCLE_RoB_Q10	Was the study apparently free of other problems that could result in high risk of bias?	Low: The study appears free of other major biases not covered above (e.g., unit of analysis errors, design flaws, funding-related bias). High: An additional problem that could result in high risk of bias is identified (e.g., unit of analysis error, high-risk conflict of interest). Unclear: Insufficient information to assess other risks of bias.

4.3 Scoring and Reporting

- **SYRCLE_Total_Score:** A calculated field representing the count of domains (Q1-Q10) judged as 'Low' risk of bias.
- **SYRCLE_Reporting_Notes:** A free-text field used to justify judgments of 'Low' or 'High' risk by quoting or paraphrasing the source text. For 'Unclear' judgments, a note was optional but recommended if the reason was not simply 'not reported'.
- **Process:** Assessments were performed independently by two reviewers. Disagreements were resolved through consensus-oriented discussion or by consulting a third reviewer.

Section 5: CAMARADES Checklist – Assessment Protocol

This section details the protocol for assessing the methodological quality and reporting completeness of included studies using the CAMARADES checklist (Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies).

5.1 Tool Overview

The CAMARADES checklist comprises ten items that evaluate key aspects of study design, conduct, and reporting known to influence the internal validity and translational value of preclinical animal studies. Each item is judged based on explicit reporting in the publication.

5.2 Assessment Items and Judgment Criteria

Two reviewers independently judged each item as “Yes”, “No”, or “Unclear” according to the criteria below.

Domain (Parameter)	Assessment Item	Judgment Criteria
CAMARADES_ Compliance	Peer-reviewed publication	Yes: Automatically scored ‘Yes’ for all included studies. All studies in this review are peer-reviewed by definition. (Do not select ‘No’ or ‘Unclear’).
CAMARADES_ Conflict_Interest	Statement of potential conflict of interest	Yes: A conflict of interest statement is explicitly provided. No: The study explicitly states that no conflicts exist. Unclear: No statement regarding conflicts of interest is provided.
CAMARADES_ Temp_Control	Statement of temperature control	Yes: Maintenance of normothermia during and/or after surgical procedures is explicitly described. No: The study explicitly states temperature was not controlled. Unclear: No mention of temperature control is made.
CAMARADES_ Randomization	Random allocation to group	Yes: Random allocation of animals to experimental groups is explicitly stated or described. No: The study explicitly states allocation was not random. Unclear: The method of allocation is not mentioned.
CAMARADES_ Blind_Intervention	Blinded induction of therapy	Yes: The study explicitly states that personnel administering the intervention (cells/vehicle) were blinded to group allocation. No: The study explicitly states that intervention induction was not blinded. Unclear: Blinding of intervention induction is not mentioned.
CAMARADES_ Blind_Assessment	Blinded assessment of outcome	Yes: The study explicitly states that outcome assessors were blinded to group allocation. No: The study explicitly states that outcome assessment was not blinded. Unclear: Blinding of outcome assessment is not mentioned.
CAMARADES_ Sample_Calc	Sample size calculation	Yes: A sample size calculation, power analysis, or reference to a pilot study is provided to justify the number of animals used. No: The study explicitly states no sample size calculation was performed. Unclear: No rationale for sample size is provided.
CAMARADES_ Model_Verification	Animal model authentication	Yes: Verification of successful injury induction is reported (e.g., via immediate post-operative functional deficit, histology, or electrophysiology). No: The study explicitly states the injury model was not verified. Unclear: Model verification is not mentioned.
CAMARADES_ Exclusion	Exclusion of comorbid animals	Yes: Any pre-defined criteria for excluding animals from analysis are mentioned (e.g., due to death, illness, or model failure). No: The study explicitly states no animals were excluded. Unclear: No information on exclusion criteria is provided.
CAMARADES_ Regulatory	Compliance with animal policy	Yes: The study mentions ethical approval, IACUC approval, or compliance with animal welfare regulations. No: The study explicitly states ethical approval was not obtained. Unclear: No statement regarding ethical approval or compliance is provided.

5.3 Scoring and Reporting

- **CAMARADES_Total_Score:** A calculated field representing the count of items judged as 'Yes'. Items judged 'No' or 'Unclear' are not counted.
- **CAMARADES_Reporting_Notes:** A free-text field. Justification by quoting source text is mandatory for 'Yes' judgments. Justification is strongly recommended for 'No' judgments. Justification for 'Unclear' judgments is optional.
- **Process:** Assessments were performed independently by two reviewers. Disagreements were resolved through consensus or by consulting a third reviewer.

Section 6: ARRIVE 2.0 Guidelines – Assessment Protocol

This section details the protocol for assessing the reporting quality of included studies against key items from the Animal Research: Reporting of In Vivo Experiments (ARRIVE) 2.0 guidelines. We focused on items considered essential for interpretation, reproducibility, and translation.

6.1 Tool Overview

The ARRIVE 2.0 guidelines consist of a comprehensive checklist designed to improve the reporting of animal research. For this systematic review, we assessed a subset of core items relevant to the design, methodological rigor, and interpretation of preclinical spinal cord injury studies.

6.2 Assessment Items and Judgment Criteria

Two reviewers independently assessed whether each of the selected ARRIVE 2.0 items was adequately reported. Each item was judged as "Yes", "No", or "Unclear". "Yes" indicates the item was explicitly and sufficiently described.

Domain (Parameter)	ARRIVE 2.0 Item (Abbreviated)	Judgment Criteria
ARRIVE_1_Title	1. Study identification	Yes: The title specifically identifies the study as an animal experiment involving spinal cord injury and cell therapy (or related key terms).

		No: The title is generic and does not reflect these specific experimental elements.
ARRIVE_2_Abstract	2. Abstract	Yes: The abstract provides an accurate and complete summary of the background, objectives, methods (including model and key interventions), main results, and conclusions. No: The abstract is incomplete or contains inaccuracies. Unclear: The abstract is structured but lacks key details required for appraisal.
ARRIVE_3_Background	3. Background / Objectives	Yes: The introduction clearly states the study's objectives and specific hypotheses. No: The study objectives or hypotheses are not stated. Unclear: Objectives are implied but not explicitly stated.
ARRIVE_4_Objectives	4. Objectives	Yes: The specific objectives/hypotheses are clearly stated. No: The objectives/hypotheses are not stated. Unclear: The objectives are implied but not explicitly stated.
ARRIVE_5_Ethics	5. Ethical statement	Yes: The study indicates relevant ethical approvals (e.g., IACUC) and consent procedures. No: No ethical statement is provided. Unclear: Ethics are mentioned indirectly (e.g., "approved by the institutional committee").
ARRIVE_6_Ethics	6. Ethical statement	Yes: The study mentions ethical review and approval, and describes compliance with animal welfare regulations. No: The study explicitly states no ethical approval was obtained. Unclear: No ethical statement is provided.
ARRIVE_7_StudyDesign	7. Study design	Yes: The experimental design is clearly described, including the number of groups, allocation method, and experimental timeline. No: The study design is not described. Unclear: The description of the design is incomplete or ambiguous.
ARRIVE_8_SampleSize	8. Sample size	Yes: The number of animals per group is provided, and a rationale for the sample size (e.g., power calculation) is given. No: The sample size per group is not provided, or the study explicitly states no justification was made. Unclear: Group sizes are provided but no justification is mentioned.
ARRIVE_9_Inclusion Exclusion	9. Inclusion/exclusion criteria	Yes: Pre-defined criteria for including or excluding animals or data from the analysis are stated. No: The study explicitly states no animals/data were excluded. Unclear: No information on inclusion/exclusion criteria is provided.
ARRIVE_10_Randomisation	10. Randomisation	Yes: The method of random allocation to experimental groups is described. No: The study explicitly states allocation was not random. Unclear: Randomisation is mentioned but the method is not described.
ARRIVE_11_Blinding	11. Blinding	Yes: Who was blinded and during which phases of the experiment (e.g., allocation, intervention, outcome assessment) is described. No: The study explicitly states blinding was not performed. Unclear: Blinding is mentioned but key details are omitted.
ARRIVE_12_Blinding	12. Blinding	Yes: The study describes who was blinded and during which processes (e.g., allocation, outcome assessment). No: Blinding is not mentioned. Unclear: Blinding is mentioned but it is unclear who was blinded or when.
ARRIVE_13_Outcomes	13. Outcomes	Yes: All primary and secondary outcome measures are clearly defined, including the assessment method and time points. No: The outcome measures are not defined. Unclear: Outcomes are listed but insufficiently defined.

ARRIVE_14_Statistics	14. Statistical methods	Yes: Statistical methods are described for each analysis, including methods for handling missing data and software used. No: Statistical methods are not described. Unclear: Statistical tests are named but details are incomplete.
ARRIVE_15_Results_GroupSize	15. Numbers analyzed	Yes: The number of animals in each group included in each analysis is stated. No: The number of animals analyzed is not stated. Unclear: The initial group size is stated but not the number analyzed.
ARRIVE_16_Results	16. Results / Animal details	Yes: Results are presented for all analysed animals, with data for each group and an indication of variability (e.g., SD, SEM). No: Results are missing for key outcomes or groups. Unclear: Results presentation is incomplete or unclear.
ARRIVE_17_AdverseEvents	17. Adverse events	Yes: The study explicitly addresses adverse events (e.g., by reporting their occurrence or explicitly stating that none were observed). No: There is no statement regarding adverse events. Unclear: The reporting is ambiguous and cannot be clearly categorized. Assessment Guidance: The assessment of adverse events should consider the Immunosuppression and Immunosuppression_regimen recorded in the Master_Data sheet, as immunosuppressive drugs themselves can be a source of adverse events.
ARRIVE_18_Interpretation	18. Interpretation/scientific implications	Yes: The interpretation of the results, balanced against the study objectives and limitations, is provided. No: The interpretation is missing or not balanced. Unclear: The interpretation is provided but does not adequately address objectives or limitations.
ARRIVE_19_Funding	19. Funding	Yes: Sources of funding and the role of funders are declared. No: The study explicitly states no specific funding was received. Unclear: No funding information is provided.
ARRIVE_20_Funding	20. Funding	Yes: Sources of funding and the role of funders are declared. No: Funding sources are not declared. Unclear: Funding is mentioned indirectly but sources are not clearly declared.

6.3 Scoring and Reporting

- **ARRIVE_Total_Score:** The total number of the above 13 items judged as 'Yes' was calculated for each study, and the percentage adherence was derived ($\text{Score}/13 * 100\%$).
- **Reporting Notes:** Justifications for judgments were recorded in free-text notes, particularly for 'No' or 'Unclear' ratings.
- **Process:** Independent assessment by two reviewers was followed by consensus resolution of any discrepancies.