

Acute Liver Failure: A Systematic Review and Network Meta-Analysis of Optimal Type of Stem Cells in Animal Models

Supplementary Table 1 Database retrieval process

Database	
PubMed	<p>#1: "stem cell"[Title/Abstract] OR "stem cells"[Title/Abstract] OR "stromal cells"[Title/Abstract] OR "stromal cell"[Title/Abstract] OR "mesenchymal cell"[Title/Abstract] OR "mesenchymal cells"[Title/Abstract] OR "cell therapy"[Title/Abstract] OR "cellular therapy"[Title/Abstract] OR "progenitor cell"[Title/Abstract] OR "progenitor cells"[Title/Abstract] OR "cytotherapy"[Title/Abstract] 428,758</p> <p>#2: "Stem Cells"[MeSH Terms] OR "Stem Cell Research"[MeSH Terms] OR "Stromal Cells"[MeSH Terms] OR "Mesenchymal Stem Cells"[MeSH Major Topic] 270,158</p> <p>#3: #1 OR #2 497,859</p> <p>#4: "liver failure"[MeSH Terms] 28,883</p> <p>#5: "liver failure"[Title/Abstract] OR "hepatic failure"[Title/Abstract] 30,879</p> <p>#6: #4 OR #5 47,646</p> <p>#7: #3 AND #6 1,240</p>
WOS	<p>(TS=("stem cell" OR "stem cells" OR "stromal cells" OR "stromal cell" OR "mesenchymal cell" OR "mesenchymal cells" OR "cell therapy" OR "cellular therapy" OR "progenitor cell" OR "progenitor cells" OR "cytotherapy")) AND TS=("liver failure" OR "hepatic failure") 2219</p>
Embase	<p>#1: 'stem cell':ab,ti OR 'stem cells':ab,ti OR 'stromal cells':ab,ti OR 'stromal cell':ab,ti OR 'cell therapy':ab,ti OR 'mesenchymal cells':ab,ti OR 'mesenchymal cell':ab,ti OR 'cellular therapy':ab,ti OR 'progenitor cell':ab,ti OR 'progenitor cells':ab,ti OR cytotherapy:ab,ti 613113</p> <p>#2: 'stem cell'/exp 448922</p> <p>#3: 'stromal cells'/exp 60788</p> <p>#4: 'mesenchymal cell'/exp 106535</p> <p>#5: 'cell therapy'/exp 245924</p> <p>#6: #1 OR #2 OR #3 OR #4 OR #5 795185</p>

#7: 'liver failure':ab,ti OR 'hepatic failure':ab,ti 48893

#8: 'liver failure'/exp 90387

#9: 'hepatic failure'/exp 90387

#10: #7 OR #8 OR #9 101814

#11: #6 AND #10 AND ([article]/lim OR [article in press]/lim) AND [animals]/lim 735

Scopus TITLE-ABS("stem cell" OR "stem cells" OR "stromal cells" OR "stromal cell" OR "mesenchymal cell" OR "mesenchymal cells" OR "cell therapy" OR "cellular therapy" OR "progenitor cell" OR "progenitor cells" OR "cytotherapy") AND TITLE-ABS("liver failure" OR "hepatic failure") 1134

Cochrane #1: MeSH descriptor: [Stem Cells] explode all trees 940

#2: MeSH descriptor: [Stromal Cells] explode all trees 251

#3: MeSH descriptor: [Cell- and Tissue-Based Therapy] explode all trees 6722

#4: ("stem cell" OR "stem cells" OR "stromal cells" OR "stromal cell" OR "mesenchymal cell" OR "mesenchymal cells" OR "cell therapy" OR "cellular therapy" OR "progenitor cell" OR "progenitor cells" OR "cytotherapy"):ti,ab,kw 17137

#5: #1 or #2 or #3 or #4 21438

#6: MeSH descriptor: [Liver Failure] explode all trees 953

#7: ("liver failure" OR "hepatic failure"):ti,ab,kw 2664

#8: #6 or #7 3207

#9: #4 and #8 108

Supplementary Table 2 Basic information of included studies

Ref.	Country	Type of study	Baseline characteristics of animals					Stem cell transplant					
			Species	Gender	Weight	Age	Sample size	Modeling method	Type	Source	Timing	Dose	
Cao 2012	China	RCT	Pigs	Male	10-12kg	/	6/6	D-GalN		PMSCs	Human placenta	18h	1.0×10^8
Chiang 2001	China	RCT	BALB/c mice	Male	25-30g	7-8 wk	23/36	TAA		iPSCs	mouse embryo	/	2×10^6
Koellensperger 2013	Germany	RCT	SD rats	Female	140-200g	/	20/20	2/3 liver resection		ADMS Cs	Human adipose tissue	/	2×10^6
Teshima 2017	Japan	Control	Dogs	Male	12.2kg	1.5 years	3/3	CCl4		ADMS Cs	Canine adipose tissue	3d	$2 \times 10^6/\text{kg}$
Kieling 2017	Brazil	RCT	Wistar rats	Male	298±60g	8 wk	39/41	90% liver resection		BMSCs	Wistar rats bone marrow	0h	/

Zhang 2018	China	RCT	SD rats	Male	220- 250g	/	12/12	D- GalN/LPS	UCMS Cs	Human umbilical cord	1d	1×10^6
Wang 2019	China	RCT	SD rats	Male	300- 350g	7-10 wk	20/20	D- GalN/LPS	UCMS Cs	Human umbilical cord	1h	5×10^6
Nie 2020	China	RCT	SD rats	Male	180- 200g	6-8 wk	8/8	CCl4	BMSCs	SD rats bone marrow	6h	2×10^6
Jin 2012	China	RCT	BALB/c mice	/	20-22g	8-10 wk	35/35	CCl4	BMSCs	Mice bone marrow	1d	1×10^6
Pan 2021	China	RCT	C57BL/ 6 mice	Male	/	6-8 wk	10/10	Con A	UCMS Cs	Human umbilical cord	0.5h	1×10^6
Xu 2022	China	RCT	C57BL/ 6 mice	Male	/	8 wk	5/5	TAA	UCMS Cs	Human umbilical	12h	1×10^6

Wang 2022	China	RCT	C57BL/ 6 mice	Male	22.0 ± / 2.0 g	8/4	APAP	UCMS Cs	Human umbilical cord	2h	1 × 10 ⁶	
Saidi 2015	USA	Control	C57BL/ 6 mice	Male	/	8-10 wk	7/7	CCl4	ADMS Cs	Human adipose tissue	0.5h before modelin g.	1-2 × 10 ⁶
Liu 2017	China	RCT	C57BL/ 6 mice	Male	20g	6 wk	12/12	D- GalN/LPS	ADMS Cs	Human adipose tissue	/	2 × 10 ⁶
Yoshizumi 2016	Japan	Control	C57BL/ 6 mice	/	/	6-10 wk	16/16	Con A	ADMS Cs	Mice adipose tissue	0.5h	1 × 10 ⁶
Ohashi 2012	Japan	Control	C57BL/ 6 mice	Male	/	5 wk	3/3	CCl4	ADMS Cs	Mice adipose tissue	1d	1 × 10 ⁵

Yukawa 2009	Japan	Control	C57BL/6 mice	Male	/	6 wk	6/6	CCl4	ADMS Cs	Mice adipose tissue	4h	1 × 10 ⁶
Xiu 2020	China	RCT	SD rats	Female	180-220g	/	8/8	D-GalN/LPS	BMSCs	SD rats bone marrow	6h	2 × 10 ⁶ /kg
Xu 2017	China	RCT	BALB/c mice	Male	/	6-8 wk	12/12	CCl4	ADMS Cs/B MSCs	Mice adipose tissue and bone marrow.	/	/
Mina 2017	Iran	RCT	BALB/c mice	/	/	8-10 wk	15/15	CCl4	MenS Cs	Women's menstrual blood.	/	8 × 10 ⁵
Li 2019	China	RCT	C57BL/6 mice	Male	/	/	8/8	Con A	LSCs	Liver of C57BL/6 mice	12h	2 × 10 ⁶

Liu 2021	China	Control	C57BL/ 6 mice	Male	20-22g	/	10/9	D- GalN/LPS	UCMS Cs	Human umbilical cord	6h	1×10^6
Chen 2021a	China	RCT	SD rats	Male	/	/	6/6	D- GalN/LPS	UCMS Cs	Human umbilical cord	2h	1×10^7
Chen 2021b	China	RCT	C57BL/ 6 mice	Male	18-22g	6-8 wk	14/14	D- GalN/LPS	MenS Cs	Women's menstrua l blood.	1h	3×10^6
Cai 2020	China	RCT	C57BL/ 6 mice	Female	/	6-8 wk	3/3	APAP	UCMS Cs	Human umbilical cord	1d	5×10^5
Liu 2018	China	RCT	C57BL/ 6 mice	/	/	6-8 wk	8/8	D- GalN/LPS	BMSCs	C57BL/6 mice bone marrow	6h	2×10^6
Zheng 2012	China	RCT	SD rats	Male	200g	8-12	15/15	D-	AFMS	SD rat	1d	1×10^6

						wk		GalN/LPS	Cs	amniotic fluid		
Zagoura 2011	China	RCT	C57BL/6 mice	Male	20g	6-8 wk	10/10	CCl4	AFMS Cs	Human amniotic fluid	1d	1.5×10^6
He 2021	China	RCT	Wistar rats	Male	120-150g	6 wk	12/12	D-GalN/LPS	UCMS Cs	Human umbilical cord	1h	2×10^6
Li 2012	China	Control	Pigs	/	8-10kg	/	15/15	D-GalN	BMSCs	Human bone marrow	6h	3×10^7
Wang 2018	China	RCT	C57BL/6 mice	Male	25-35g	6-7 wk	20/20	D-GalN/LPS	BMSCs	C57BL/6 mice bone marrow	12h	1×10^6
Wang 2017	China	Control	C57BL/6 mice	Male	/	6-8 wk	15/15	Con A	ADMS Cs	Mice adipose	2h	/

Feng 2015	China	RCT	SD rats	Male	180-220g	6-8 wk	12/12	CCl4	UCMS Cs	tissue Human umbilical cord	1d	$3-5 \times 10^6$
Varaa 2018	Iran	RCT	Albino rats	Male	250-300g	/	6/6	CCl4	UCMS Cs	Human umbilical cord	4d	1×10^6
Chang 2012	China	RCT	BALB/c mice	Male	25-30g	8 wk	6/6	CCl4	iPSCs	Mouse embryo	1d	5×10^6
Banas 2008	Japan	Control	BALB/c mice	Female	/	/	3/3	CCl4	ADMS Cs	Human adipose tissue	1d	1.5×10^6
Kubo 2011	Japan	RCT	BALB/c mice	Female	/	8-12 wk	15/15	Con A	ADMS Cs	Mice adipose tissue	0.5h	1×10^6
Wang 2018	China	RCT	SD rats	Male	180-200g	6-8 wk	20/20	D-GalN	BMSCs	SD rats bone	1d	1×10^6

Chen 2019	China	RCT	SD rats	Male	/	/	5/5	D-GalN/LPS	UCMS Cs	Human marrow umbilical cord	2h	1×10^7
Mina 2019	Iran	RCT	BALB/c mice	Female	20-22g	8-10 wk	10/5	CCl4	MenS Cs/B MSCs	Women's menstrua l blood.	2d	8×10^5
Hwang 2019	Korea	Control	BALB/c mice	Male	/	8 wk	5/5	APAP	ADMS Cs	Human adipose tissue	3d	4×10^5
Qiao 2019	China	RCT	ICR mice	Male	20g	6 wk	4/4	CCl4	UCMS Cs	Human umbilical cord	1d	1×10^6
Belardinelli 2008	Brazil	RCT	Wistar rats	Female	180- 220g	/	59/35	APAP	BMSCs	Wistar rats bone marrow	1d	1×10^6
Gazdic 2018	Serbia	RCT	C57BL/	Male	/	6-8 wk	10/10	D-GalN	BMSCs	C57BL/6	0h	5×10^5

			6 mice							mice		
										bone		
										marrow		
Kong 2020	China	RCT	C57BL/ 6 mice	Male	/	8-10 wk	8/8	APAP	UCMS Cs	Human umbilical cord	1d	2×10^6
Liu 2020	China	RCT	BALB/c mice	Male	20-22g	6-8 wk	25/25	D-GalN	ADMS Cs	Porcine adipose tissue	1d	1×10^6
Shi 2010	China	Control	SD rats	Male	160- 200g	/	20/20	CCl4	UCMS Cs	Human umbilical cord	1d	5×10^6
Jin 2011	China	RCT	BALB/c mice	/	20-22g	8-10 wk	35/35	CCl4	BMSCs	Human bone marrow	1d	5×10^6
Ramanathan 2017	India	RCT	Swiss albino	Male	25±5g	/	6/6	D-GalN	UCMS Cs	Human umbilical	0h	5×10^5

Wabitsch 2019	Germany	RCT	BALB/c mice	/	20-22g	7-9 wk	8/8	70% liver resection	BMSCs	Human bone marrow	cord	1d	1×10^6
Itaba 2018	Japan	RCT	BALB/c mice	/	20-22g	8 wk	10/10	CCl4	BMSCs	Human bone marrow		1d	/
Yang 2019	China	RCT	Wistar rats	Male	200±50g	/	20/20	D-GalN/LPS	BMSCs	Wistar rats bone marrow		/	1×10^7
Li 2018	China	RCT	NOD-SCID mice	Male	20g	6 wk	4/4	D-GalN/LPS	ADMS Cs	Human adipose tissue		6h	2×10^6
Liao 2021	China	RCT	BALB/c mice	Female	20-22g	6-8 wk	28/28	D-GalN/LPS	UCMS Cs	Human umbilical cord		12h	5×10^6
Wang 2021	China	RCT	SD rats	/	200-	8-12	6/6	90% liver	BMSCs	SD rats		/	5×10^6

					300g	wk		resection		bone marrow			
Jin 2009	China	RCT	BALB/c mice	Male	20-22g	8-10 wk	30/30	CCl4	BMSCs	BALB/c mice	1d	1×10^6	
Wang 2017	China	RCT	SD rats	Male	80-100g	4 wk	12/12	D-GalN/LPS	BMSCs	SD rats	2d	1.0×10^7 /kg	\times
Regmi 2019	China	RCT	BALB/c mice	Male	/	7-8 wk	4/4	D-GalN/LPS	ADMS Cs	Human adipose tissue	5h	1×10^6	
Bi 2019	China	RCT	C57BL/6 mice	Male	22-25g	/	30/30	Con A	LSCs	Human liver tissue	/	2×10^6	
Zhang 2012	China	RCT	NOD-SCID	Male	/	/	11/11	CCl4	UCMS Cs	Human umbilical	18h	4×10^7 /kg	

Ezzat 2012	Egypt	RCT	mice C57BL/ 6 mice	Male	20-25g	5-6 wk	20/20	APAP	ESCs	cord C57BL/6 mice	4h	5×10^6
Cen 2019	China	RCT	Pigs	Male	8-12kg	/	20/20	D-GalN	MenS Cs	embryos Women's menstrua l blood.	/	2.5×10^6 /kg
Kim 2011	Korea	RCT	C57BL/ 6 mice	Male	/	8 wk	5/5	CCl4	ADMS Cs	Human adipose tissue	1d	1.5×10^6
Milosavljevi c 2017	Switzerla nd	RCT	C57BL/ 6 mice	Male	/	8-10 wk	10/10	D- GalN/LPS	BMSCs	C57BL/6 mice bone marrow	1d	5×10^5
Ju 2010	China	RCT	ICR mice	/	/	/	8/8	CCl4	BMSCs	Mice bone marrow	/	1×10^6

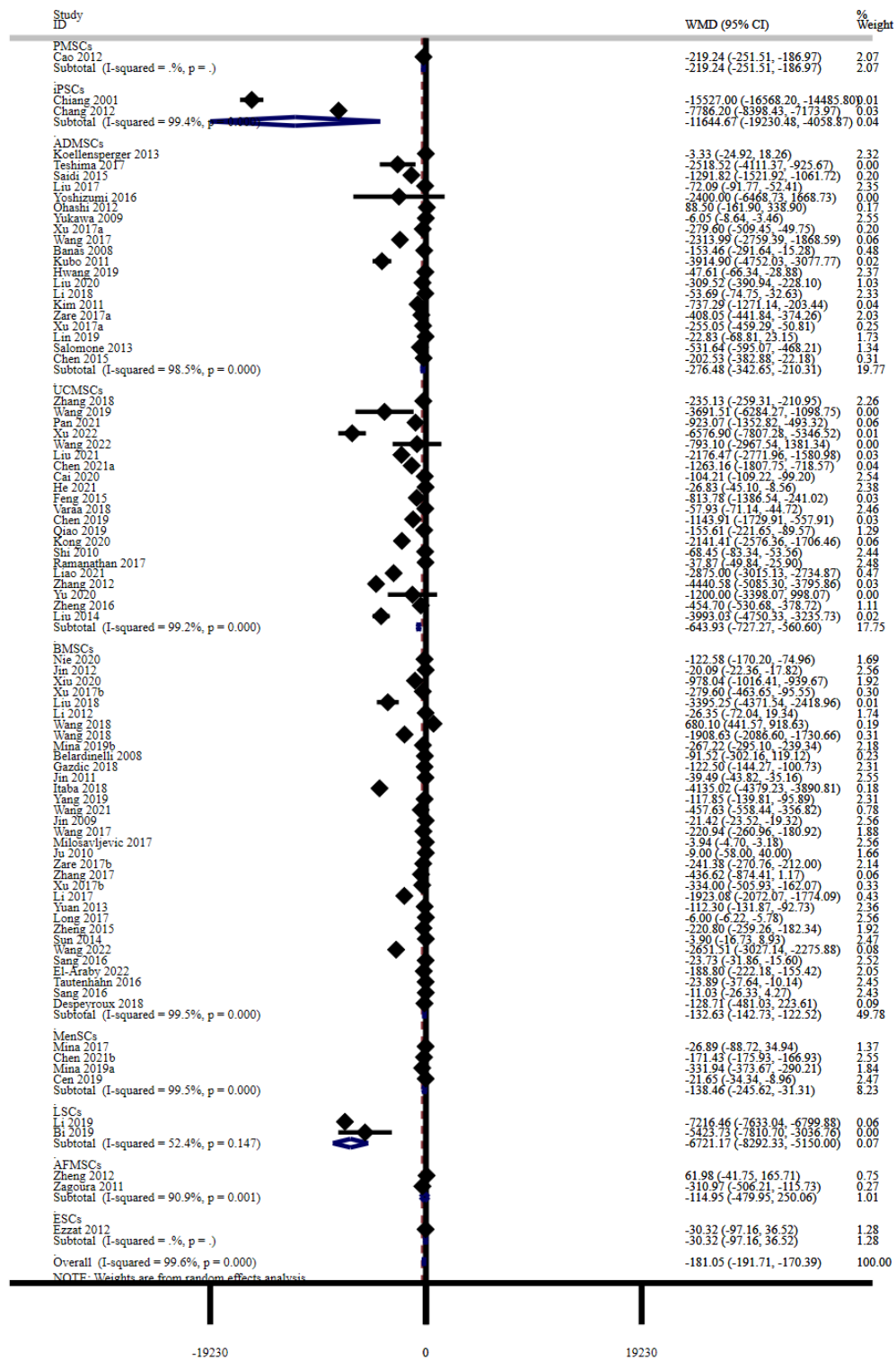
Zare 2017	India	RCT	ICR mice	Male	/	8 wk	20/20	CCl4	ADMS Cs/B MSCs	Mice	1d	1×10^6
Jiang 2022	China	RCT	SD rats	Male	200±10g	6-8 wk	20/20	TAA	BMSCs	SD rats bone marrow	1d	1×10^6
Kang 2018	Korea	RCT	C57BL/6 mice	Male	/	6 wk	20/20	TAA	BMSCs	Human bone marrow	/	1×10^6
Zhang 2017	China	RCT	SD rats	Male	190-200g	6-7 wk	10/10	D-GalN/LPS	BMSCs	SD rats bone marrow	1h	1×10^6
Xu 2017	China	RCT	C57BL/6 mice	Male	/	6 wk	8/8	CCl4	ADMS Cs/B MSCs	Mice	1d	1×10^6
Li 2017	China	RCT	Wistar rats	Male	190±20g	/	16/10	D-GalN/LPS	BMSCs	Wistar rats bone	12h	5.5×10^5

Lin 2019	China	RCT	Pigs	Male	10-15kg	/	10/6	IRI	ADMS Cs	Human marrow adipose tissue	1.5h	1.6-2.4 × 10 ⁶ /kg
Yuan 2013	China	Control	SD rats	Male	250- 300g	/	30/30	D- GalN/LPS	BMSCs	SD rats bone marrow	/	1.4 × 10 ⁷ /kg
Yu 2020	China	Control	C57BL/ 6 mice	Male	20-25g	6-8 wk	8/8	D- GalN/LPS	UCMS Cs	Human umbilical cord	1d	5 × 10 ⁶
Long 2017	China	Control	SD rats	Male	250±50g	/	20/20	D- GalN/LPS	BMSCs	SD rats bone marrow	1d	1 × 10 ⁷ /kg
Zheng 2016	China	RCT	SD rats	Male	130- 180g	/	12/12	CCl ₄	UCMS Cs	Human umbilical cord	/	3-5 × 10 ⁶
Zheng 2015	China	RCT	SD rats	Male	200-	/	30/30	D-	BMSCs	SD rats	1h	1 × 10 ⁷

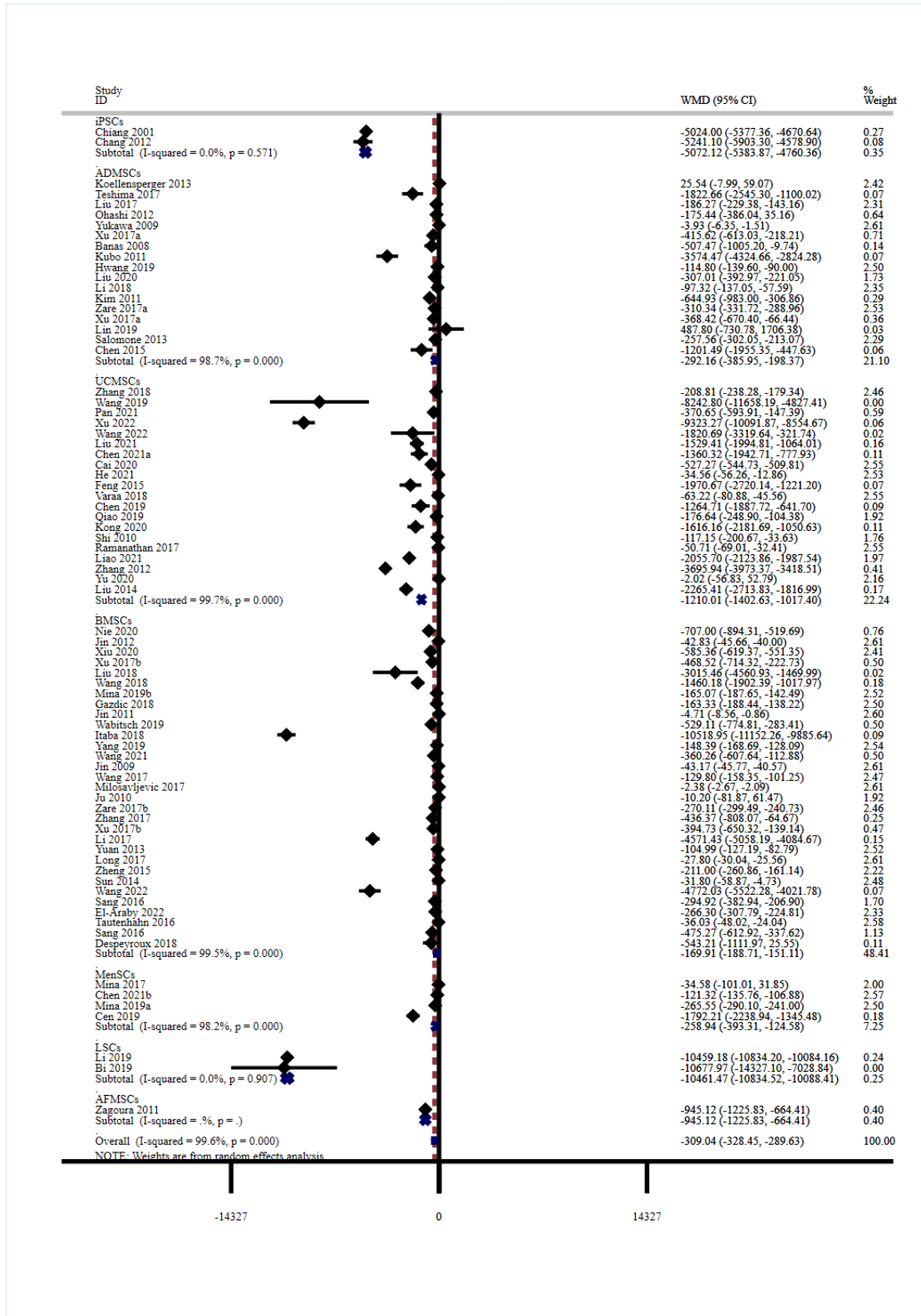
					250g				GalN/LPS	bone marrow			
Sun 2014	China	RCT	SD rats	Male	250-280g	/	16/16	D-GalN/LPS	BMSCs	SD rats	0h		2×10^7
Zhao 2016	China	RCT	Wistar rats	Male	180-220g	6-8 wk	16/16	D-GalN/LPS	BMSCs	SD rats	/		2×10^7
Liu 2014	China	RCT	C57BL/6 mice	Male	18-20g	/	12/12	APAP	UCMS Cs	Human umbilical cord	/		1×10^6
Salomone 2013	Italy	RCT	SD rats	Female	200g	/	6/6	APAP	ADMS Cs	Human adipose tissue	2h		2×10^5
Wang 2022	China	RCT	C57BL/6 mice	Male	/	4-6 wk	20/20	D-GalN/LPS	BMSCs	C57BL/6 mice	12h		1×10^6
										bone			

Sang 2016	China	RCT	Pigs	/	15±3kg	5-8 month s	6/6	D-GalN	BMSCs	marrow Pigs bone marrow	1d	1 × 10 ⁷
Chen 2015	China	RCT	SD rats	Male	/	4-6 wk	15/15	D-GalN	ADMS Cs	Human adipose tissue	1d	5 × 10 ⁶
Wang 2021	China	RCT	C57BL/ 6 mice	Male	20-25g	6-8 wk	10/10	D-GalN	BMSCs	C57BL/6 mice bone marrow	6h	2 × 10 ⁶
El - Araby 2022	Egypt	RCT	Albino rats	Male	150- 200g	/	10/10	APAP	BMSCs	Albino rats bone marrow	/	1 × 10 ⁶
Tautenhahn 2016	Denmark	RCT	F344- Fischer rats		/	/	6/6	90% liver resection	BMSCs	F344- Fischer rats bone	/	1 × 10 ⁶

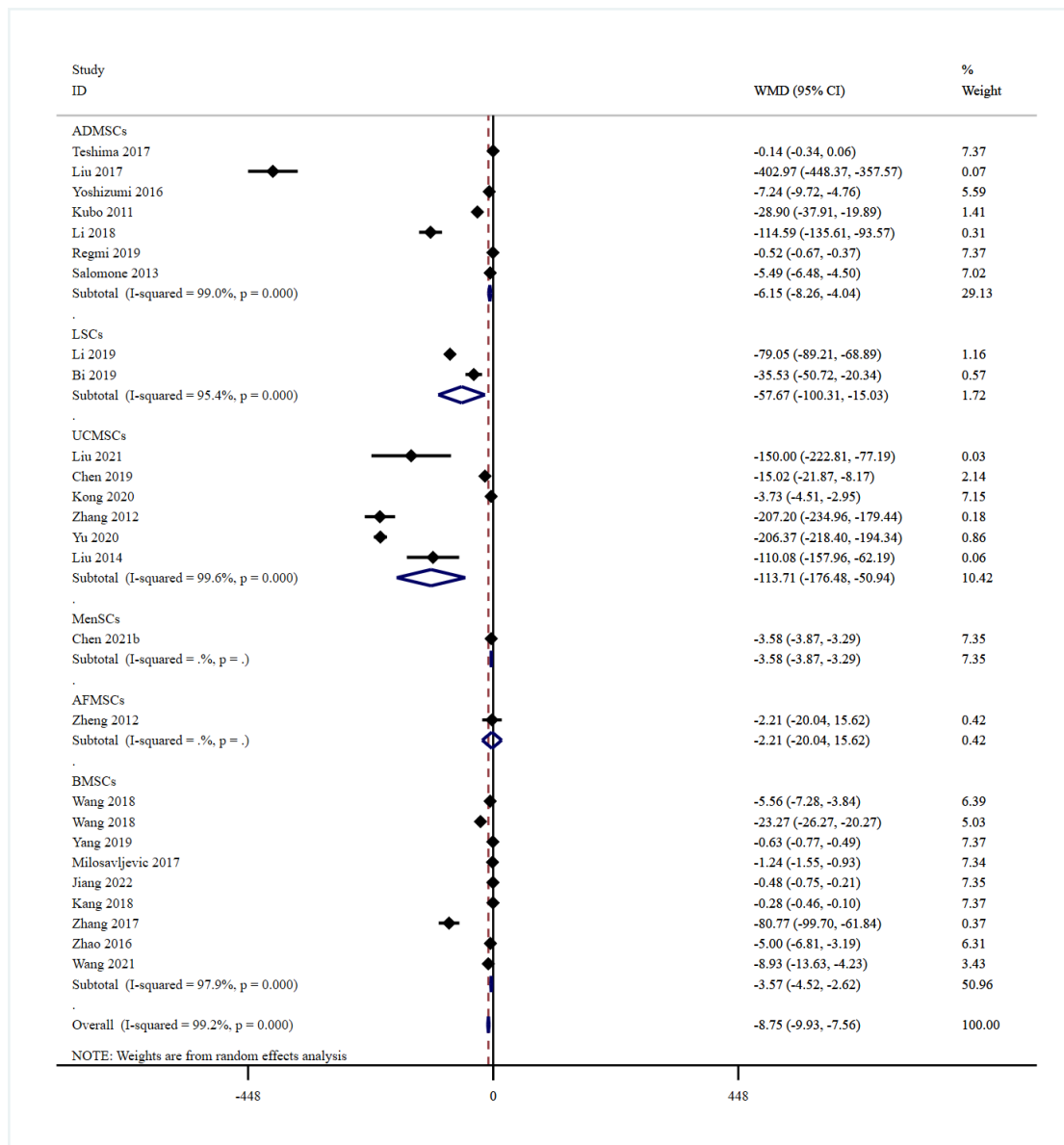
Sang 2016	China	RCT	Pigs	/	15±3kg	5-8 month s	6/6	85% resection	liver	BMSCs	marrow Pigs bone marrow	1d	1 × 10 ⁸
Despeyroux 2018	France	Control	C57BL/ 6 mice	Female	17.5- 22.5g	9 wk	40/40	80% resection	liver	BMSCs	C57BL/6 mice bone marrow	/	5 × 10 ⁵



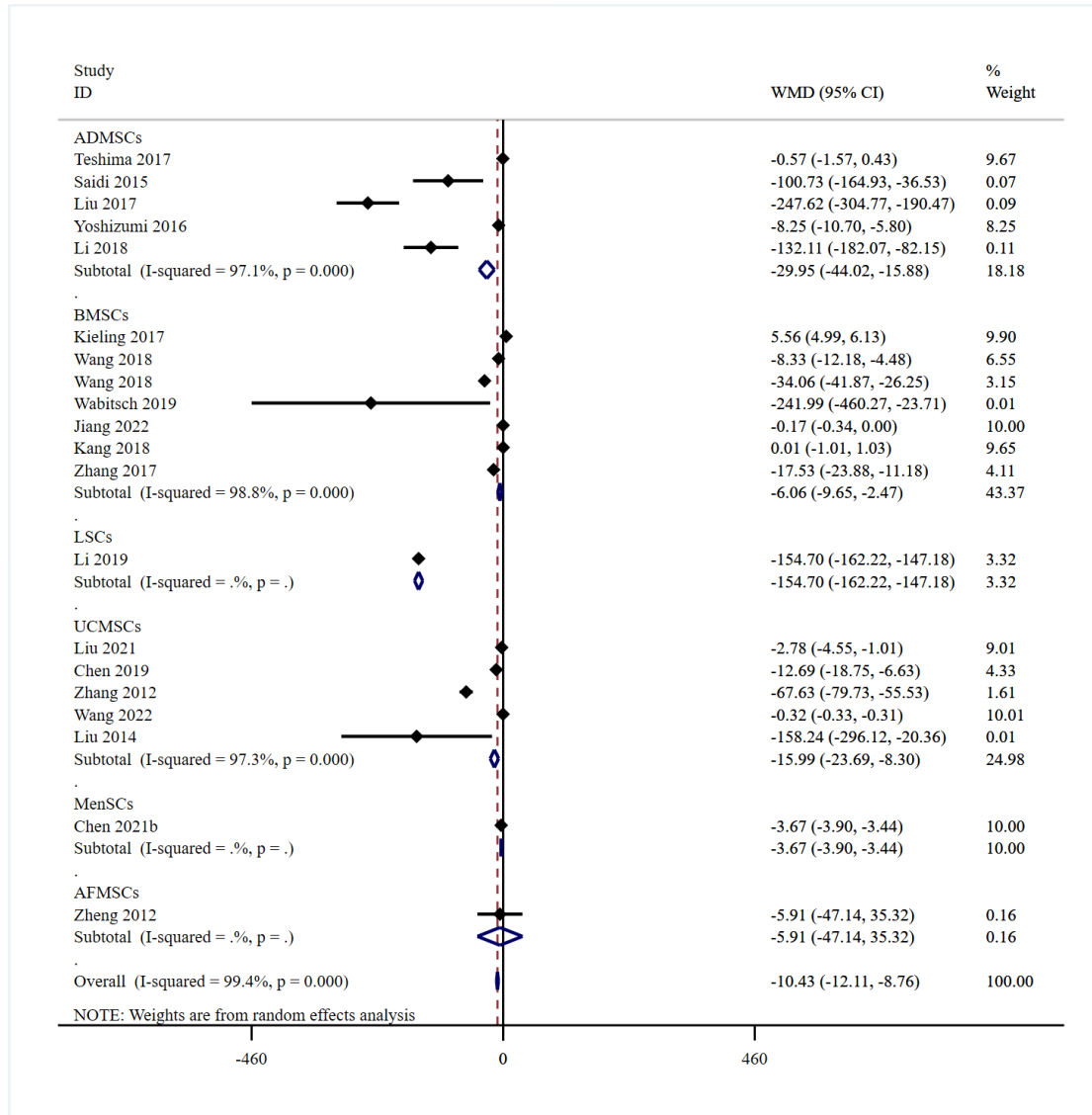
Supplementary Figure 1 Traditional meta-analysis of ALT.



Supplementary Figure 2 Traditional meta-analysis of AST.



Supplementary Figure 3 Traditional meta-analysis of TNF-α.



Supplementary Figure 4 Traditional meta-analysis of IL-6.