

Mouse models of diabetes-related ulcers: a systematic review and network meta-analysis

Running title: Mouse models of diabetes-related ulcers

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Supplementary data

Supplementary table S1. Search key words.....	2
Supplementary table S2. Summary of included studies	3
Supplementary table S3. Evaluation of heterogeneity (τ and I²) and the global inconsistency at each time point.....	32
Supplementary table S4. Evaluation of the inconsistency using the Separate indirect from direct evidence (SIDE) back calculation method at day 3, 7, 11, and 15.	33
Supplementary table S4. League table presenting the result of network meta-analyses at day 3 and 7.	45
Supplementary table S5. League table presenting the result of network meta-analyses at day 11 and 15.	46
Supplementary table S6. Comparison of wound healing over time between each control mice strains and C57Bl6.	47
Supplementary table S7. League table of the frequentist network meta-analysis comparing the impact of strain at day 3.	49
Supplementary Figure S1. Network plots when separating the wild type group by strain.	50
Supplementary Figure S2. Comparison-adjusted funnel plots.....	51
Systematic review protocol.....	52
PRISMA 2020 flow diagram	58

Supplementary table S1. Search key words.

Database	Key words	Number of references
Embase	#1('wound healing'/exp OR 'wound healing') AND [animal model]/lim AND ('mouse' OR 'mouse'/exp OR mouse) AND ('diabetes mellitus'/exp OR 'diabetes mellitus')	1,257
	#3 AND [embase]/lim NOT ([embase]/lim AND [medline]/lim)	439
	#1 #3 AND 'article'/it	146
Pubmed	“models, animal” OR “disease models, animal” AND “diabetes mellitus” AND “wound healing” AND “mice”	672

Supplementary table S2. Summary of included studies

ID	Title	Autors	Journal	Year	Diabetic model
5	Wound healing effect of naringin gel in alloxan induced diabetic mice	Okur, M.E. and Sakul, A.A. and Ayla, S. and Karadag, A.E. and SenyÄ¼z, C.S. and Batur, S. and Daylan, B. and Ä¼zdemir, E.M. and Palabiyik-YÄ¼cellik, S. and SipahI, H. and Aydin, A.	Ankara Universitesi Eczacilik Fakultesi Dergisi	2020	Alloxan
49	Role of Chemokine Receptor CCR4 and Regulatory T Cells in Wound Healing of Diabetic Mice	Barros JF, Waclawiak I, Pecli C, Borges PA, Georgii JL, Ramos-Junior ES, Canetti C, Courau T, Klatzmann D, Kunkel SL, Penido C, Canto FB, Benjamim CF.	J Invest Dermatol	2019	Alloxan
63	Synthesis of newly functionalized 1,4-naphthoquinone derivatives and their effects on wound healing in alloxan-induced diabetic mice	Cardoso SH, de Oliveira CR, GuimarÃ£es AS, Nascimento J, de Oliveira Dos Santos Carmo J, de Souza Ferro JN, de Carvalho Correia AC, Barreto E.	Chem Biol Interact. 2018	2018	Alloxan
111	Oral administration of antioxidants improves skin wound healing in diabetic mice.	Pessoa AF, Florim JC, Rodrigues HG, Andrade-Oliveira V, Teixeira SA, Vitzel KF, Curi R, Saraiva CÃ§mara NO, MuscarÃ¼ MN, Lamers ML, Santos MF.	Wound Repair Regen. 2016	2016	Alloxan
114	Ameliorative effect of dietary genistein on diabetes induced hyper-inflammation and oxidative stress during early stage of wound healing in alloxan induced diabetic mice.	Eo H, Lee HJ, Lim Y.	Biochem Biophys Res Commun. 2016	2016	Alloxan
221	Healing potential of Rosmarinus officinalis L. on full-thickness excision cutaneous wounds in alloxan-induced-diabetic BALB/c mice.	Abu-Al-Basal MA.	J Ethnopharmacol. 2010	2010	Alloxan
173	Ganglioside GM3 Depletion Reverses Impaired Wound Healing in Diabetic Mice by activating IGF-1 and Insulin Receptors	Wang, XQ. et al 2014 [57]	Journal of Investigate Dermatology	2014	High Fat Diet (HFD)
94	Hydrogen sulfide improves diabetic wound healing in ob/ob mice via attenuating inflammation	Zhao, H. et al 2017 [82]	Journal of Diabetes and its complications	2017	Lep ^{ob} or ob/ob (-/-)

104	Cytochrome P450 (CYP) epoxygenases as potential targets in the management of impaired diabetic wound healing	Zhao, H. et al 2017 [81]	laboratory investigation	2017	Lep ^{ob} or ob/ob (-/-)
166	Angiopoietin-like 4 stimulates STAT3-mediated iNOS expression and enhances angiogenesis to accelerate wound healing in diabetic mice.	Chong HC, Chan JS, Goh CQ, Gounko NV, Luo B, Wang X, Foo S, Wong MT, Choong C, Kersten S, Tan NS.	Mol Ther. 2014	2014	Lep ^{ob} or ob/ob (-/-)
212	Wound healing in mice with high-fat diet- or ob gene-induced diabetes-obesity syndromes: a comparative study.	Seitz O, SchÄ¼rmann C, Hermes N, MÄ¼ller E, Pfeilschifter J, Frank S, Goren I.	Exp Diabetes Res. 2010	2010	Lep ^{ob} or ob/ob (-/-) and High Fat Diet (HFD)
154	Protein tyrosine phosphatase 1B impairs diabetic wound healing through vascular endothelial growth factor receptor 2 dephosphorylation.	Zhang J, Li L, Li J, Liu Y, Zhang CY, Zhang Y, Zen K.	Arterioscler Thromb Vasc Biol. 2015	2015	Lep ^{ob} or ob/ob (-/-) and Streptozotocin (STZ)
1	Comparison of systemic inflammatory and hematology parameters in normal C57B1/6 and genetically diabetic db/db mice during local wound repair	Åšitum, K. and BokuliÄž, A. and IvetiÄž-TkalÄž • eviÄž, V. and Parnham, M.J. and ÄEuÄ¼Äž, S. and DuriÄž, K. and GlojnariÄž, I. and Ä eveljeviÄž, D. and BrajÄžja, K.	Biochemia Medica	2007	Lepr ^{db} or db/db (-/-)
4	Preparation of hydrogel by radiation for the healing of diabetic ulcer	Nho, Y.-C. and Park, J.-S. and Lim, Y.-M.	Radiat. Phys. Chem.	2014	Lepr ^{db} or db/db (-/-)
6	Healing of Pseudomonas aeruginosa-infected wounds in diabetic db/db mice by weakly acidic hypochlorous acid cleansing and silver nanoparticle/chitin-nanofiber sheet covering	Kuwabara, M. and Sato, Y. and Ishihara, M. and Takayama, T. and Nakamura, S. and Fukuda, K. and Murakami, K. and Yokoe, H. and Kiyosawa, T.	Wound Med.	2020	Lepr ^{db} or db/db (-/-)
10	Selective MMP-9 Inhibitor (R)-ND-336 Alone or in Combination with Linezolid Accelerates Wound Healing in Infected Diabetic Mice	Peng, Z. and Nguyen, T.T. and Song, W. and Anderson, B. and Wolter, W.R. and Schroeder, V.A. and Heseck, D. and Lee, M. and Mobashery, S. and Chang, M.	ACS Pharm. Transl. Sci.	2021	Lepr ^{db} or db/db (-/-)
13	Examination of the Therapeutic Potential of Mouse Oral Mucosa Stem Cells in a Wound-Healing Diabetic Mice Model	Kuperman S, Efraty R, Arie I, Rahmanov A, Rahmanov Gavriellov M, Noff M, Fishel R, Pitaru S.	Int J Environ Res Public Health	2020	Lepr ^{db} or db/db (-/-)
16	Cas9-AAV6-engineered human mesenchymal stromal cells improved cutaneous wound healing in diabetic mice	Srifa W, Kosaric N, Amarin A, Jadi O, Park Y, Mantri S, Camarena J, Gurtner GC, Porteus M.	Nat Commun	2020	Lepr ^{db} or db/db (-/-)

20	Embryonic stem cell extracts improve wound healing in diabetic mice	Loretelli C, Ben Nasr M, Giatsidis G, Bassi R, Lancerotto L, D'Addio F, Valderrama-Vasquez A, Scherer SS, Salvatore L, Madaghiele M, Abdelsalam A, Ippolito E, Assi E, Usuelli V, El Essawy B, Sannino A, Pietramaggiore G, Zuccotti GV, Orgill DP, Fiorina P.	Acta Diabetol	2020	Lepr ^{db} or db/db (-/-)
22	Hydrogen sulfide improves vessel formation of the ischemic adductor muscle and wound healing in diabetic db/db mice	Wang, G.-G. and Li, W.	Iran. J. Basic Med. Sci.	2019	Lepr ^{db} or db/db (-/-)
26	The fabrication of a highly efficient self-healing hydrogel from natural biopolymers loaded with exosomes for the synergistic promotion of severe wound healing	Wang C , Liang C , Wang R , Yao X , Guo P , Yuan W , Liu Y , Song Y , Li Z , Xie X .	Biomater Sci	2019	Lepr ^{db} or db/db (-/-)
28	Rosiglitazone accelerates wound healing by improving endothelial precursor cell function and angiogenesis in db/db mice	Zhou, G. and Han, X. and Wu, Z. and Shi, Q. and Bao, X.	PeerJ	2019	Lepr ^{db} or db/db (-/-)
31	New Peroxisome Proliferator-Activated Receptor Agonist (GQ-11) Improves Wound Healing in Diabetic Mice	Silva, J.C. and Pitta, M.G.R. and Pitta, I.R. and Koh, T.J. and Abdalla, D.S.P.	Adv. Wound Care	2019	Lepr ^{db} or db/db (-/-)
34	Insulin treatment enhances pseudomonas aeruginosa biofilm formation by increasing intracellular cyclic di-gmp levels, leading to chronic wound infection and delayed wound healing	Wei, Q. and Zhang, Z. and Luo, J. and Kong, J. and Ding, Y. and Chen, Y. and Wang, K.	Am. J. Transl. Res.	2019	Lepr ^{db} or db/db (-/-)
45	Periostin and CCN2 Scaffolds Promote the Wound Healing Response in the Skin of Diabetic Mice	Elliott CG, Wang J, Walker JT, Michelsons S, Dunmore-Buyze J, Drangova M, Leask A, Hamilton DW.	Tissue Eng Part A	2019	Lepr ^{db} or db/db (-/-)
48	Modified VEGF-A mRNA induces sustained multifaceted microvascular response and accelerates diabetic wound healing	Sun N, Ning B, Hansson KM, Bruce AC, Seaman SA, Zhang C, Rikard M, DeRosa CA, Fraser CL, Wågberg M, Fritsche-Danielson R, Wikström J, Chien KR, Lundahl A, Hölttä M, Carlsson LG, Peirce SM, Hu S.	Sci Rep	2018	Lepr ^{db} or db/db (-/-)

52	Hydrogen sulfide primes diabetic wound to close through inhibition of NETosis	Yang CT, Chen L, Chen WL, Li N, Chen MJ, Li X, Zheng X, Zhao YZ, Wu YX, Xian M, Liu J.	Mol Cell Endocrinol	2019	Lepr ^{db} or db/db (-/-)
54	An electrochemically deposited collagen wound matrix combined with adipose-derived stem cells improves cutaneous wound healing in a mouse model of type 2 diabetes	Edwards N, Feliens D, Zhao Q, Stone R, Christy R, Cheng X.	J Biomater Appl	2018	Lepr ^{db} or db/db (-/-)
57	Sleep fragmentation delays wound healing in a mouse model of type 2 diabetes	McLain JM, Alami WH, Glovak ZT, Cooley CR, Burke SJ, Collier JJ, Baghdoyan HA, Karlstad MD, Lydic R.	Sleep	2018	Lepr ^{db} or db/db (-/-)
58	Hyperbaric oxygen increases stem cell proliferation, angiogenesis and wound-healing ability of WJ-MSCs in diabetic mice	PeA±a-Villalobos, I. and Casanova-Maldonado, I. and Lois, P. and Prieto, C. and Pizarro, C. and Lattus, J. and Osorio, G. and Palma, V.	Front. Physiol.	2018	Lepr ^{db} or db/db (-/-)
61	Acceleration of Diabetic Wound Regeneration using an In Situ-Formed Stem-Cell-Based Skin Substitute	Dong Y, Rodrigues M, Kwon SH, Li X, A S, Brett EA, Elvassore N, Wang W, Gurtner GC.	Adv Healthc Mater	2018	Lepr ^{db} or db/db (-/-)
62	Promotion of wound healing through low-fluence ablative fractional laser treatment in diabetic mice	Lee HN, Bae JM, Goo BCL, Park YM.	Lasers Med Sci	2019	Lepr ^{db} or db/db (-/-)
64	Beta-glucan-loaded nanofiber dressing improves wound healing in diabetic mice	Grip J, Engstad RE, Skjæveland I, Škalko-Basnet N, Isaksson J, Basnet P, Holsæter AM.	Eur J Pharm Sci	2018	Lepr ^{db} or db/db (-/-)
68	Multidomain Peptide Hydrogel Accelerates Healing of Full-Thickness Wounds in Diabetic Mice	Carrejo, N.C. and Moore, A.N. and Lopez Silva, T.L. and Leach, D.G. and Li, I.-C. and Walker, D.R. and Hartgerink, J.D.	ACS Biomater. Sci. Eng.	2018	Lepr ^{db} or db/db (-/-)
70	Effects of CD100 promote wound healing in diabetic mice.	Wang F, Liu B, Yu Z, Wang T, Song Y, Zhuang R, Wu Y, Su Y, Guo S.	J Mol Histol. 2018	2018	Lepr ^{db} or db/db (-/-)
74	Targeted Nrf2 activation therapy with RTA 408 enhances regenerative capacity of diabetic wounds.	Rabbani PS, Ellison T, Waqas B, Sultan D, Abdou S, David JA, Cohen JM, Gomez-Viso A, Lam G, Kim C, Thomson J, Ceradini DJ.	Diabetes Res Clin Pract. 2018	2018	Lepr ^{db} or db/db (-/-)

78	Diabetes impairs wound healing by Dnmt1-dependent dysregulation of hematopoietic stem cells differentiation towards macrophages	Yan, J. et al 2018 [89]	nature communications	2018	Lepr ^{db} or db/db (-/-)
80	Activation of the EPOR-Î² common receptor complex by cibinetide ameliorates impaired wound healing in mice with genetic diabetes.	Bitto A, Irrera N, Pizzino G, Pallio G, Mannino F, Vaccaro M, Arcoraci V, AliquÃ² F, Minutoli L, Colonna MR, Galeano MR, Brines M, De Ponte C, Collino M, Squadrito F, Altavilla D.	Biochim Biophys Acta Mol Basis Dis. 2018	2018	Lepr ^{db} or db/db (-/-)
84	Topical Reformulation of Valsartan for Treatment of Chronic Diabetic Wounds	Abadir P, Hosseini S, Faghieh M, Ansari A, Lay F, Smith B, Beselman A, Vuong D, Berger A, Tian J, Rini D, Keenahan K, Budman J, Inagami T, Fedarko N, Marti G, Harmon J, Walston J.	J Invest Dermatol	2018	Lepr ^{db} or db/db (-/-)
85	Metformin accelerates wound healing in type 2 diabetic db/db mice.	Han X, Tao Y, Deng Y, Yu J, Sun Y, Jiang G.	Mol Med Rep. 2017	2017	Lepr ^{db} or db/db (-/-)
86	Delivery of monocyte lineage cells in a biomimetic scaffold enhances tissue repair	Hu MS, Walmsley GG, Barnes LA, Weiskopf K, Rennert RC, Duscher D, Januszyk M, Maan ZN, Hong WX, Cheung AT, Leavitt T, Marshall CD, Ransom RC, Malhotra S, Moore AL, Rajadas J, Lorenz HP, Weissman IL, Gurtner GC, Longaker MT.	JCI Insight	2017	Lepr ^{db} or db/db (-/-)
87	Mature B cells accelerate wound healing after acute and chronic diabetic skin lesions.	SÃ©rbulescu RF, Boehm CK, Soon E, Wilks MQ, IlieÅ I, Yuan H, Maxner B, Chronos N, Kaittanis C, Normandin MD, El Fakhri G, Orgill DP, Sluder AE, Poznansky MC.	Wound Repair Regen. 2017	2017	Lepr ^{db} or db/db (-/-)
91	In situ depot comprising phase-change materials that can sustainably release a gasotransmitter H(2)S to treat diabetic wounds.	Lin WC, Huang CC, Lin SJ, Li MJ, Chang Y, Lin YJ, Wan WL, Shih PC, Sung HW.	Biomaterials. 2017	2017	Lepr ^{db} or db/db (-/-)
98	6-Formylindolo[3,2-b]Carbazole Accelerates Skin Wound Healing viaÅ Activation of ERK, but Not ArylÅ Hydrocarbon Receptor.	Morino-Koga S, Uchi H, Mitoma C, Wu Z, Kiyomatsu M, Fuyuno Y, Nagae K, Yasumatsu M, Suico MA, Kai H, Furue M.	J Invest Dermatol. 2017	2017	Lepr ^{db} or db/db (-/-)

100	An injectable non-cross-linked hyaluronic-acid gel containing therapeutic spheroids of human adipose-derived stem cells.	Feng J, Mineda K, Wu SH, Mashiko T, Doi K, Kuno S, Kinoshita K, Kanayama K, Asahi R, Sunaga A, Yoshimura K.	Sci Rep. 2017	2017	Lepr ^{db} or db/db (-/-)
102	Novel lipoproteoplex delivers Keap1 siRNA based gene therapy to accelerate diabetic wound healing.	Rabbani PS, Zhou A, Borab ZM, Frezzo JA, Srivastava N, More HT, Rifkin WJ, David JA, Berens SJ, Chen R, Hameedi S, Junejo MH, Kim C, Sartor RA, Liu CF, Saadeh PB, Montclare JK, Ceradini DJ.	Biomaterials. 2017	2017	Lepr ^{db} or db/db (-/-)
103	Acarbose Accelerates Wound Healing via Akt/eNOS Signaling in db/db Mice.	Han X, Deng Y, Yu J, Sun Y, Ren G, Cai J, Zhu J, Jiang G.	Oxid Med Cell Longev. 2017	2017	Lepr ^{db} or db/db (-/-)
107	Diabetic wounds exhibit decreased yml and arginase expression with increased expression of IL-17 and IL-20	Finley, P.J. and DeClue, C.E. and Sell, S.A. and DeBartolo, J.M. and Shornick, L.P.	Adv. Wound Care	2016	Lepr ^{db} or db/db (-/-)
110	AGEs Induced Autophagy Impairs Cutaneous Wound Healing via Stimulating Macrophage Polarization to M1 in Diabetes.	Guo Y, Lin C, Xu P, Wu S, Fu X, Xia W, Yao M.	Sci Rep. 2016	2016	Lepr ^{db} or db/db (-/-)
112	Diabetic wound regeneration using peptide-modified hydrogels to target re-epithelialization.	Xiao Y, Reis LA, Feric N, Knee EJ, Gu J, Cao S, Laschinger C, Londono C, Antolovich J, McGuigan AP, Radisic M.	Proc Natl Acad Sci U S A. 2016	2016	Lepr ^{db} or db/db (-/-)
113	Inositol-Requiring Enzyme 1 Facilitates Diabetic Wound Healing Through Modulating MicroRNAs.	Wang JM, Qiu Y, Yang ZQ, Li L, Zhang K.	Diabetes. 2017	2017	Lepr ^{db} or db/db (-/-)
132	Mesenchymal stem cell-laden anti-inflammatory hydrogel enhances diabetic wound healing.	Chen S, Shi J, Zhang M, Chen Y, Wang X, Zhang L, Tian Z, Yan Y, Li Q, Zhong W, Xing M, Zhang L, Zhang L.	Sci Rep. 2015	2015	Lepr ^{db} or db/db (-/-)
133	Acceleration of diabetic wound healing using a novel proteaseanti-protease combination therapy	Gao, M. and Nguyen, T.T. and Suckow, M.A. and Wolter, W.R. and Gooyit, M. and Mobashery, S. and Chang, M.	Proc. Natl. Acad. Sci. U. S. A.	2015	Lepr ^{db} or db/db (-/-)
139	The murine excisional wound model: Contraction revisited.	Chen L, Mirza R, Kwon Y, DiPietro LA, Koh TJ.	Wound Repair Regen. 2015	2015	Lepr ^{db} or db/db (-/-)
140	SDF-1 liposomes promote sustained cell proliferation in mouse diabetic wounds.	Olekson MA, Faulknor R, Bandekar A, Sempkowski M, Hsia HC, Berthiaume F.	Wound Repair Regen. 2015	2015	Lepr ^{db} or db/db (-/-)

145	Pseudomonas aeruginosa uses T3SS to inhibit diabetic wound healing.	Goldufsky J, Wood SJ, Jayaraman V, Majdobehe O, Chen L, Qin S, Zhang C, DiPietro LA, Shafikhani SH.	Wound Repair Regen. 2015	2015	Lepr ^{db} or db/db (-/-)
149	Targeted metabolic profiling of wounds in diabetic and nondiabetic mice.	Sood RF, Gu H, Djukovic D, Deng L, Ga M, Muffley LA, Raftery D, Hocking AM.	Wound Repair Regen. 2015	2015	Lepr ^{db} or db/db (-/-)
152	Normalizing dysfunctional purine metabolism accelerates diabetic wound healing	Weinstein, A.L. and Lalezarzadeh, F.D. and Soares, M.A. and Saadeh, P.B. and Ceradini, D.J.	Wound Repair Regen.	2015	Lepr ^{db} or db/db (-/-)
156	Thymosin beta 4 improves dermal burn wound healing via downregulation of receptor of advanced glycation end products in db/db mice	Kim, S. and Kwon, J.	Biochim. Biophys. Acta Gen. Subj.	2014	Lepr ^{db} or db/db (-/-)
159	A short peptide from frog skin accelerates diabetic wound healing.	Liu H, Duan Z, Tang J, Lv Q, Rong M, Lai R.	FEBS J. 2014	2014	Lepr ^{db} or db/db (-/-)
160	Wound administration of M2-polarized macrophages does not improve murine cutaneous healing responses.	Jetten N, Roumans N, Gijbels MJ, Romano A, Post MJ, de Winther MP, van der Hulst RR, Xanthoulea S.	PLoS One. 2014	2014	Lepr ^{db} or db/db (-/-)
165	Topical naltrexone as treatment for type 2 diabetic cutaneous wounds	Immonen, J.A. and Zagon, I.S. and McLaughlin, P.J.	Adv. Wound Care	2014	Lepr ^{db} or db/db (-/-)
168	Combination therapy accelerates diabetic wound closure.	Allen RJ Jr, Soares MA, Haberman ID, Szpalski C, Schachar J, Lin CD, Nguyen PD, Saadeh PB, Warren SM.	PLoS One. 2014	2014	Lepr ^{db} or db/db (-/-)
171	Skin Electroporation of a Plasmid Encoding hCAP-18/LL-37 Host Defense Peptide Promotes Wound Healing	Steinstraesser, L. et al 2014 [56]	The American Society of Gene & Cell Therapy	2014	Lepr ^{db} or db/db (-/-)
175	A nanoscaffold impregnated with human wharton's jelly stem cells or its secretions improves healing of wounds.	Tam K, Cheyyatraviendran S, Venugopal J, Biswas A, Choolani M, Ramakrishna S, Bongso A, Fong CY.	J Cell Biochem. 2014	2014	Lepr ^{db} or db/db (-/-)
181	Enhanced healing of diabetic wounds by subcutaneous administration of human umbilical cord derived stem cells and their conditioned media	Shrestha, C. and Zhao, L. and Chen, K. and He, H. and Mo, Z.	Intl. J. Endocrinol.	2013	Lepr ^{db} or db/db (-/-)
182	A chemical biological strategy to facilitate diabetic wound healing	Gooyit, M. et al 2014 [52]	ACS chemical biology	2014	Lepr ^{db} or db/db (-/-)

193	Impaired therapeutic capacity of autologous stem cells in a model of type 2 diabetes.	Shin L, Peterson DA.	Stem Cells Transl Med. 2012	2012	Lepr ^{db} or db/db (-/-)
196	Innate defense regulator peptide 1018 in wound healing and wound infection.	Steinstraesser L, Hirsch T, Schulte M, Kueckelhaus M, Jacobsen F, Mersch EA, Stricker I, Afacan N, Jenssen H, Hancock RE, Kindrachuk J.	PLoS One. 2012	2012	Lepr ^{db} or db/db (-/-)
200	Plasminogen is a key proinflammatory regulator that accelerates the healing of acute and diabetic wounds.	Shen Y, Guo Y, Mikus P, Sulniute R, Wilczynska M, Ny T, Li J.	Blood. 2012	2012	Lepr ^{db} or db/db (-/-)
206	Lack of FGF-7 further delays cutaneous wound healing in diabetic mice.	Peng C, Chen B, Kao HK, Murphy G, Orgill DP, Guo L.	Plast Reconstr Surg. 2011	2011	Lepr ^{db} or db/db (-/-)
210	Topical prolyl hydroxylase domain-2 silencing improves diabetic murine wound closure.	Wetterau M, George F, Weinstein A, Nguyen PD, Tutela JP, Knobel D, Cohen Ba O, Warren SM, Saadeh PB.	Wound Repair Regen. 2011	2011	Lepr ^{db} or db/db (-/-)
213	Inhibition of stromal cell-derived factor-1 α further impairs diabetic wound healing.	Bermudez DM, Xu J, Herdrich BJ, Radu A, Mitchell ME, Liechty KW.	J Vasc Surg. 2011	2011	Lepr ^{db} or db/db (-/-)
215	Manganese superoxide dismutase expression in endothelial progenitor cells accelerates wound healing in diabetic mice.	Marrotte EJ, Chen DD, Hakim JS, Chen AF.	J Clin Invest. 2010	2010	Lepr ^{db} or db/db (-/-)
217	Effects of human cord blood mesenchymal stem cells on cutaneous wound healing in leprdb mice.	Tark KC, Hong JW, Kim YS, Hahn SB, Lee WJ, Lew DH.	Ann Plast Surg. 2010	2010	Lepr ^{db} or db/db (-/-)
220	Application of the chemokine CXCL12 expression plasmid restores wound healing to near normal in a diabetic mouse model.	Restivo TE, Mace KA, Harken AH, Young DM.	J Trauma. 2010	2010	Lepr ^{db} or db/db (-/-)
223	Decreased circulating progenitor cell number and failed mechanisms of stromal cell-derived factor-1 α mediated bone marrow mobilization impair diabetic tissue repair.	Tepper OM, Carr J, Allen RJ Jr, Chang CC, Lin CD, Tanaka R, Gupta SM, Levine JP, Saadeh PB, Warren SM.	Diabetes. 2010	2010	Lepr ^{db} or db/db (-/-)
224	Molecular mechanisms of enhanced wound healing by copper oxide-impregnated dressings.	Borkow G, Gabbay J, Dardik R, Eidelman AI, Lavie Y, Grunfeld Y, Ikher S, Huszar M, Zatzoff RC, Marikovsky M.	Wound Repair Regen. 2010	2010	Lepr ^{db} or db/db (-/-)

225	Laser photobiomodulation of wound healing in diabetic and non-diabetic mice: effects in splinted and unsplinted wounds.	Chung TY, Peplow PV, Baxter GD.	Photomed Laser Surg. 2010	2010	Lepr ^{db} or db/db (-/-)
227	Poly(methacrylic acid-co-methyl methacrylate) beads promote vascularization and wound repair in diabetic mice.	Martin DC, Semple JL, Sefton MV.	J Biomed Mater Res A. 2010	2010	Lepr ^{db} or db/db (-/-)
229	Heme oxygenase-1 accelerates cutaneous wound healing in mice.	Grochot-Przeczek A, Lach R, Mis J, Skrzypek K, Gozdecka M, Sroczynska P, Dubiel M, Rutkowski A, Kozakowska M, Zagorska A, Walczynski J, Was H, Kotlinowski J, Drukala J, Kurowski K, Kieda C, Herault Y, Dulak J, Jozkowicz A.	PLoS One. 2009	2009	Lepr ^{db} or db/db (-/-)
233	Stabilization of HIF-1alpha is critical to improve wound healing in diabetic mice.	Botusan IR, Sunkari VG, Savu O, Catrina AI, GrÅ¼nler J, Lindberg S, Pereira T, YlÅ±-Herttuala S, Poellinger L, Brismar K, Catrina SB.	Proc Natl Acad Sci U S A. 2008	2008	Lepr ^{db} or db/db (-/-)
237	Pulsed Electromagnetic Fields Accelerate Normal and Diabetic Wound Healing by Increasing Endogenous FGF-2 Release	Callaghan, MJ. et al 2008 [29]	Plastic and Reconstructive Surgery	2008	Lepr ^{db} or db/db (-/-)
238	Aminated beta-1,3-D-glucan improves wound healing in diabetic db/db mice.	Berdal M, Appelbom HI, Eikrem JH, Lund A, Zykova S, Busund LT, Seljelid R, Jenssen T.	Wound Repair Regen. 2007	2007	Lepr ^{db} or db/db (-/-)
240	Sustained expression of Hif-1alpha in the diabetic environment promotes angiogenesis and cutaneous wound repair.	Mace KA, Yu DH, Paydar KZ, Boudreau N, Young DM.	Wound Repair Regen. 2007	2007	Lepr ^{db} or db/db (-/-)
241	Side population hematopoietic stem cells promote wound healing in diabetic mice.	Chan RK, Garfein E, Gigante PR, Liu P, Agha RA, Mulligan R, Orgill DP.	Plast Reconstr Surg. 2007	2007	Lepr ^{db} or db/db (-/-)
244	The effects of topical treatment with acidified nitrite on wound healing in normal and diabetic mice.	Weller R, Finnen MJ.	Nitric Oxide. 2006	2006	Lepr ^{db} or db/db (-/-)

245	Effect of recombinant platelet-derived growth factor (Regranex) on wound closure in genetically diabetic mice.	Chan RK, Liu PH, Pietramaggiore G, Ibrahim SI, Hechtman HB, Orgill DP.	J Burn Care Res. 2006	2006	Lepr ^{db} or db/db (-/-)
246	COMP-angiopoietin-1 promotes wound healing through enhanced angiogenesis, lymphangiogenesis, and blood flow in a diabetic mouse model.	Cho CH, Sung HK, Kim KT, Cheon HG, Oh GT, Hong HJ, Yoo OJ, Koh GY.	Proc Natl Acad Sci U S A. 2006	2006	Lepr ^{db} or db/db (-/-)
247	Plasmin modulates vascular endothelial growth factor-A-mediated angiogenesis during wound repair.	Roth D, Piekarek M, Paulsson M, Christ H, Bloch W, Krieg T, Davidson JM, Eming SA.	Am J Pathol. 2006	2006	Lepr ^{db} or db/db (-/-)
249	Acceleration of wound healing in healing-impaired db/db mice with a photocrosslinkable chitosan hydrogel containing fibroblast growth factor-2.	Obara K, Ishihara M, Fujita M, Kanatani Y, Hattori H, Matsui T, Takase B, Ozeki Y, Nakamura S, Ishizuka T, Tominaga S, Hiroi S, Kawai T, Maehara T.	Wound Repair Regen. 2005	2005	Lepr ^{db} or db/db (-/-)
251	Effect of a diode laser on wound healing by using diabetic and nondiabetic mice.	Kawalec JS, Hetherington VJ, Pfennigwerth TC, Dockery DS, Dolce M.	J Foot Ankle Surg. 2004	2004	Lepr ^{db} or db/db (-/-)
254	Discordant effects of a soluble VEGF receptor on wound healing and angiogenesis.	Jacobi J, Tam BY, Sundram U, von Degenfeld G, Blau HM, Kuo CJ, Cooke JP.	Gene Ther. 2004	2004	Lepr ^{db} or db/db (-/-)
257	Effect of chitosan film containing basic fibroblast growth factor on wound healing in genetically diabetic mice.	Mizuno K, Yamamura K, Yano K, Osada T, Saeki S, Takimoto N, Sakurai T, Nimura Y.	J Biomed Mater Res A. 2003	2003	Lepr ^{db} or db/db (-/-)
265	Effect of topical application of a stable prostacyclin analogue, SM-10902 on wound healing in diabetic mice.	Yamamoto T, Horikawa N, Komuro Y, Hara Y.	Eur J Pharmacol. 1996	1996	Lepr ^{db} or db/db (-/-)
40	Resveratrol promotes diabetic wound healing via SIRT1-FoxO1-c-Myc signaling pathway-mediated angiogenesis	Huang, X. and Sun, J. and Chen, G. and Niu, C. and Wang, Y. and Zhao, C. and Sun, J. and Huang, H. and Huang, S. and Liang, Y. and Shen, Y. and Cong, W. and Jin, L. and Zhu, Z.	Front. Pharmacol.	2019	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)

43	Ameliorating Methylglyoxal-Induced Progenitor Cell Dysfunction for Tissue Repair in Diabetes	Li H, O'Meara M, Zhang X, Zhang K, Seyoum B, Yi Z, Kaufman RJ, Monks TJ, Wang JM.	Diabetes	2019	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
44	Dynamic Histological Events and Molecular Changes in Excisional Wound Healing of Diabetic DB/DB Mice	Wang XT, McKeever CC, Vonu P, Patterson C, Liu PY.	J Surg Res	2019	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
53	Effect of N-acyl-dopamines on beta cell differentiation and wound healing in diabetic mice	Jiménez-Jiménez C, Lara-Chica M, Palomares B, Collado JA, Lopez-Miranda J, Muñoz E, Calzado MA.	Biochim Biophys Acta Mol Cell Res	2018	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
88	Glycoprotein Nonmelanoma Clone B Regulates the Crosstalk between Macrophages and Mesenchymal Stem Cells toward Wound Repair	Yu B, Alboslemy T, Safadi F, Kim MH.	J Invest Dermatol	2018	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
92	Mitochondria-Targeted Antioxidant SkQ1 Improves Dermal Wound Healing in Genetically Diabetic Mice.	Demyanenko IA, Zakharova VV, Ilyinskaya OP, Vasilieva TV, Fedorov AV, Manskikh VN, Zinovkin RA, Pletjushkina OY, Chernyak BV, Skulachev VP, Popova EN.	Oxid Med Cell Longev. 2017	2017	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
108	Mono-epoxy-tocotrienol- $\hat{\pm}$ enhances wound healing in diabetic mice and stimulates in vitro angiogenesis and cell migration.	Xu C, Bentinger M, Savu O, Moshfegh A, Sunkari V, Dallner G, Swiezewska E, Catrina SB, Brismar K, Tekle M.	J Diabetes Complications. 2017	2017	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
116	Enforced Expression of Hoxa3 Inhibits Classical and Promotes Alternative Activation of Macrophages In Vitro and In Vivo.	Al Sadoun H, Burgess M, Hentges KE, Mace KA.	J Immunol. 2016	2016	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
131	Restoration of Nrf2 signaling normalizes the regenerative niche	Soares, MA. et al 2016 [70]	Diabetes	2015	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)

147	Macrophage PPAR α and impaired wound healing in type 2 diabetes.	Mirza RE, Fang MM, Novak ML, Urao N, Sui A, Ennis WJ, Koh TJ.	J Pathol. 2015	2015	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
167	Full-thickness splinted skin wound healing models in db/db and heterozygous mice: implications for wound healing impairment.	Park SA, Teixeira LB, Raghunathan VK, Covert J, Dubielzig RR, Isseroff RR, Schurr M, Abbott NL, McAnulty J, Murphy CJ.	Wound Repair Regen. 2014	2014	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
170	Hydrogen sulfide improves wound healing via restoration of endothelial progenitor cell functions and activation of angiopoietin-1 in type 2 diabetes.	Liu F, Chen DD, Sun X, Xie HH, Yuan H, Jia W, Chen AF.	Diabetes. 2014	2014	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
176	MicroRNA miR-27b rescues bone marrow-derived angiogenic cell function and accelerates wound healing in type 2 diabetes mellitus.	Wang JM, Tao J, Chen DD, Cai JJ, Irani K, Wang Q, Yuan H, Chen AF.	Arterioscler Thromb Vasc Biol. 2014	2014	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
190	Integration of silver nanoparticle-impregnated polyelectrolyte multilayers into murine-splinted cutaneous wound beds.	Guthrie KM, Agarwal A, Teixeira LB, Dubielzig RR, Abbott NL, Murphy CJ, Singh H, McAnulty JF, Schurr MJ.	J Burn Care Res. 2013	2013	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
203	Downregulation of endothelial microRNA-200b supports cutaneous wound angiogenesis by desilencing GATA binding protein 2 and vascular endothelial growth factor receptor 2.	Chan YC, Roy S, Khanna S, Sen CK.	Arterioscler Thromb Vasc Biol. 2012	2012	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
207	Dysregulation of monocyte/macrophage phenotype in wounds of diabetic mice.	Mirza R, Koh TJ.	Cytokine. 2011	2011	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
235	Wound closure and metabolic parameter variability in a db/db mouse model for diabetic ulcers.	Trousdale RK, Jacobs S, Simhaee DA, Wu JK, Lustbader JW.	J Surg Res. 2009	2009	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)

256	Effects of vascular endothelial growth factor on wound closure rates in the genetically diabetic mouse model	Kirchner, LM. et al 2003 [24]	Wound repair and regeneration	2003	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
258	The role of oxidised regenerated cellulose/collagen in wound repair : effects in vitro on fibroblast biology and in vivo in a model of compromised healing	Hart, J., et al 2002 [22]	The international Journal of Biochemistry & Cell Biology	2002	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
260	Differential Expression of Matrix Metalloproteinases During Impaired Wound Healing of the Diabetes Mouse	Wall, SJ. et al 2002 [23]	The Society for Investigate Dermatology	2002	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
261	Topical Application of Yeast Extract Accelerates the Wound Healing of Diabetic Mice	Crowe, MJ. et al 1999 [21]	Journal of Burn Care & Rehabilitation	1999	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
263	Apoptosis down-regulates inflammation under the advancing epithelial wound edge : Delayed patterns in diabetes and improvement with topical growth factors	Brown, DL. et al 1997 [19]	Surgery	1997	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
264	Acceleration of wound healing in diabetic mice by basic fibroblast growth factor.	Okumura M, Okuda T, Nakamura T, Yajima M.	Biol Pharm Bull. 1996	1996	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
266	PDGF and TGF- α Act Synergistically to Improve Wound Healing in the Genetically Diabetic Mouse	Brown, RL. et al 1994 [17]	JOURNAL OF SURGICAL RESEARCH	1994	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)
267	PDGF and FGF stimulate wound healing in the genetically diabetic mouse.	Greenhalgh DG, Sprugel KH, Murray MJ, Ross R.	Am J Pathol. 1990	1990	Lepr ^{db} or db/db (-/-) and Db/db heterozygous (+/-)

248	Effect of SR58611A, a potent beta-3 adrenoceptor agonist, on cutaneous wound healing in diabetic and obese mice.	Schaeffer P, Bernat A, Arnone M, Manara L, Gallas JF, Dol-Gleizes F, Millet L, Grosset A, Herbert JM.	Eur J Pharmacol. 2006	2006	Lepr ^{db} or db/db (-/-) and Lep ^{ob} or ob/ob (-/-) and Other diabetic model
8	Development of stabilized dual growth factor-loaded hyaluronate collagen dressing matrix	Kim, J. and Lee, K.-M. and Han, S.H. and Ko, E.A. and Yoon, D.S. and Park, I.K. and Shin, H.-C. and Park, K.H. and Lee, J.W.	J. Tissue Eng.	2021	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ)
14	Topical GDF11 accelerates skin wound healing in both type 1 and 2 diabetic mouse models	Li Q, Jiao L, Shao Y, Li M, Gong M, Zhang Y, Tan Z, Wang Y, Yang X, Wang Z, Zhang Y.	Biochem Biophys Res Commun	2020	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ)
81	Effects of structurally stabilized EGF and bFGF on wound healing in type I and type II diabetic mice.	Choi SM, Lee KM, Kim HJ, Park IK, Kang HJ, Shin HC, Baek D, Choi Y, Park KH, Lee JW.	Acta Biomater. 2018	2018	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ)
115	Activation of Dopamine D1 Receptors in Dermal Fibroblasts Restores Vascular Endothelial Growth Factor-A Production by These Cells and Subsequent Angiogenesis in Diabetic Cutaneous Wound Tissues.	Chakroborty D, Sarkar C, Lu K, Bhat M, Dasgupta PS, Basu S.	Am J Pathol. 2016	2016	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ)
135	Improvement of skin wound healing in diabetic mice by kinin B2 receptor blockade.	Desposito D, Chollet C, Taveau C, Descamps V, Alhenc-Gelas F, Roussel R, Bouby N, Waeckel L.	Clin Sci (Lond). 2016	2016	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ)
239	db/db mice exhibit severe wound-healing impairments compared with other murine diabetic strains in a silicone-splinted excisional wound model.	Michaels J 5th, Churgin SS, Blechman KM, Greives MR, Aarabi S, Galiano RD, Gurtner GC.	Wound Repair Regen. 2007	2007	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ) and Akita
35	Cutaneous Wound Healing in Diabetic Mice Is Improved by Topical Mineralocorticoid Receptor Blockade	Nguyen VT, Farman N, Palacios-Ramirez R, Sbeih M, Behar-Cohen F, Aractingi S, Jaisser F.	J Invest Dermatol	2020	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ) and Db/db heterozygous (+/-)

42	Triggering of a Dll4-Notch1 loop impairs wound healing in diabetes	Zheng X, Narayanan S, Sunkari VG, Eliasson S, Botusan IR, Grünler J, Catrina AI, Radtke F, Xu C, Zhao A, Ekberg NR, Lendahl U, Catrina SB.	Proc Natl Acad Sci U S A	2019	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ) and Db/db heterozygous (+/-)
129	Application of Electron Paramagnetic Resonance (EPR) Oximetry to Monitor Oxygen in Wounds in Diabetic Models.	Desmet CM, Lafosse A, VÃ©riter S, Porporato PE, Sonveaux P, Dufrane D, LevÃªque P, Gallez B.	PLoS One.	2015	2015 Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ) and Db/db heterozygous (+/-)
216	Limitations of the db/db mouse in translational wound healing research: Is the NONcNZO10 polygenic mouse model superior?	Fang RC, Kryger ZB, Buck DW 2nd, De la Garza M, Galiano RD, Mustoe TA.	Wound Repair Regen.	2010	Lepr ^{db} or db/db (-/-) and Streptozotocin (STZ) and NONcNZO10/Ltj (NON/NZ)
146	Accelerated healing in NONcNZO10/LtJ type 2 diabetic mice by FGF-1.	Blaber SI, Diaz J, Blaber M.	Wound Repair Regen.	2015	NONcNZO10/Ltj (NON/NZ)
192	In vivo bioluminescence imaging to evaluate systemic and topical antibiotics against community-acquired methicillin-resistant Staphylococcus aureus-infected skin wounds in mice.	Guo Y, Ramos RI, Cho JS, Donegan NP, Cheung AL, Miller LS.	Antimicrob Agents Chemother.	2013	NONcNZO10/Ltj (NON/NZ)
142	Ultrasonic Stimulation of Mouse Skin Reverses the Healing Delays in Diabetes and Aging by Activation of Rac1.	Roper JA, Williamson RC, Bally B, Cowell CAM, Brooks R, Stephens P, Harrison AJ, Bass MD.	J Invest Dermatol.	2015	Other diabetic model
179	Deficient cytokine expression and neutrophil oxidative burst contribute to impaired cutaneous wound healing in diabetic, biofilm-containing chronic wounds.	Nguyen KT, Seth AK, Hong SJ, Geringer MR, Xie P, Leung KP, Mustoe TA, Galiano RD.	Wound Repair Regen.	2013	Other diabetic model
199	Obesity impairs wound closure through a vasculogenic mechanism	Wagner, II. et al 2012 [47]	Wound repair and regeneration	2012	Other diabetic model
208	The TallyHo polygenic mouse model of diabetes: implications in wound healing.	Buck DW 2nd, Jin DP, Geringer M, Hong SJ, Galiano RD, Mustoe TA.	Plast Reconstr Surg.	2011	Other diabetic model

250	Tissue Factor as a Link Between Wounding and Tissue Repair	Chen, J. et al 2005 [26]	Diabetes	2005	Other diabetic model
255	Effects of recombinant human tissue inhibitor of metalloproteinases-2 (rh-TIMP-2) on migration of epidermal keratinocytes in vitro and wound healing in vivo.	Terasaki K, Kanzaki T, Aoki T, Iwata K, Saiki I.	J Dermatol.	2003	Other diabetic model
2	Wound healing activity of standardized extract of <i>Curculigo orchoides</i> in streptozotocin-induced diabetic mice	Singh, A. and Bajpai, S. and Singh, N. and Kumar, V. and Gour, J.K. and Singh, P.K. and Singh, R.K.	Asian Pac. J. Trop. Dis.	2014	Streptozotocin (STZ)
3	Topical Nitric oxide in nanoformulation enhanced wound healing in experimental diabetes in mice	Samaha, R. and Othman, A.I. and El-Sherbiny, I.M. and Amer, M.A. and Elhusseini, F. and ElMissiry, M.A. and Amin, A.H. and Saad, M.A.A.A.	Res. J. Pharm., Biol. Chem. Sci.	2017	Streptozotocin (STZ)
7	Bioactive skin-mimicking hydrogel band-aids for diabetic wound healing and infectious skin incision treatment	Yang, Y. and Zhao, X. and Yu, J. and Chen, X. and Wang, R. and Zhang, M. and Zhang, Q. and Zhang, Y. and Wang, S. and Cheng, Y.	Bioact. Mater.	2021	Streptozotocin (STZ)
9	Improved diabetic wound healing by LFcInB is associated with relevant changes in the skin immune response and microbiota	Mouritzen, M.V. and Petkovic, M. and Qvist, K. and Poulsen, S.S. and Alarico, S. and Leal, E.C. and Dalgaard, L.T. and Empadinhas, N. and Carvalho, E. and Jenssen, H.	Mol. Ther. Methods Clin. Dev.	2021	Streptozotocin (STZ)
11	In situ sprayed NIR-responsive, analgesic black phosphorus-based gel for diabetic ulcer treatment	Ouyang J, Ji X, Zhang X, Feng C, Tang Z, Kong N, Xie A, Wang J, Sui X, Deng L, Liu Y, Kim JS, Cao Y, Tao W.	Proc Natl Acad Sci U S A	2020	Streptozotocin (STZ)
12	Deregulated immune cell recruitment orchestrated by FOXM1 impairs human diabetic wound healing	Sawaya AP, Stone RC, Brooks SR, Pastar I, Jozic I, Hasneen K, O'Neill K, Mehdizadeh S, Head CR, Strbo N, Morasso MI, Tomic-Canic M.	Nat Commun	2020	Streptozotocin (STZ)
15	Lack of lymphocytes impairs macrophage polarization and angiogenesis in diabetic wound healing	Seraphim PM, Leal EC, Moura J, Gonçalves P, Gonçalves JP, Carvalho E.	Life Sci	2020	Streptozotocin (STZ)
17	MiRNA-221-3p in endothelial progenitor cell-derived exosomes accelerates skin wound healing in diabetic mice	Xu, J. and Bai, S. and Cao, Y. and Liu, L. and Fang, Y. and Du, J. and Luo, L. and Chen, M. and Shen, B. and Zhang, Q.	Diabetes Metab. Syndr. Obes. Targets Ther.	2020	Streptozotocin (STZ)

18	Improved diabetic wound healing by EGF encapsulation in gelatin-alginate coacervates	Jeong, S. and Kim, B.W. and Park, M. and Ban, E. and Lee, S.-H. and Kim, A.	Pharmaceutics	2020	Streptozotocin (STZ)
19	Autologous blood transfusion stimulates wound healing in diabetic mice through activation of the HIF-1 α pathway by improving the blood preservation solution	Zhu NN, Lu MJ, Chen YQ, Jin XJ, Zhou X, Wei HW, Liu XQ, Duan LS, Yin L, Guo JR.	FASEB J	2020	Streptozotocin (STZ)
21	A Synthetic Curcuminoid Analog, (2E,6E)-2,6-bis(2-(trifluoromethyl)benzylidene)cyclohexanone, Ameliorates Impaired Wound Healing in Streptozotocin-Induced Diabetic Mice by Increasing miR-146a	Huang J, Fu J, Liu B, Wang R, You T.	Molecules	2020	Streptozotocin (STZ)
23	Umbilical cord-matrix stem cells induce the functional restoration of vascular endothelial cells and enhance skin wound healing in diabetic mice via the polarized macrophages	Zhang S, Chen L, Zhang G, Zhang B.	Stem Cell Res Ther	2020	Streptozotocin (STZ)
24	Preparation and characterization of epigallocatechin gallate, ascorbic acid, gelatin, chitosan nanoparticles and their beneficial effect on wound healing of diabetic mice	Sun M, Xie Q, Cai X, Liu Z, Wang Y, Dong X, Xu Y.	Int J Biol Macromol	2020	Streptozotocin (STZ)
25	CD271 promotes STZ-induced diabetic wound healing and regulates epidermal stem cell survival in the presence of the pTrkA receptor	Zhang M, Zhang R, Li X, Cao Y, Huang K, Ding J, Liu M, Feng Z, Yin S, Ma J, Zhang H, Wang Y.	Cell Tissue Res	2020	Streptozotocin (STZ)
27	The wound healing effects of the Tilapia collagen peptide mixture TY001 in streptozotocin diabetic mice	Xiong X, Liang J, Xu Y, Liu J, Liu Y.	J Sci Food Agric	2020	Streptozotocin (STZ)
29	Chitosan-based nitric oxide-releasing dressing for anti-biofilm and in vivo healing activities in MRSA biofilm-infected wounds	Choi M, Hasan N, Cao J, Lee J, Hlaing SP, Yoo JW.	Int J Biol Macromol	2020	Streptozotocin (STZ)
30	An aligned porous electrospun fibrous scaffold with embedded asiatic acid for accelerating diabetic wound healing	Han Y, Jiang Y, Li Y, Wang M, Fan T, Liu M, Ke Q, Xu H, Yi Z.	J Mater Chem B	2019	Streptozotocin (STZ)

32	Preparation and in vivo evaluation of a topical hydrogel system incorporating highly skin-permeable growth factors, quercetin, and oxygen carriers for enhanced diabetic wound-healing therapy	Jee JP, Pangei R, Jha SK, Byun Y, Park JW.	Int J Nanomedicine	2019	Streptozotocin (STZ)
33	Accelerated wound healing in diabetes by reprogramming the macrophages with particle-induced clustering of the mannose receptors	Gan J, Liu C, Li H, Wang S, Wang Z, Kang Z, Huang Z, Zhang J, Wang C, Lv D, Dong L.	Biomaterials	2019	Streptozotocin (STZ)
36	CCL2-Mediated Reversal of Impaired Skin Wound Healing in Diabetic Mice by Normalization of Neovascularization and Collagen Accumulation	Ishida Y, Kuninaka Y, Nosaka M, Furuta M, Kimura A, Taruya A, Yamamoto H, Shimada E, Akiyama M, Mukaida N, Kondo T.	J Invest Dermatol	2019	Streptozotocin (STZ)
38	Edaravone-Loaded Alginate-Based Nanocomposite Hydrogel Accelerated Chronic Wound Healing in Diabetic Mice	Fan Y, Wu W, Lei Y, Gaucher C, Pei S, Zhang J, Xia X.	Mar Drugs	2019	Streptozotocin (STZ)
39	Interleukin 6 Function in the Skin and Isolated Keratinocytes Is Modulated by Hyperglycemia	Lee EG, Luckett-Chastain LR, Calhoun KN, Frempham B, Bastian A, Gallucci RM.	J Immunol Res	2019	Streptozotocin (STZ)
41	A new alternative insight of nanoemulsion conjugated with κ -carrageenan for wound healing study in diabetic mice: In vitro and in vivo evaluation	Shanmugapriya K, Kim H, Kang HW.	Eur J Pharm Sci	2019	Streptozotocin (STZ)
46	Long noncoding RNA-antisense noncoding RNA in the INK4 locus accelerates wound healing in diabetes by promoting lymphangiogenesis via regulating miR-181a/Prox1 axis	He ZY, Wei TH, Zhang PH, Zhou J, Huang XY.	J Cell Physiol	2019	Streptozotocin (STZ)
47	Sustained release of recombinant thrombomodulin from cross-linked gelatin/hyaluronic acid hydrogels potentiate wound healing in diabetic mice	Hsu YY, Liu KL, Yeh HH, Lin HR, Wu HL, Tsai JC.	Eur J Pharm Biopharm	2019	Streptozotocin (STZ)
50	SIRT1 activation promotes angiogenesis in diabetic wounds by protecting endothelial cells against oxidative stress	Li, X., et al. 2019 [92]	Archives of Biochemistry and Biophysics	2019	Streptozotocin (STZ)
51	Bee venom improves diabetic wound healing by protecting functional macrophages from apoptosis and enhancing Nrf2, Ang-1 and Tie-2 signaling	Hozzein WN, Badr G, Badr BM, Allam A, Ghamdi AA, Al-Wadaan MA, Al-Waili NS.	Mol Immunol	2018	Streptozotocin (STZ)

55	Impaired wound healing in type 1 diabetes is dependent on 5-lipoxygenase products	Ramalho T, Filgueiras L, Silva-Jr IA, Pessoa AFM, Jancar S.	Sci Rep	2018	Streptozotocin (STZ)
56	Matrix-entrapped cellular secretome rescues diabetes-induced EPC dysfunction and accelerates wound healing in diabetic mice	Deshpande R, Kanitkar M, Kadam S, Dixit K, Chhabra H, Bellare J, Datar S, Kale VP.	PLoS One	2018	Streptozotocin (STZ)
59	Wound healing can be improved by (-)-epigallocatechin gallate through targeting Notch in streptozotocin-induced diabetic mice	Huang YW, Zhu QQ, Yang XY, Xu HH, Sun B, Wang XJ, Sheng J.	FASEB J	2019	Streptozotocin (STZ)
60	Dimethyl fumarate accelerates wound healing under diabetic condition	Li Y, Ma F, Li H, Song Y, Zhang H, Jiang Z, Wu H.	J Mol Endocrinol	2018	Streptozotocin (STZ)
66	High dose oral vitamin C and mesenchymal stem cells aid wound healing in a diabetic mouse model	Chokesuwattanaskul S, Sukpat S, Duangpatra J, Buppajarntham S, Decharatanachart P, Mutirangura A, Patumraj S.	J Wound Care	2018	Streptozotocin (STZ)
67	Vitamin D Ameliorates Impaired Wound Healing in Streptozotocin-Induced Diabetic Mice by Suppressing Endoplasmic Reticulum Stress.	Yuan YF, Das SK, Li MQ.	J Diabetes Res. 2018	2018	Streptozotocin (STZ)
69	FOXO1 inhibition potentiates endothelial angiogenic functions in diabetes via suppression of ROCK/Drp1-mediated mitochondrial fission	Shi, Y. et al 2018 [87]	Molecular Basis of Disease	2018	Streptozotocin (STZ)
72	Deficiency of liver-derived insulin-like growth factor-I (IGF-I) does not interfere with the skin wound healing rate.	Botusan IR, Zheng X, Narayanan S, GrÄ¼nler J, Sunkari VG, Calissendorff FS, Ansurudeen I, Illies C, Svensson J, Jansson JO, Ohlsson C, Brismar K, Catrina SB.	PLoS One. 2018	2018	Streptozotocin (STZ)
73	Folic Acid Promotes Wound Healing in Diabetic Mice by Suppression of Oxidative Stress.	Zhao M, Zhou J, Chen YH, Yuan L, Yuan MM, Zhang XQ, Hu Y, Yu H.	J Nutr Sci Vitaminol (Tokyo). 2018	2018	Streptozotocin (STZ)
75	Specific PKC β II inhibitor: one stone two birds in the treatment of diabetic foot ulcers	Das SK, Yuan YF, Li MQ.	Biosci Rep	2018	Streptozotocin (STZ)
77	Vitamin D ameliorates impaired wound healing in streptozotocin-induced diabetic mice by suppressing NF-kB-mediated inflammatory genes.	Yuan Y, Das SK, Li M.	Biosci Rep. 2018	2018	Streptozotocin (STZ)

79	IL-15 enhances activation and IGF-1 production of dendritic epidermal T cells to promote wound healing in diabetic mice	Wang, Y. and Bai, Y. and Li, Y. and Liang, G. and Jiang, Y. and Liu, Z. and Liu, M. and Hao, J. and Zhang, X. and Hu, X. and Chen, J. and Wang, R. and Yin, Z. and Wu, J. and Luo, G. and He, W.	Front. Immunol.	2017	Streptozotocin (STZ)
82	Prospect of Using Cell Product for the Therapy of Skin Defects in Diabetes Mellitus.	Lykov AP, Bondarenko NA, Poveshchenko OV, Miller TV, Poveshchenko AF, Surovtseva MA, Bgatova NP, Konenkov VI.	Bull Exp Biol Med.	2017	Streptozotocin (STZ)
83	Blocking AGE-RAGE Signaling Improved Functional Disorders of Macrophages in Diabetic Wound.	Wang Q, Zhu G, Cao X, Dong J, Song F, Niu Y.	J Diabetes Res.	2017	Streptozotocin (STZ)
89	Cytocompatible Anti-microbial Dressings of Syzygium cumini Cellulose Nanocrystals Decorated with Silver Nanoparticles Accelerate Acute and Diabetic Wound Healing	Singla R, Soni S, Patial V, Kulurkar PM, Kumari A, S M, Padwad YS, Yadav SK.	Sci Rep	2017	Streptozotocin (STZ)
90	Acellular dermal matrix scaffolds coated with connective tissue growth factor accelerate diabetic wound healing by increasing fibronectin through PKC signalling pathway	Yan W, Liu H, Deng X, Jin Y, Wang N, Chu J.	J Tissue Eng Regen Med	2018	Streptozotocin (STZ)
93	Weakened IL-15 Production and Impaired mTOR Activation Alter Dendritic Epidermal T Cell Homeostasis in Diabetic Mice	Liu Z, Liang G, Gui L, Li Y, Liu M, Bai Y, Zhang X, Hu X, Chen J, Huang C, Liu X, Luo G, Wu J, He W.	Sci Rep	2017	Streptozotocin (STZ)
95	A bioluminescent Pseudomonas aeruginosa wound model reveals increased mortality of type 1 diabetic mice to biofilm infection	Agostinho Hunt AM, Gibson JA, Larrivee CL, O'Reilly S, Navitskaya S, Needle DB, Abramovitch RB, Busik JV, Waters CM.	J Wound Care	2017	Streptozotocin (STZ)
96	IL-33 improves wound healing through enhanced M2 macrophage polarization in diabetic mice.	He R, Yin H, Yuan B, Liu T, Luo L, Huang P, Dai L, Zeng K.	Mol Immunol.	2017	Streptozotocin (STZ)
97	In vivo diabetic wound healing potential of nanobiocomposites containing bamboo cellulose nanocrystals impregnated with silver nanoparticles.	Singla R, Soni S, Patial V, Kulurkar PM, Kumari A, S M, Padwad YS, Yadav SK.	Int J Biol Macromol.	2017	Streptozotocin (STZ)
99	Interleukin-6 stimulates Akt and p38 MAPK phosphorylation and fibroblast migration in non-diabetic but not diabetic mice.	Nishikai-Yan Shen T, Kanazawa S, Kado M, Okada K, Luo L, Hayashi A, Mizuno H, Tanaka R.	PLoS One.	2017	Streptozotocin (STZ)

101	Raman spectroscopy enables noninvasive biochemical identification of the collagen regeneration in cutaneous wound healing of diabetic mice treated with MSCs.	Yan W, Liu H, Deng X, Jin Y, Sun H, Li C, Wang N, Chu J.	Lasers Med Sci. 2017	2017	Streptozotocin (STZ)
105	Gamma-tocopherol supplementation ameliorated hyper-inflammatory response during the early cutaneous wound healing in alloxan-induced diabetic mice.	Shin J, Yang SJ, Lim Y.	Exp Biol Med (Maywood). 2017	2017	Streptozotocin (STZ)
106	Protein Phosphotyrosine Phosphatase 1B (PTP1B) in Calpain-dependent Feedback Regulation of Vascular Endothelial Growth Factor Receptor (VEGFR2) in Endothelial Cells: IMPLICATIONS IN VEGF-DEPENDENT ANGIOGENESIS AND DIABETIC WOUND HEALING.	Zhang Y, Li Q, Youn JY, Cai H.	J Biol Chem. 2017	2017	Streptozotocin (STZ)
109	Hyperglycaemia inhibits REG3A expression to exacerbate TLR3-mediated skin inflammation in diabetes	Wu, Y. et al 2016 [73]_A	nature communications	2016	Streptozotocin (STZ)
117	Treatment of refractory cutaneous ulcers with mixed sheets consisting of peripheral blood mononuclear cells and fibroblasts.	Ueno K, Takeuchi Y, Samura M, Tanaka Y, Nakamura T, Nishimoto A, Murata T, Hosoyama T, Hamano K.	Sci Rep. 2016	2016	Streptozotocin (STZ)
118	Engineered human vascularized constructs accelerate diabetic wound healing.	Shen YI, Cho H, Papa AE, Burke JA, Chan XY, Duh EJ, Gerecht S.	Biomaterials. 2016	2016	Streptozotocin (STZ)
119	Metformin improves the angiogenic functions of endothelial progenitor cells via activating AMPK/eNOS pathway in diabetic mice	Yu, JW. et al 2016 [74]	Cardiovascular Diabetology	2016	Streptozotocin (STZ)
120	High-Density Lipoproteins Rescue Diabetes-Impaired Angiogenesis via Scavenger Receptor Class B Type I.	Tan JT, Prosser HC, Dunn LL, Vanags LZ, Ridiandries A, Tsatralis T, Lecce L, Clayton ZE, Yuen SC, Robertson S, Lam YT, Celermajer DS, Ng MK, Bursill CA.	Diabetes. 2016	2016	Streptozotocin (STZ)
121	Pleiotropic Effects of Simvastatin on Wound Healing in Diabetic Mice.	Sukpat S, Israsena N, Patumraj S.	J Med Assoc Thai. 2016	2016	Streptozotocin (STZ)

123	Mast Cells Regulate Wound Healing in Diabetes.	Tellechea A, Leal EC, Kafanas A, Auster ME, Kuchibhotla S, Ostrovsky Y, Tecilazich F, Baltzis D, Zheng Y, Carvalho E, Zabolotny JM, Weng Z, Petra A, Patel A, Panagiotidou S, Pradhan-Nabzdyk L, Theoharides TC, Veves A.	Diabetes. 2016	2016	Streptozotocin (STZ)
124	Cell recruiting chemokine-loaded sprayable gelatin hydrogel dressings for diabetic wound healing.	Yoon DS, Lee Y, Ryu HA, Jang Y, Lee KM, Choi Y, Choi WJ, Lee M, Park KM, Park KD, Lee JW.	Acta Biomater. 2016	2016	Streptozotocin (STZ)
125	Diazoxide accelerates wound healing by improving EPC function.	Li ZP, Xin RJ, Yang H, Jiang GJ, Deng YP, Li DJ, Shen FM.	Front Biosci (Landmark Ed). 2016	2016	Streptozotocin (STZ)
126	Vascular Endothelial Growth Factor Receptor Type 1 Signaling Prevents Delayed Wound Healing in Diabetes by Attenuating the Production of IL-1 β by Recruited Macrophages.	Okizaki S, Ito Y, Hosono K, Oba K, Ohkubo H, Kojo K, Nishizawa N, Shibuya M, Shichiri M, Majima M.	Am J Pathol. 2016	2016	Streptozotocin (STZ)
127	Bee Venom Accelerates Wound Healing in Diabetic Mice by Suppressing Activating Transcription Factor-3 (ATF-3) and Inducible Nitric Oxide Synthase (iNOS)-Mediated Oxidative Stress and Recruiting Bone Marrow-Derived Endothelial Progenitor Cells.	Badr G, Hozzein WN, Badr BM, Al Ghamdi A, Saad Eldien HM, Garraud O.	J Cell Physiol. 2016	2016	Streptozotocin (STZ)
128	An Essential Role of NRF2 in Diabetic Wound Healing.	Long M, Rojo de la Vega M, Wen Q, Bharara M, Jiang T, Zhang R, Zhou S, Wong PK, Wondrak GT, Zheng H, Zhang DD.	Diabetes. 2016	2016	Streptozotocin (STZ)
130	Activation of $\alpha 7$ nAChR Promotes Diabetic Wound Healing by Suppressing AGE-Induced TNF- α Production.	Dong MW, Li M, Chen J, Fu TT, Lin KZ, Ye GH, Han JG, Feng XP, Li XB, Yu LS, Fan YY.	Inflammation. 2016	2016	Streptozotocin (STZ)
136	Topical application of propolis enhances cutaneous wound healing by promoting TGF- β /Smad-mediated collagen production in a streptozotocin-induced type I diabetic mouse model.	Hozzein WN, Badr G, Al Ghamdi AA, Sayed A, Al-Waili NS, Garraud O.	Cell Physiol Biochem. 2015	2015	Streptozotocin (STZ)

137	Interleukin-22 Promotes Wound Repair in Diabetes by Improving Keratinocyte Pro-Healing Functions.	Avitabile S, Odorisio T, Madonna S, Eyerich S, Guerra L, Eyerich K, Zambruno G, Cavani A, Cianfarani F.	J Invest Dermatol. 2015	2015	Streptozotocin (STZ)
138	Akt/hypoxia-inducible factor-1 α signaling deficiency compromises skin wound healing in a type 1 diabetes mouse model	Jing, L. and Li, S. and Li, Q.	Exp. Ther. Med.	2015	Streptozotocin (STZ)
141	Adenosine accelerates the healing of diabetic ischemic ulcers by improving autophagy of endothelial progenitor cells grown on a biomaterial.	Chen W, Wu Y, Li L, Yang M, Shen L, Liu G, Tan J, Zeng W, Zhu C.	Sci Rep. 2015	2015	Streptozotocin (STZ)
143	Alginate and DNA Gels Are Suitable Delivery Systems for Diabetic Wound Healing.	Tellechea A, Silva EA, Min J, Leal EC, Auster ME, Pradhan-Nabzdyk L, Shih W, Mooney DJ, Veves A.	Int J Low Extrem Wounds. 2015	2015	Streptozotocin (STZ)
144	FOXO1 differentially regulates both normal and diabetic wound healing.	Zhang C, Ponugoti B, Tian C, Xu F, Tarapore R, Batres A, Alsadun S, Lim J, Dong G, Graves DT.	J Cell Biol. 2015	2015	Streptozotocin (STZ)
148	Substance P promotes wound healing in diabetes by modulating inflammation and macrophage phenotype.	Leal EC, Carvalho E, Tellechea A, Kafanas A, Tecilazich F, Kearney C, Kuchibhotla S, Auster ME, Kokkotou E, Mooney DJ, LoGerfo FW, Pradhan-Nabzdyk L, Veves A.	Am J Pathol. 2015	2015	Streptozotocin (STZ)
150	Inhibition of PAI-1 Via PAI-039 Improves Dermal Wound Closure in Diabetes.	Rebalka IA, Raleigh MJ, D'Souza DM, Coleman SK, Rebalka AN, Hawke TJ.	Diabetes. 2015	2015	Streptozotocin (STZ)
151	Suppressed recruitment of alternatively activated macrophages reduces TGF- β 1 and impairs wound healing in streptozotocin-induced diabetic mice.	Okizaki S, Ito Y, Hosono K, Oba K, Ohkubo H, Amano H, Shichiri M, Majima M.	Biomed Pharmacother. 2015	2015	Streptozotocin (STZ)
153	Therapeutic Potential of Adipose-Derived SSEA-3-Positive Muse Cells for Treating Diabetic Skin Ulcers.	Kinoshita K, Kuno S, Ishimine H, Aoi N, Mineda K, Kato H, Doi K, Kanayama K, Feng J, Mashiko T, Kurisaki A, Yoshimura K.	Stem Cells Transl Med. 2015	2015	Streptozotocin (STZ)
157	The role of mast cells in cutaneous wound healing in streptozotocin-induced diabetic mice.	Nishikori Y, Shiota N, Okunishi H.	Arch Dermatol Res. 2014	2014	Streptozotocin (STZ)

158	Processing of CXCL12 impedes the recruitment of endothelial progenitor cells in diabetic wound healing.	Feng G, Hao D, Chai J.	FEBS J. 2014	2014	Streptozotocin (STZ)
161	An application of embryonic skin cells to repair diabetic skin wound: a wound reparation trail.	Qian de J, Guo XK, Duan HC, Han ZH, Meng F, Liu J, Wang Y.	Exp Biol Med (Maywood). 2014	2014	Streptozotocin (STZ)
162	Proinsulin C-peptide prevents impaired wound healing by activating angiogenesis in diabetes.	Lim YC, Bhatt MP, Kwon MH, Park D, Na S, Kim YM, Ha KS.	J Invest Dermatol. 2015	2015	Streptozotocin (STZ)
163	Galectin-1 accelerates wound healing by regulating the neuropilin-1/Smad3/NOX4 pathway and ROS production in myofibroblasts.	Lin YT, Chen JS, Wu MH, Hsieh IS, Liang CH, Hsu CL, Hong TM, Chen YL.	J Invest Dermatol. 2015	2015	Streptozotocin (STZ)
164	Reduction of ARNT in myeloid cells causes immune suppression and delayed wound healing.	Scott C, Bonner J, Min D, Boughton P, Stokes R, Cha KM, Walters SN, Maslowski K, Sierro F, Grey ST, Twigg S, McLennan S, Gunton JE.	Am J Physiol Cell Physiol. 2014	2014	Streptozotocin (STZ)
169	GTP cyclohydrolase I prevents diabetic-impaired endothelial progenitor cells and wound healing by suppressing oxidative stress/thrombospondin-1.	Tie L, Chen LY, Chen DD, Xie HH, Channon KM, Chen AF.	Am J Physiol Endocrinol Metab. 2014	2014	Streptozotocin (STZ)
172	Selective blockade of estrogen receptor beta improves wound healing in diabetes.	Sunkari VG, Botusan IR, Savu O, GrÅ¼nler J, Zheng X, Gustafsson JÅ., Brismar K, Catrina SB.	Endocrine. 2014	2014	Streptozotocin (STZ)
174	Genetic reduction of vascular endothelial growth factor receptor 2 rescues aberrant angiogenesis caused by epsin deficiency.	Tessneer KL, Pasula S, Cai X, Dong Y, McManus J, Liu X, Yu L, Hahn S, Chang B, Chen Y, Griffin C, Xia L, Adams RH, Chen H.	Arterioscler Thromb Vasc Biol. 2014	2014	Streptozotocin (STZ)
177	Neurotensin-loaded collagen dressings reduce inflammation and improve wound healing in diabetic mice.	Moura LI, Dias AM, Suesca E, Casadiegos S, Leal EC, Fontanilla MR, Carvalho L, de Sousa HC, Carvalho E.	Biochim Biophys Acta. 2014	2014	Streptozotocin (STZ)
178	Chitosan-based dressings loaded with neurotensin-an efficient strategy to improve early diabetic wound healing	Moura, LIF. et al 2014 [54]	Acta Materialia	2013	Streptozotocin (STZ)
180	Loss of innervation and axon plasticity accompanies impaired diabetic wound healing.	Cheng C, Singh V, Krishnan A, Kan M, Martinez JA, Zochodne DW.	PLoS One. 2013	2013	Streptozotocin (STZ)

183	Enhanced growth of endothelial precursor cells on PCG-matrix facilitates accelerated, fibrosis-free, wound healing: a diabetic mouse model.	Kanitkar M, Jaiswal A, Deshpande R, Bellare J, Kale VP.	PLoS One. 2013	2013	Streptozotocin (STZ)
184	Vasculoprotective effects of combined endothelial progenitor cells and mesenchymal stem cells in diabetic wound care: their potential role in decreasing wound-oxidative stress.	Sukpat S, Isarasena N, Wongphoom J, Patumraj S.	Biomed Res Int. 2013	2013	Streptozotocin (STZ)
185	Amelioration in wound healing in diabetic toll-like receptor-4 knockout mice.	Dasu MR, Jialal I.	J Diabetes Complications. 2013	2013	Streptozotocin (STZ)
186	Quality-control culture system restores diabetic endothelial progenitor cell vasculogenesis and accelerates wound closure.	Tanaka R, Vaynrub M, Masuda H, Ito R, Kobori M, Miyasaka M, Mizuno H, Warren SM, Asahara T.	Diabetes. 2013	2013	Streptozotocin (STZ)
187	Accelerated healing of diabetic wound using artificial dermis constructed with adipose stem cells and poly (L-glutamic acid)/chitosan scaffold.	Shen T, Pan ZG, Zhou X, Hong CY.	Chin Med J (Engl). 2013	2013	Streptozotocin (STZ)
188	The influence of Flightless I on Toll-like-receptor-mediated inflammation in a murine model of diabetic wound healing.	Ruzehaji N, Mills SJ, Melville E, Arkell R, Fitridge R, Cowin AJ.	Biomed Res Int. 2013	2013	Streptozotocin (STZ)
189	Camel whey protein enhances diabetic wound healing in a streptozotocin-induced diabetic mouse model: the critical role of β -Defensin-1, -2 and -3.	Badr G.	Lipids Health Dis. 2013	2013	Streptozotocin (STZ)
191	Microfluidic wound bandage: localized oxygen modulation of collagen maturation.	Lo JF, Brennan M, Merchant Z, Chen L, Guo S, Eddington DT, DiPietro LA.	Wound Repair Regen. 2013	2013	Streptozotocin (STZ)
194	Soluble ST2 is regulated by p75 neurotrophin receptor and predicts mortality in diabetic patients with critical limb ischemia.	Caporali A, Meloni M, Miller AM, Vierlinger K, Cardinali A, Spinetti G, Nailor A, Faglia E, Losa S, Gotti A, Fortunato O, Mitic T, Hofner M, Noehammer C, Madeddu P, Emanuelli C.	Arterioscler Thromb Vasc Biol. 2012	2012	Streptozotocin (STZ)
195	Pseudomonas aeruginosa biofilms perturb wound resolution and antibiotic tolerance in diabetic mice.	Watters C, DeLeon K, Trivedi U, Griswold JA, Lyte M, Hampel KJ, Wargo MJ, Rumbaugh KP.	Med Microbiol Immunol. 2013	2013	Streptozotocin (STZ)

197	Genistein accelerates refractory wound healing by suppressing superoxide and FoxO1/iNOS pathway in type 1 diabetes.	Tie L, An Y, Han J, Xiao Y, Xiaokaiti Y, Fan S, Liu S, Chen AF, Li X.	J Nutr Biochem. 2013	2013	Streptozotocin (STZ)
198	Treatment of diabetic mice with undenatured whey protein accelerates the wound healing process by enhancing the expression of MIP-1 α , MIP-2, KC, CX3CL1 and TGF- β 2 in wounded tissue.	Badr G, Badr BM, Mahmoud MH, Mohany M, Rabah DM, Garraud O.	BMC Immunol. 2012	2012	Streptozotocin (STZ)
201	Ganoderma lucidum polysaccharide accelerates refractory wound healing by inhibition of mitochondrial oxidative stress in type 1 diabetes.	Tie L, Yang HQ, An Y, Liu SQ, Han J, Xu Y, Hu M, Li WD, Chen AF, Lin ZB, Li XJ.	Cell Physiol Biochem. 2012	2012	Streptozotocin (STZ)
202	Supplementation with undenatured whey protein during diabetes mellitus improves the healing and closure of diabetic wounds through the rescue of functional long-lived wound macrophages.	Badr G.	Cell Physiol Biochem. 2012	2012	Streptozotocin (STZ)
204	Pressure ulcers: description of a new model and use of mesenchymal stem cells for repair.	de la Garza-Rodea AS, Knaflitz-Shanzer S, van Bekkum DW.	Dermatology. 2011	2011	Streptozotocin (STZ)
205	Pressure ulcers: description of a new model and use of mesenchymal stem cells for repair.	de la Garza-Rodea AS, Knaflitz-Shanzer S, van Bekkum DW.	Dermatology. 2011	2011	Streptozotocin (STZ)
209	Effect of selenium on connexin expression, angiogenesis, and antioxidant status in diabetic wound healing.	Bajpai S, Mishra M, Kumar H, Tripathi K, Singh SK, Pandey HP, Singh RK.	Biol Trace Elem Res. 2011	2011	Streptozotocin (STZ)
211	Fibronectin potentiates topical erythropoietin-induced wound repair in diabetic mice.	Hamed S, Ullmann Y, Egozi D, Daod E, Hellou E, Ashkar M, Gilhar A, Teot L.	J Invest Dermatol. 2011	2011	Streptozotocin (STZ)
214	Defective recruitment, survival and proliferation of bone marrow-derived progenitor cells at sites of delayed diabetic wound healing in mice	Albiero, M. et al 2011 [37]	Diabetologia	2011	Streptozotocin (STZ)
218	Skin wound healing in diabetic β 6 integrin-deficient mice.	Jacobsen JN, Steffensen B, Hämäläinen L, Krogfelt KA, Larjava HS.	APMIS. 2010	2010	Streptozotocin (STZ)
219	TLR2 expression and signaling-dependent inflammation impair wound healing in diabetic mice.	Dasu MR, Thangappan RK, Bourgette A, DiPietro LA, Isseroff R, Jialal I.	Lab Invest. 2010	2010	Streptozotocin (STZ)

222	The redox enzyme p66Shc contributes to diabetes and ischemia-induced delay in cutaneous wound healing.	Fadini GP, Albiero M, Menegazzo L, Boscaro E, Pagnin E, Iori E, Cosma C, Lapolla A, Pengo V, Stendardo M, Agostini C, Pelicci PG, Giorgio M, Avogaro A.	Diabetes. 2010	2010	Streptozotocin (STZ)
226	Granulocyte-macrophage colony-stimulating factor enhances wound healing in diabetes via upregulation of proinflammatory cytokines.	Fang Y, Shen J, Yao M, Beagley KW, Hambly BD, Bao S.	Br J Dermatol. 2010	2010	Streptozotocin (STZ)
228	Sonic hedgehog improves delayed wound healing via enhancing cutaneous nitric oxide function in diabetes.	Luo JD, Hu TP, Wang L, Chen MS, Liu SM, Chen AF.	Am J Physiol Endocrinol Metab. 2009	2009	Streptozotocin (STZ)
230	Human CD133+ progenitor cells promote the healing of diabetic ischemic ulcers by paracrine stimulation of angiogenesis and activation of Wnt signaling.	Barcelos LS, Duplaa C, KrÄnkel N, Graiani G, Invernici G, Katare R, Siragusa M, Meloni M, Campesi I, Monica M, Simm A, Campagnolo P, Mangialardi G, Stevanato L, Alessandri G, Emanuelli C, Madeddu P.	Circ Res. 2009	2009	Streptozotocin (STZ)
231	Endothelium-specific GTP cyclohydrolase I overexpression accelerates refractory wound healing by suppressing oxidative stress in diabetes.	Tie L, Li XJ, Wang X, Channon KM, Chen AF.	Am J Physiol Endocrinol Metab. 2009	2009	Streptozotocin (STZ)
232	Effect of fenofibrate on microcirculation and wound healing in healthy and diabetic mice.	Valentin S, Rudolph J, Goertz O, Botteck N, Langer S, Schneider S.	Eur J Med Res. 2009	2009	Streptozotocin (STZ)
234	Sonoporation of the minicircle-VEGF(165) for wound healing of diabetic mice.	Yoon CS, Jung HS, Kwon MJ, Lee SH, Kim CW, Kim MK, Lee M, Park JH.	Pharm Res. 2009	2009	Streptozotocin (STZ)
236	High-Mobility Group Box 1 Protein in Human and Murine Skin : Involvement in Wound Healing	Straino, S. et al 2008 [30]	The Society for Investigate Dermatology	2008	Streptozotocin (STZ)

242	Diabetic impairments in NO-mediated endothelial progenitor cell mobilization and homing are reversed by hyperoxia and SDF-1 alpha.	Gallagher KA, Liu ZJ, Xiao M, Chen H, Goldstein LJ, Buerk DG, Nedeau A, Thom SR, Velazquez OC.	J Clin Invest. 2007	2007	Streptozotocin (STZ)
243	Placenta growth factor in diabetic wound healing: altered expression and therapeutic potential.	Cianfarani F, Zambruno G, Brogelli L, Sera F, Lacal PM, Pesce M, Capogrossi MC, Failla CM, Napolitano M, Odorisio T.	Am J Pathol. 2006	2006	Streptozotocin (STZ)
252	Gene therapy of endothelial nitric oxide synthase and manganese superoxide dismutase restores delayed wound healing in type 1 diabetic mice.	Luo JD, Wang YY, Fu WL, Wu J, Chen AF.	Circulation. 2004	2004	Streptozotocin (STZ)
253	Nerve growth factor promotes reparative angiogenesis and inhibits endothelial apoptosis in cutaneous wounds of Type 1 diabetic mice	Graiani, G. et al 2004 [25]	Diabetologia	2004	Streptozotocin (STZ)
259	Adenovirus-mediated VEGF(165) gene transfer enhances wound healing by promoting angiogenesis in CD1 diabetic mice.	Romano Di Peppe S, Mangoni A, Zambruno G, Spinetti G, Melillo G, Napolitano M, Capogrossi MC.	Gene Ther. 2002	2002	Streptozotocin (STZ)
122	Overexpressing IRS1 in Endothelial Cells Enhances Angioblast Differentiation and Wound Healing in Diabetes and Insulin Resistance.	Katagiri S, Park K, Maeda Y, Rao TN, Khamaisi M, Li Q, Yokomizo H, Mima A, Lancerotto L, Wagers A, Orgill DP, King GL.	Diabetes. 2016	2016	Streptozotocin (STZ) and High Fat Diet (HFD)
65	PEGylated graphene oxide-mediated quercetin-modified collagen hybrid scaffold for enhancement of MSCs differentiation potential and diabetic wound healing.	Chu J, Shi P, Yan W, Fu J, Yang Z, He C, Deng X, Liu H.	Nanoscale. 2018	2018	Streptozotocin and High Fat Diet (STZ + HFD)
71	Dynamic multiphoton imaging of acellular dermal matrix scaffolds seeded with mesenchymal stem cells in diabetic wound healing	Chu J, Shi P, Deng X, Jin Y, Liu H, Chen M, Han X, Liu H.	J Biophotonics	2018	Streptozotocin and High Fat Diet (STZ + HFD)
76	Sheng-ji Hua-yu formula promotes diabetic wound healing of re-epithelization via Activin/Follistatin regulation.	Kuai L, Zhang JT, Deng Y, Xu S, Xu XZ, Wu MF, Guo DJ, Chen Y, Wu RJ, Zhao XQ, Nian H, Li B, Li FL.	BMC Complement Altern Med. 2018	2018	Streptozotocin and High Fat Diet (STZ + HFD)

134	Co-Transplantation of Skin-Derived Precursors and Collagen Sponge Facilitates Diabetic Wound Healing by Promoting Local Vascular Regeneration.	Ke T, Yang M, Mao D, Zhu M, Che Y, Kong D, Li C.	Cell Physiol Biochem. 2015	2015	Streptozotocin and High Fat Diet (STZ + HFD)
155	Mesenchymal stromal cells enhance wound healing by ameliorating impaired metabolism in diabetic mice.	Gao D, Gu C, Wu Y, Xie J, Yao B, Li J, Feng C, Wang J, Wu X, Huang S, Fu X.	Cytotherapy. 2014	2014	Streptozotocin and High Fat Diet (STZ + HFD)
37	Heparin-ploxamer hydrogel-encapsulated rhFGF21 enhances wound healing in diabetic mice	Liu H, Zhao Y, Zou Y, Huang W, Zhu L, Liu F, Wang D, Guo K, Hu J, Chen J, Ye L, Li X, Lin L.	FASEB J	2019	Streptozotocin and High Fat Diet (STZ + HFD)
262	Wound healing is accelerated by agonists of adenosine A2 (G alpha s-linked) receptors.	Montesinos MC, Gadangi P, Longaker M, Sung J, Levine J, Nilsen D, Reibman J, Li M, Jiang CK, Hirschhorn R, Recht PA, Ostad E, Levin RI, Cronstein BN.	J Exp Med. 1997	1997	Wild type (+/+)

Supplementary table S3. Evaluation of heterogeneity (τ and I^2) and the global inconsistency at each time point.

Time point	Heterogeneity τ	Heterogeneity I^2	Cochrane Q (between design)	Cochrane Q (design-by-treatment interaction)
Day 3	1.1667	83.2%	89.92 (p<0.0001)	13.18 (p=0.512)
Day 7	1.5667	88.3%	107.59 (p<0.0001)	16.48 (p=0.420)
Day 11	1.6011	88.4%	77.44 (p<0.0001)	8.55 (p=0.479)
Day 15	1.5997	88.9%	97.45 (p<0.0001)	11.95 (p=0.154)

Supplementary table S4. Evaluation of the inconsistency using the Separate indirect from direct evidence (SIDE) back calculation method at day 3, 7, 11, and 15.

Comparisons at Day 3	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (SMD) in network meta-analysis	Estimated treatment effect (SMD) derived from direct evidence	Estimated treatment effect (SMD) derived from indirect evidence.	Difference between direct and indirect treatment estimates	z-value of test for disagreement (direct versus indirect)	p-value of test for disagreement (direct versus indirect)
akita:alloxan	0	0	0.57	.	0.57	.	.	.
akita:cNZO1	0	0	0.90	.	0.90	.	.	.
akita:db_db	1	0.67	-0.62	-0.47	-0.95	0.48	0.23	0.81
akita:db_het	0	0	1.10	.	1.10	.	.	.
akita:high_fat_diet	0	0	0.15	.	0.15	.	.	.
akita:ob_ob	0	0	-0.75	.	-0.75	.	.	.
akita:other_DM_model	0	0	0.31	.	0.31	.	.	.
akita:STZ	1	0.67	-0.26	0.19	-1.17	1.36	0.65	0.51
akita:STZhigh_fat_diet	0	0	-0.80	.	-0.80	.	.	.
akita:wild_type	1	0.67	0.98	0.38	2.20	-1.82	-0.88	0.37
alloxan:cNZO1	0	0	0.33	.	0.33	.	.	.
alloxan:db_db	0	0	-1.19	.	-1.19	.	.	.
alloxan:db_het	0	0	0.54	.	0.54	.	.	.
alloxan:high_fat_diet	0	0	-0.41	.	-0.41	.	.	.
alloxan:ob_ob	0	0	-1.31	.	-1.31	.	.	.
alloxan:other_DM_model	0	0	-0.26	.	-0.26	.	.	.
alloxan:STZ	0	0	-0.83	.	-0.83	.	.	.
alloxan:STZhigh_fat_diet	0	0	-1.37	.	-1.37	.	.	.
alloxan:wild_type	6	1.00	0.41	0.41

cNZO1:db_db	0	0	-1.52	.	-1.52	.	.	.
cNZO1:db_het	0	0	0.21	.	0.21	.	.	.
cNZO1:high_fat_diet	0	0	-0.75	.	-0.75	.	.	.
cNZO1:ob_ob	0	0	-1.65	.	-1.65	.	.	.
cNZO1:other_DM_model	0	0	-0.59	.	-0.59	.	.	.
cNZO1:STZ	0	0	-1.16	.	-1.16	.	.	.
cNZO1:STZhigh_fat_diet	0	0	-1.70	.	-1.70	.	.	.
cNZO1:wild_type	2	1.00	0.08	0.08
db_db:db_het	34	0.99	1.73	1.72	2.34	-0.62	-0.27	0.78
db_db:high_fat_diet	1	0.19	0.78	0.06	0.95	-0.89	-0.63	0.53
db_db:ob_ob	1	0.20	-0.12	0.09	-0.17	0.27	0.19	0.85
db_db:other_DM_model	1	0.15	0.93	0.26	1.05	-0.79	-0.57	0.56
db_db:STZ	8	0.16	0.37	1.29	0.19	1.10	2.20	0.02
db_db:STZhigh_fat_diet	0	0	-0.17	.	-0.17	.	.	.
db_db:wild_type	70	0.91	1.60	1.52	2.39	-0.86	-1.62	0.10
db_het:high_fat_diet	0	0	-0.95	.	-0.95	.	.	.
db_het:ob_ob	0	0	-1.85	.	-1.85	.	.	.
db_het:other_DM_model	0	0	-0.80	.	-0.80	.	.	.
db_het:STZ	0	0	-1.36	.	-1.36	.	.	.
db_het:STZhigh_fat_diet	0	0	-1.90	.	-1.90	.	.	.
db_het:wild_type	1	0.04	-0.13	0.22	-0.14	0.36	0.27	0.78
high_fat_diet:ob_ob	0	0	-0.90	.	-0.90	.	.	.
high_fat_diet:other_DM_model	0	0	0.15	.	0.15	.	.	.
high_fat_diet:STZ	0	0	-0.41	.	-0.41	.	.	.
high_fat_diet:STZhigh_fat_diet	1	0.25	-0.95	-0.46	-1.11	0.65	0.45	0.65
high_fat_diet:wild_type	5	0.88	0.82	0.66	2.02	-1.36	-0.81	0.41
ob_ob:other_DM_model	1	0.30	1.05	0.16	1.43	-1.26	-0.83	0.40
ob_ob:STZ	0	0	0.49	.	0.49	.	.	.
ob_ob:STZhigh_fat_diet	0	0	-0.05	.	-0.05	.	.	.

ob_ob:wild_type	5	0.91	1.72	1.70	1.93	-0.23	-0.11	0.90
other_DM_model:STZ	0	0	-0.57	.	-0.57	.	.	.
other_DM_model:STZhigh_fat_diet	0	0	-1.11	.	-1.11	.	.	.
other_DM_model:wild_type	7	0.94	0.67	0.52	2.86	-2.33	-1.18	0.23
STZ:STZhigh_fat_diet	0	0	-0.54	.	-0.54	.	.	.
STZ:wild_type	139	0.96	1.24	1.28	0.20	1.07	1.85	0.06
STZhigh_fat_diet:wild_type	14	0.98	1.78	1.76	2.58	-0.82	-0.32	0.75

Comparisons at Day 7	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (SMD) in network meta-analysis	Estimated treatment effect (SMD) derived from direct evidence	Estimated treatment effect (SMD) derived from indirect evidence.	Difference between direct and indirect treatment estimates	z-value of test for disagreement (direct versus indirect)	p-value of test for disagreement (direct versus indirect)
akita:alloxan	0	0	-0.87	.	-0.87	.	.	.
akita:cNZO1	0	0	1.00	.	1.00	.	.	.
akita:db_db	1	0.67	-1.21	-0.71	-2.24	1.53	0.55	0.58
akita:db_het	0	0	1.88	.	1.88	.	.	.
akita:high_fat_diet	0	0	-0.49	.	-0.49	.	.	.
akita:ob_ob	0	0	-1.32	.	-1.32	.	.	.
akita:other_DM_model	0	0	-0.32	.	-0.32	.	.	.
akita:STZ	1	0.67	-0.36	0.13	-1.37	1.50	0.54	0.58
akita:STZhigh_fat_diet	0	0	-1.58	.	-1.58	.	.	.
akita:wild_type	1	0.67	1.35	0.36	3.36	-3.00	-1.09	0.27
alloxan:cNZO1	0	0	1.88	.	1.88	.	.	.
alloxan:db_db	0	0	-0.34	.	-0.34	.	.	.
alloxan:db_het	0	0	2.75	.	2.75	.	.	.
alloxan:high_fat_diet	0	0	0.38	.	0.38	.	.	.
alloxan:ob_ob	0	0	-0.44	.	-0.44	.	.	.
alloxan:other_DM_model	0	0	0.55	.	0.55	.	.	.
alloxan:STZ	0	0	0.51	.	0.51	.	.	.
alloxan:STZhigh_fat_diet	0	0	-0.70	.	-0.70	.	.	.
alloxan:wild_type	5	1.00	2.22	2.22
cNZO1:db_db	0	0	-2.22	.	-2.22	.	.	.
cNZO1:db_het	0	0	0.88	.	0.88	.	.	.
cNZO1:high_fat_diet	0	0	-1.50	.	-1.50	.	.	.

cNZO1:ob_ob	0	0	-2.32	.	-2.32	.	.	.
cNZO1:other_DM_model	0	0	-1.33	.	-1.33	.	.	.
cNZO1:STZ	0	0	-1.37	.	-1.37	.	.	.
cNZO1:STZhigh_fat_diet	0	0	-2.58	.	-2.58	.	.	.
cNZO1:wild_type	3	1.00	0.35	0.35
db_db:db_het	32	0.99	3.09	3.11	2.13	0.98	0.35	0.72
db_db:high_fat_diet	1	0.16	0.72	-0.20	0.90	-1.10	-0.61	0.54
db_db:ob_ob	1	0.14	-0.11	0.20	-0.15	0.35	0.20	0.84
db_db:other_DM_model	1	0.13	0.89	0.36	0.97	-0.61	-0.34	0.73
db_db:STZ	7	0.12	0.85	2.56	0.62	1.94	2.82	0.004
db_db:STZhigh_fat_diet	0	0	-0.37	.	-0.37	.	.	.
db_db:wild_type	85	0.93	2.56	2.45	4.09	-1.64	-2.24	0.02
db_het:high_fat_diet	0	0	-2.37	.	-2.37	.	.	.
db_het:ob_ob	0	0	-3.20	.	-3.20	.	.	.
db_het:other_DM_model	0	0	-2.20	.	-2.20	.	.	.
db_het:STZ	0	0	-2.24	.	-2.24	.	.	.
db_het:STZhigh_fat_diet	0	0	-3.46	.	-3.46	.	.	.
db_het:wild_type	1	0.05	-0.53	-0.60	-0.53	-0.08	-0.05	0.96
high_fat_diet:ob_ob	1	0.22	-0.83	-1.55	-0.62	-0.94	-0.47	0.63
high_fat_diet:other_DM_model	0	0	0.17	.	0.17	.	.	.
high_fat_diet:STZ	0	0	0.13	.	0.13	.	.	.
high_fat_diet:STZhigh_fat_diet	1	0.21	-1.09	-0.98	-1.12	0.14	0.07	0.94
high_fat_diet:wild_type	6	0.84	1.84	1.98	1.11	0.87	0.50	0.61
ob_ob:other_DM_model	1	0.23	1.00	0.16	1.25	-1.09	-0.58	0.56
ob_ob:STZ	0	0	0.96	.	0.96	.	.	.
ob_ob:STZhigh_fat_diet	0	0	-0.26	.	-0.26	.	.	.
ob_ob:wild_type	8	0.90	2.67	2.63	3.04	-0.41	-0.21	0.83
other_DM_model:STZ	0	0	-0.04	.	-0.04	.	.	.
other_DM_model:STZhigh_fat_diet	0	0	-1.26	.	-1.26	.	.	.

other_DM_model:wild_type	8	0.94	1.67	1.51	4.33	-2.82	-1.13	0.25
STZ:STZhigh_fat_diet	0	0	-1.22	.	-1.22	.	.	.
STZ:wild_type	151	0.97	1.71	1.78	-0.38	2.15	2.65	0.008
STZhigh_fat_diet:wild_type	15	0.98	2.93	2.91	3.63	-0.72	-0.22	0.82

Comparisons at Day 11	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (SMD) in network meta-analysis	Estimated treatment effect (SMD) derived from direct evidence	Estimated treatment effect (SMD) derived from indirect evidence.	Difference between direct and indirect treatment estimates	z-value of test for disagreement (direct versus indirect)	p-value of test for disagreement (direct versus indirect)
akita:alloxan	0	0	-0.57	.	-0.57	.	.	.
akita:cNZO1	0	0	1.05	.	1.05	.	.	.
akita:db_db	1	0.67	-1.33	-1.03	-1.96	0.94	0.33	0.74
akita:db_het	0	0	2.24	.	2.24	.	.	.
akita:ob_ob	0	0	-1.13	.	-1.13	.	.	.
akita:other_DM_model	0	0	1.45	.	1.45	.	.	.
akita:STZ	1	0.67	-0.33	0.31	-1.64	1.96	0.69	0.48
akita:STZhigh_fat_diet	0	0	-1.29	.	-1.29	.	.	.
akita:wild_type	1	0.67	1.48	0.54	3.40	-2.86	-1.02	0.30
alloxan:cNZO1	0	0	1.62	.	1.62	.	.	.
alloxan:db_db	0	0	-0.76	.	-0.76	.	.	.
alloxan:db_het	0	0	2.81	.	2.81	.	.	.
alloxan:ob_ob	0	0	-0.56	.	-0.56	.	.	.
alloxan:other_DM_model	0	0	2.02	.	2.02	.	.	.
alloxan:STZ	0	0	0.24	.	0.24	.	.	.
alloxan:STZhigh_fat_diet	0	0	-0.72	.	-0.72	.	.	.
alloxan:wild_type	4	1.00	2.05	2.05
cNZO1:db_db	0	0	-2.38	.	-2.38	.	.	.
cNZO1:db_het	0	0	1.19	.	1.19	.	.	.
cNZO1:ob_ob	0	0	-2.18	.	-2.18	.	.	.
cNZO1:other_DM_model	0	0	0.40	.	0.40	.	.	.
cNZO1:STZ	0	0	-1.38	.	-1.38	.	.	.

cNZO1:STZhigh_fat_diet	0	0	-2.34	.	-2.34	.	.	.
cNZO1:wild_type	1	1.00	0.43	0.43
db_db:db_het	25	0.98	3.58	3.65	-0.56	4.22	1.52	0.12
db_db:ob_ob	1	0.44	0.21	-0.78	0.98	-1.76	-0.78	0.43
db_db:other_DM_model	0	0	2.78	.	2.78	.	.	.
db_db:STZ	8	0.17	1.01	1.99	0.81	1.18	1.71	0.08
db_db:STZhigh_fat_diet	0	0	0.04	.	0.04	.	.	.
db_db:wild_type	65	0.91	2.82	2.68	4.14	-1.45	-1.98	0.04
db_het:ob_ob	0	0	-3.37	.	-3.37	.	.	.
db_het:other_DM_model	0	0	-0.80	.	-0.80	.	.	.
db_het:STZ	0	0	-2.57	.	-2.57	.	.	.
db_het:STZhigh_fat_diet	0	0	-3.53	.	-3.53	.	.	.
db_het:wild_type	1	0.06	-0.76	1.00	-0.88	1.88	1.10	0.27
ob_ob:other_DM_model	0	0	2.58	.	2.58	.	.	.
ob_ob:STZ	0	0	0.80	.	0.80	.	.	.
ob_ob:STZhigh_fat_diet	0	0	-0.16	.	-0.16	.	.	.
ob_ob:wild_type	2	0.85	2.61	2.35	4.07	-1.72	-0.55	0.57
other_DM_model:STZ	0	0	-1.78	.	-1.78	.	.	.
other_DM_model:STZhigh_fat_diet	0	0	-2.74	.	-2.74	.	.	.
other_DM_model:wild_type	3	1.00	0.03	0.03
STZ:STZhigh_fat_diet	0	0	-0.96	.	-0.96	.	.	.
STZ:wild_type	104	0.95	1.81	1.87	0.67	1.20	1.56	0.11
STZhigh_fat_diet:wild_type	9	1.00	2.77	2.77
akita:alloxan	0	0	-0.57	.	-0.57	.	.	.
akita:cNZO1	0	0	1.05	.	1.05	.	.	.
akita:db_db	1	0.67	-1.33	-1.03	-1.96	0.94	0.33	0.74
akita:db_het	0	0	2.24	.	2.24	.	.	.
akita:ob_ob	0	0	-1.13	.	-1.13	.	.	.
akita:other_DM_model	0	0	1.45	.	1.45	.	.	.

akita:STZ	1	0.67	-0.33	0.31	-1.64	1.96	0.69	0.48
akita:STZhigh_fat_diet	0	0	-1.29	.	-1.29	.	.	.
akita:wild_type	1	0.67	1.48	0.54	3.40	-2.86	-1.02	0.30
alloxan:cNZO1	0	0	1.62	.	1.62	.	.	.

Comparisons at Day 15	Number of studies providing direct evidence	Direct evidence proportion	Estimated treatment effect (SMD) in network meta-analysis	Estimated treatment effect (SMD) derived from direct evidence	Estimated treatment effect (SMD) derived from indirect evidence.	Difference between direct and indirect treatment estimates	z-value of test for disagreement (direct versus indirect)	p-value of test for disagreement (direct versus indirect)
akita:alloxan	0	0	-0.31	.	-0.31	.	.	.
akita:cNZO1	0	0	0.62	.	0.62	.	.	.
akita:db_db	1	0.68	-1.76	-0.68	-4.00	3.32	1.17	0.24
akita:db_het	0	0	1.31	.	1.31	.	.	.
akita:high_fat_diet	0	0	1.48	.	1.48	.	.	.
akita:ob_ob	0	0	-1.20	.	-1.20	.	.	.
akita:other_DM_model	0	0	1.29	.	1.29	.	.	.
akita:STZ	1	0.67	-0.18	0.11	-0.79	0.91	0.32	0.74
akita:STZhigh_fat_diet	0	0	-0.96	.	-0.96	.	.	.
akita:wild_type	1	0.67	1.48	0.11	4.26	-4.15	-1.47	0.14
alloxan:cNZO1	0	0	0.93	.	0.93	.	.	.
alloxan:db_db	0	0	-1.45	.	-1.45	.	.	.
alloxan:db_het	0	0	1.62	.	1.62	.	.	.
alloxan:high_fat_diet	0	0	1.78	.	1.78	.	.	.
alloxan:ob_ob	0	0	-0.89	.	-0.89	.	.	.
alloxan:other_DM_model	0	0	1.59	.	1.59	.	.	.
alloxan:STZ	0	0	0.13	.	0.13	.	.	.
alloxan:STZhigh_fat_diet	0	0	-0.66	.	-0.66	.	.	.
alloxan:wild_type	3	1.00	1.78	1.78
cNZO1:db_db	0	0	-2.38	.	-2.38	.	.	.
cNZO1:db_het	0	0	0.69	.	0.69	.	.	.
cNZO1:high_fat_diet	0	0	0.86	.	0.86	.	.	.

cNZO1:ob_ob	0	0	-1.82	.	-1.82	.	.	.
cNZO1:other_DM_model	0	0	0.67	.	0.67	.	.	.
cNZO1:STZ	0	0	-0.80	.	-0.80	.	.	.
cNZO1:STZhigh_fat_diet	0	0	-1.58	.	-1.58	.	.	.
cNZO1:wild_type	2	1.00	0.86	0.86
db_db:db_het	25	0.98	3.07	3.11	1.02	2.08	0.75	0.45
db_db:high_fat_diet	0	0	3.23	.	3.23	.	.	.
db_db:ob_ob	1	0.36	0.56	-0.63	1.22	-1.85	-0.88	0.38
db_db:other_DM_model	1	0.24	3.04	0.21	3.95	-3.74	-1.93	0.05
db_db:STZ	5	0.14	1.58	2.48	1.43	1.06	1.24	0.21
db_db:STZhigh_fat_diet	0	0	0.79	.	0.79	.	.	.
db_db:wild_type	50	0.91	3.23	3.14	4.21	-1.07	-1.25	0.21
db_het:high_fat_diet	0	0	0.16	.	0.16	.	.	.
db_het:ob_ob	0	0	-2.51	.	-2.51	.	.	.
db_het:other_DM_model	0	0	-0.03	.	-0.03	.	.	.
db_het:STZ	0	0	-1.49	.	-1.49	.	.	.
db_het:STZhigh_fat_diet	0	0	-2.28	.	-2.28	.	.	.
db_het:wild_type	1	0.07	0.16	0.29	0.15	0.14	0.08	0.93
high_fat_diet:ob_ob	0	0	-2.68	.	-2.68	.	.	.
high_fat_diet:other_DM_model	0	0	-0.19	.	-0.19	.	.	.
high_fat_diet:STZ	0	0	-1.66	.	-1.66	.	.	.
high_fat_diet:STZhigh_fat_diet	0	0	-2.44	.	-2.44	.	.	.
high_fat_diet:wild_type	1	1.00	0.00	0.00
ob_ob:other_DM_model	1	0.49	2.49	0.84	4.10	-3.26	-1.37	0.17
ob_ob:STZ	0	0	1.02	.	1.02	.	.	.
ob_ob:STZhigh_fat_diet	0	0	0.24	.	0.24	.	.	.
ob_ob:wild_type	3	0.85	2.68	2.39	4.33	-1.94	-0.70	0.48
other_DM_model:STZ	0	0	-1.47	.	-1.47	.	.	.
other_DM_model:STZhigh_fat_diet	0	0	-2.25	.	-2.25	.	.	.

other_DM_model:wild_type	4	0.91	0.19	-0.40	5.98	-6.37	-2.30	0.02
STZ:STZhigh_fat_diet	0	0	-0.78	.	-0.78	.	.	.
STZ:wild_type	84	0.96	1.66	1.71	0.56	1.15	1.24	0.21
STZhigh_fat_diet:wild_type	6	1.00	2.44	2.44

Supplementary table S4. League table presenting the results of network meta-analyses at day 3 and 7.

Day 3										
ob/ob	-0.12 (-1.23 to 0.99)	-0.49 (-1.59 to 0.61)	-0.75 (-2.94 to 1.45)	-1.05 (-2.42 to 0.31)	-0.05 (-1.35 to 1.24)	-0.90 (-2.42 to 0.62)	-1.31 (-2.81 to 0.18)	-1.65 (-3.72 to 0.43)	<u>-1.85</u> (-3.05;-0.65)	<u>-1.72</u> (-2.80;-0.64)
-0.11 (-1.30 to 1.09)	db/db	<u>-0.37</u> (-0.72;-0.01)	-0.62 (-2.54 to 1.29)	-0.93 (-1.90 to 0.04)	-0.17 (-0.95 to 0.60)	-0.78 (-1.87 to 0.32)	<u>-1.19</u> (-2.27;-0.11)	-1.52 (-3.32 to 0.27)	<u>-1.73</u> (-2.19;-1.27)	<u>-1.60</u> (-1.90;-1.30)
-0.96 (-2.14 to 0.22)	<u>-0.85</u> (-1.29;-0.41)	STZ	-0.26 (-2.17 to 1.65)	-0.57 (-1.52 to 0.39)	-0.54 (-1.29 to 0.21)	-0.41 (-1.50 to 0.67)	-0.83 (-1.89 to 0.23)	-1.16 (-2.94 to 0.63)	<u>-1.36</u> (-1.94;-0.78)	<u>-1.24</u> (-1.45;-1.02)
-1.32 (-4.11 to 1.47)	-1.21 (-3.76 to 1.34)	-0.36 (-2.91 to 2.18)	Akita	-0.31 (-2.43 to 1.81)	-0.80 (-2.84 to 1.24)	-0.15 (-2.34 to 2.03)	-0.57 (-2.74 to 1.61)	-0.90 (-3.51 to 1.71)	-1.10 (-3.08 to 0.87)	-0.98 (-2.89 to 0.93)
-1.00 (-2.56 to 0.57)	-0.89 (-2.08 to 0.30)	0.04 (-1.13 to 1.21)	-0.32 (-3.11 to 2.46)	Other diabetic model	-1.11 (-2.28 to 0.07)	-0.15 (-1.57 to 1.26)	-0.26 (-1.65 to 1.13)	-0.59 (-2.59 to 1.41)	-0.80 (-1.87 to 0.28)	-0.67 (-1.60 to 0.26)
-0.26 (-1.71 to 1.19)	-0.37 (-1.33 to 0.60)	<u>-1.22</u> (-2.16;-0.28)	-1.58 (-4.27 to 1.12)	-1.26 (-2.71 to 0.20)	STZ + HFD	-0.95 (-2.19 to 0.28)	<u>-1.37</u> (-2.63;-0.11)	-1.70 (-3.61 to 0.21)	<u>-1.90</u> (-2.80;-1.00)	<u>-1.78</u> (-2.49;-1.06)
-0.83 (-2.45 to 0.80)	-0.72 (-2.01 to 0.57)	-0.13 (-1.41 to 1.15)	-0.49 (-3.32 to 2.34)	-0.17 (-1.86 to 1.52)	-1.09 (-2.58 to 0.40)	HFD	-0.41 (-1.90 to 1.07)	-0.75 (-2.81 to 1.32)	-0.95 (-2.14 to 0.24)	-0.82 (-1.89 to 0.24)
-0.44 (-2.34 to 1.45)	-0.34 (-1.89 to 1.22)	-0.51 (-2.05 to 1.03)	-0.87 (-3.83 to 2.08)	-0.55 (-2.45 to 1.34)	-0.70 (-2.47 to 1.06)	-0.38 (-2.35 to 1.58)	Alloxan	-0.33 (-2.39 to 1.72)	-0.54 (-1.71 to 0.64)	-0.41 (-1.45 to 0.63)
<u>-2.32</u> (-4.52;-0.12)	<u>-2.22</u> (-4.13;-0.31)	-1.37 (-3.26 to 0.53)	-1.00 (-4.16 to 2.16)	-1.33 (-3.52 to 0.87)	<u>-2.58</u> (-4.66;-0.50)	-1.50 (-3.75 to 0.76)	-1.88 (-4.29 to 0.53)	NON/NZ	-0.21 (-2.06 to 1.65)	-0.08 (-1.85 to 1.70)
<u>-3.20</u> (-4.54;-1.86)	<u>-3.09</u> (-3.71;-2.48)	<u>-2.24</u> (-2.99;-1.50)	-1.88 (-4.50 to 0.74)	<u>-2.20</u> (-3.54;-0.87)	<u>-3.46</u> (-4.60;-2.32)	-2.37 (-3.80;-0.95)	-2.75 (-4.42;-1.09)	-0.88 (-2.88 to 1.13)	db +/-	-0.13 (-0.67 to 0.42)
<u>-2.67</u> (-3.82;-1.52)	<u>-2.56</u> (-2.92;-2.20)	<u>-1.71</u> (-1.98;-1.44)	-1.35 (-3.89 to 1.19)	<u>-1.67</u> (-2.81;-0.53)	<u>-2.93</u> (-3.83;-2.03)	-1.84 (-3.10;-0.59)	-2.22 (-3.74;-0.71)	-0.35 (-2.22 to 1.53)	-0.53 (-1.24 to 0.17)	Wild type
Day 7										

Data are expressed as standardized mean differences (SMD) with their 95% confidence intervals (95% CI). Underlined results are statistically significant. HFD: high fat diet; NON/NZ: NONcNZO10/LtJ; STZ: streptozotocin.

Supplementary table S5. League table presenting the results of network meta-analyses at day 11 and 15.

Day 11										
ob/ob	-0.21 (-2.40 to 1.99)	-0.80 (-3.01 to 1.40)	-1.13 (-4.52 to 2.26)	-2.58 (-5.48 to 0.32)	-0.16 (-2.66 to 2.34)	..	-0.56 (-3.34 to 2.22)	-2.18 (-6.09 to 1.73)	<u>-3.37</u> (-5.69;-1.06)	<u>-2.61</u> (-4.80;0.43)
-0.56 (-2.54 to 1.43)	db/db	<u>-1.01</u> (-1.52;-0.50)	-1.33 (-3.94 to 1.27)	<u>-2.78</u> (-4.74;-0.83)	-0.04 (-1.33 to 1.24)	..	-0.76 (-2.53 to 1.00)	-2.38 (-5.65 to 0.88)	<u>-3.58</u> (-4.30 to -2.86)	<u>-2.82</u> (-3.23;-2.40)
-1.02 (-3.00 to 0.96)	-1.58 (-2.16;-0.99)	STZ	-0.33 (-2.93 to 2.28)	-1.78 (-3.71 to 0.16)	-0.96 (-2.22 to 0.30)	..	-0.24 (-1.99 to 1.51)	-1.38 (-4.63 to 1.88)	<u>-2.57</u> (-3.45;-1.70)	<u>-1.81</u> (-2.14;-1.48)
-1.20 (-4.44 to 2.04)	-1.76 (-4.37 to 0.85)	-0.18 (-2.78 to 2.42)	Akita	-1.45 (-4.67 to 1.77)	-1.29 (-4.16 to 1.58)	..	-0.57 (-3.69 to 2.54)	-1.05 (-5.20 to 3.10)	-2.24 (-4.95 to 0.46)	-1.48 (-4.08 to 1.11)
<u>-2.49</u> (-4.82;-0.16)	<u>-3.04</u> (-4.67;-1.42)	-1.47 (-3.08 to 0.15)	-1.29 (-4.32 to 1.75)	Other diabetic model	<u>-2.74</u> (-5.00;-0.48)	..	-2.02 (-4.59 to 0.55)	-0.40 (-4.16 to 3.36)	-0.80 (-2.87 to 1.28)	-0.03 (-1.94 to 1.87)
-0.24 (-2.72 to 2.24)	-0.79 (-2.40 to 0.82)	-0.78 (-2.36 to 0.80)	-0.96 (-3.98 to 2.05)	<u>-2.25</u> (-4.45;-0.05)	STZ + HFD	..	-0.72 (-2.83 to 1.39)	-2.34 (-5.80 to 1.12)	<u>-3.58</u> (-4.30;-2.86)	<u>-2.77</u> (-3.99;-1.55)
-2.68 (-6.57 to 1.21)	-3.23 (-6.64 to 0.17)	-1.66 (-5.05 to 1.73)	-1.48 (-5.73 to 2.78)	0.19 (-3.53 to 3.91)	-2.44 (-6.15 to 1.26)	HFD
-0.89 (-3.63 to 1.84)	-1.45 (-3.43 to 0.53)	-0.13 (-2.08 to 1.83)	-0.31 (-3.54 to 2.92)	-1.59 (-4.08 to 0.89)	-0.66 (-3.12 to 1.80)	-1.78 (-5.67 to 2.10)	Alloxan	-1.62 (-5.29 to 2.05)	<u>-2.81</u> (-4.72;-0.91)	-2.05 (-3.77;-0.33)
-1.82 (-4.84 to 1.20)	<u>-2.38</u> (-4.74;-0.01)	-0.80 (-3.14 to 1.54)	-0.62 (-4.10 to 2.86)	-0.67 (-3.47 to 2.13)	-1.58 (-4.36 to 1.20)	-0.86 (-4.95 to 3.23)	-0.93 (-3.93 to 2.08)	NON/NZ	-1.19 (-4.54 to 2.15)	-0.43 (-3.67 to 2.81)
<u>-2.51</u> (-4.62;-0.41)	<u>-3.07</u> (-3.78;-2.36)	<u>-1.49</u> (-2.40;-0.58)	-1.31 (-4.02 to 1.39)	-0.03 (-1.80 to 1.74)	<u>-2.28</u> (-4.03;-0.52)	0.16 (-3.31 to 3.64)	-1.62 (-3.72 to 0.48)	-0.69 (-3.16 to 1.77)	db +/-	-0.76 (-1.58 to 0.06)
<u>-2.68</u> (-4.62;-0.73)	<u>-3.23</u> (-3.71;-2.76)	<u>-1.66</u> (-2.03;-1.29)	-1.48 (-4.08 to 1.12)	-0.19 (-1.76 to 1.38)	<u>-2.44</u> (-3.98;-0.91)	-0.00 (-3.37 to 3.37)	-1.78 (-3.71 to 0.14)	-0.86 (-3.17 to 1.46)	-0.16 (-1.01 to 0.68)	Wild type
Day 15										

Data are expressed as standardized mean differences (SMD) with their 95% confidence intervals (95% CI). Underlined results are statistically significant. .. : Missing data. HFD: high fat diet; NON/NZ: NONcNZO10/LtJ; STZ: streptozotocin.

Table S6. Ranking of mouse model at each time point using P-scores.

	Day 3	Day 7	Day 11	Day 15	Average
db_db	0.83	0.79	0.85	0.93	0.85
STZ + HFD	0.87	0.89	0.82	0.76	0.84
ob_ob	0.83	0.81	0.76	0.80	0.80
STZ	0.64	0.48	0.56	0.59	0.57
akita	0.55	0.44	0.52	0.53	0.51
high_fat_diet	0.49	0.54	..	0.26	0.43
other_DM_model	0.43	0.49	0.23	0.24	0.34
alloxan	0.33	0.66	0.64	0.61	0.56
cNZO1	0.25	0.21	0.33	0.40	0.30
wild_type	0.17	0.14	0.22	0.17	0.17
db_het	0.12	0.03	0.06	0.22	0.11

.. : Missing data. HFD: high fat diet; NON/NZ: NONcNZO10/LtJ; STZ: streptozotocin.

Supplementary table S7. Comparison of wound healing over time between each control mice strains and C57Bl6.

Strain	J3	J7	J11	J15
Balb_c	0.35 [-0.33 to 1.02]	0.61 [-0.16 to 1.37]	0.52 [-0.43 to 1.46]	1.23 [0.19 to 2.26]
CD1	0.46 [-0.59 to 1.51]	-0.09 [-1.46 to 1.28]	2.22 [-0.04 to 4.48]	1.31 [0.19 to 2.26]
FVB_N	0.63 [-0.90 to 2.15]	1.62 [-0.27 to 3.52]	1.36 [-0.96 to 3.68]	1.89 [-0.54 to 4.33]
ICR mice	-0.54 [-1.30 to 0.22]	-1.33 [-2.27 to -0.39]	-0.68 [-1.73 to 0.37]	-0.33 [-1.49 to 0.82]
NODSCID	1.83 [-0.57 to 4.23]	3.18 [1.32 to 5.04]	2.63 [0.72 to 4.55]	1.41 [-1.03 to 3.84]
NODShiLt	0.33 [-2.35 to 3.00]	-0.82 [-4.24 to 2.61]
SCID	0.58 [-1.99 to 3.15]	1.15 [-1.10 to 3.40]	-0.26 [-3.65 to 3.13]	0.18 [-2.31 to 2.68]
SV129	0.03 [-1.38 to 1.44]	0.16 [-1.55 to 1.88]	-0.38 [-3.78 to 3.02]	0.44 [-2.12 to 2.99]
SWR_J	0.80 [-0.03 to 1.56]	-0.37 [-1.49 to 0.75]	-1.02 [-2.20 to 0.17]	-0.91 [-3.14 to 1.32]
C57Bl6_J	reference			

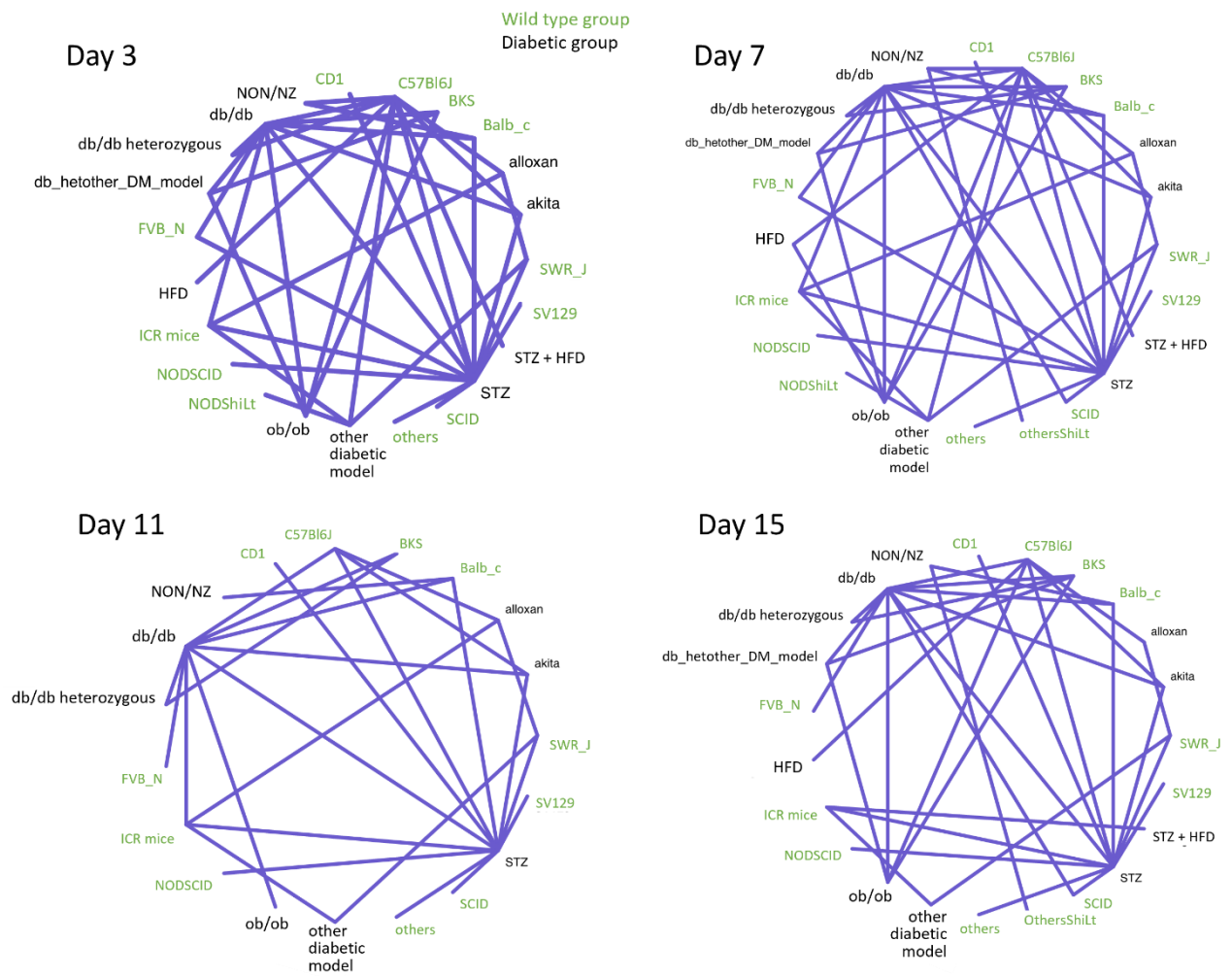
Data are expressed as standardized mean differences (SMD) with their 95% confidence intervals. .. : Missing data.

Supplementary table S8. League table of the frequentist network meta-analysis comparing the impact of strain at day 3.

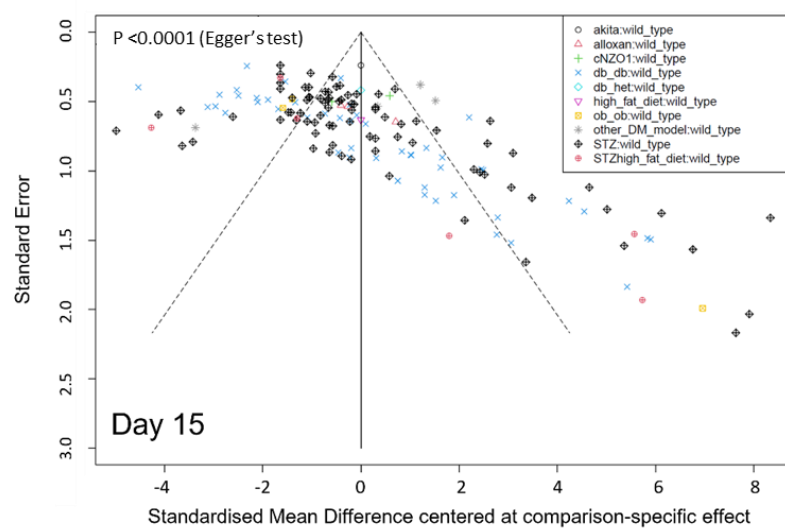
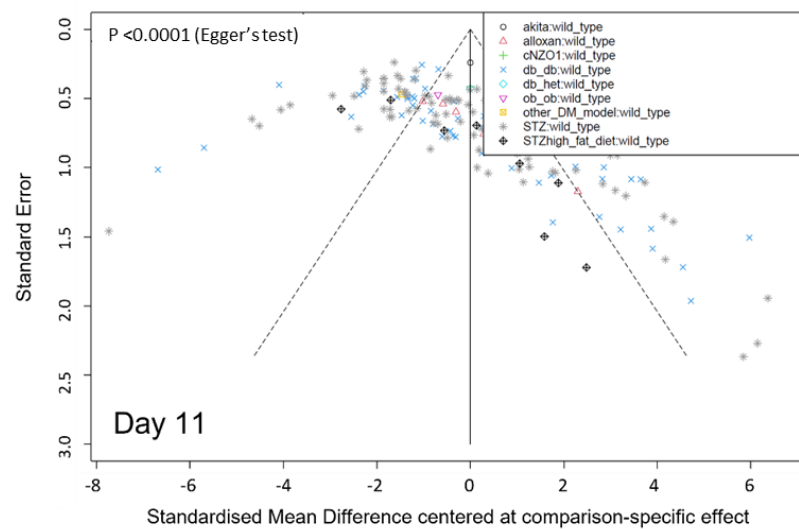
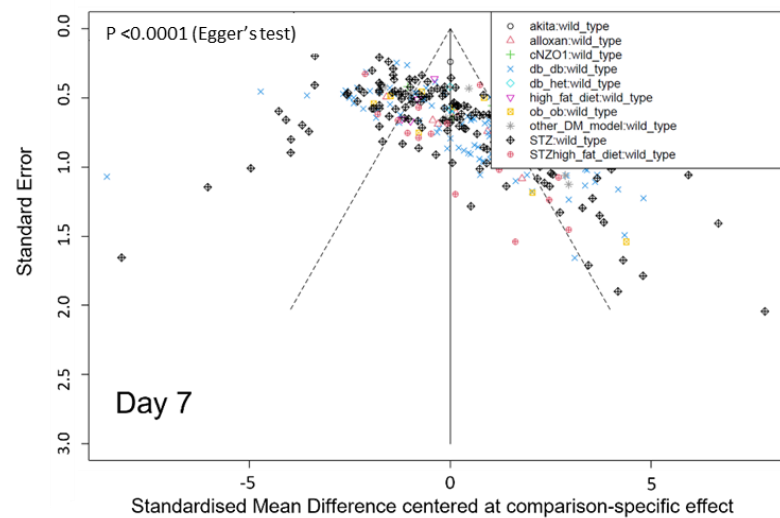
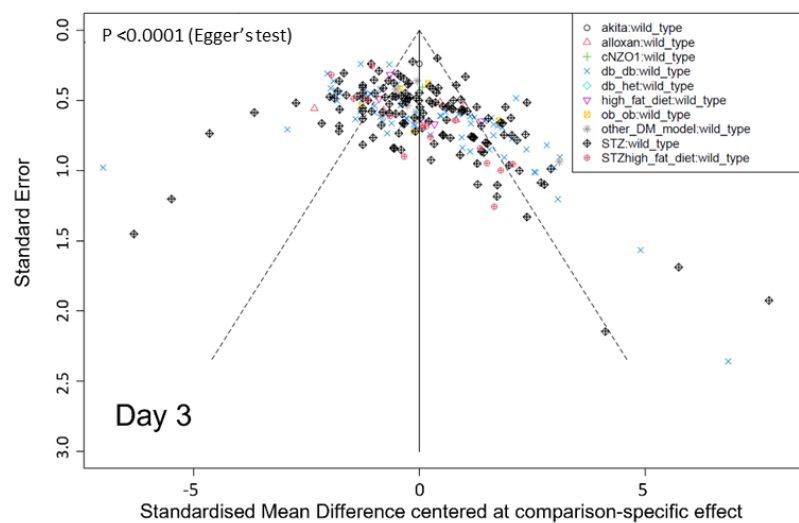
ICR mice										
-0.53 (-1.26 to 0.19)	C57Bl6_J									
-0.58 (-2.13 to 0.96)	-0.05 (-1.46 to 1.36)	SV129								
-0.90 (-1.84 to 0.03)	-0.37 (-1.04 to 0.30)	-0.32 (-1.85 to 1.21)	Balb_c							
-0.87 (-3.58 to 1.84)	-0.34 (-3.00 to 2.33)	-0.29 (-3.29 to 2.72)	0.03 (-2.71 to 2.77)	NODShiLt						
-1.02 (-2.24 to 0.21)	-0.48 (-1.53 to 0.57)	-0.43 (-2.15 to 1.28)	-0.11 (-1.32 to 1.09)	-0.15 (-3.00 to 2.71)	CD1					
-1.14 (-3.78 to 1.51)	-0.60 (-3.17 to 1.97)	-0.55 (-3.46 to 2.35)	-0.23 (-2.87 to 2.40)	-0.27 (-3.96 to 3.43)	-0.12 (-2.87 to 2.63)	SCID				
<u>-1.17</u> (-2.29 to -0.06)	-0.64 (-1.56 to 0.28)	-0.59 (-2.23 to 1.05)	-0.27 (-1.36 to 0.82)	-0.30 (-3.11 to 2.50)	-0.16 (-1.50 to 1.19)	-0.04 (-2.74 to 2.66)	Others			
-1.18 (-2.84 to 0.48)	-0.64 (-2.16 to 0.88)	-0.60 (-2.65 to 1.46)	-0.28 (-1.91 to 1.36)	-0.31 (-3.37 to 2.75)	-0.16 (-1.99 to 1.67)	-0.04 (-3.02 to 2.93)	-0.01 (-1.76 to 1.75)	FVB_N		
<u>-1.35</u> (-2.31 to -0.38)	<u>-0.81</u> (-1.58 to -0.05)	-0.76 (-2.33 to 0.80)	-0.44 (-1.41 to 0.53)	-0.48 (-3.15 to 2.20)	-0.33 (-1.58 to 0.92)	-0.21 (-2.87 to 2.45)	-0.17 (-1.31 to 0.97)	-0.17 (-1.85 to 1.52)	SWR_J	
-2.39 (-4.87 to 0.09)	-1.85 (-4.25 to 0.54)	-1.80 (-4.56 to 0.95)	-1.49 (-3.95 to 0.98)	-1.52 (-5.09 to 2.06)	-1.37 (-3.96 to 1.22)	-1.25 (-4.75 to 2.24)	-1.22 (-3.75 to 1.32)	-1.21 (-4.03 to 1.62)	-1.04 (-3.53 to 1.45)	NODSCID

Data are expressed as standardized mean differences (SMD) with their 95% confidence intervals. Underlined results are statistically significant.

Supplementary Figure S1. Network plots when separating the wild type group by strain.



Supplementary Figure S2. Comparison-adjusted funnel plots.



Systematic review protocol

Mouse models of diabetes-related ulcers: a systematic review and network meta-analysis

Citation

Axel Couturier, Clément Calissi, Charles Khouri, Matthieu Roustit. Mouse models of diabetes-related ulcers: a systematic review and network meta-analysis. PROSPERO 2021 CRD42021286873 Available from: https://www.crd.york.ac.uk/prospERO/display_record.php?ID=CRD42021286873

Review question [1 change]

Our aim is to describe and compare the different mouse models of diabetes-related ulcers.

Context and rationale

Diabetic foot ulcers (DFUs) are a common and serious complication of diabetes and associated with important morbidity. Despite available treatments, they are responsible for a lower limb loss every 30 seconds somewhere in the world. Due to the complexity of the pathophysiology and the heterogeneity of the disease, drug development has been particularly challenging in this field, with many failures at the clinical stage. Appropriate animal models may improve screening, and subsequently the success rate of clinical trials. Preclinical research on DFUs has mostly relied on mouse models. However, there are many different models, based on specific genetic strains or use of toxic agents/or diabetogenic diet, various ulceration protocols, the use of splint, covering, etc. The effect of each model (or component) on wound healing remains poorly studied, since most studies rely on small sample sizes. This prevents from establishing standards that would be more predictive of the response in humans. We thus propose a systematic review with a component network meta-analysis to gather direct and indirect evidence, and compare the different mouse models of diabetes-related ulcers. This will provide valuable information to standardize the models and improve the screening of drug candidates.

Searches [1 change]

We have searched on two databases, PubMed and Embase, with the same keys words.

("models, animal"[MeSH Terms] OR "disease models, animal"[MeSH Terms]) AND "diabetes mellitus"[MeSH Terms] AND "wound healing"[MeSH Terms] AND "mice"[MeSH Terms]

We don't restrict about publication period but we include only publication written in English. Other than that, no other restrictions.

Study designs to be included [1 change]

Inclusion criteria:

All controlled studies were eligible

Exclusion criteria:

Studies with only one group

Human disease modelled

Diabetic foot ulcers (DFUs) are a common and serious complication of diabetes and associated with important morbidity. This disease is associated with cutaneous microvascular impairment characterized by an impaired capillary structure and endothelial dysfunction.

Animals/population [1 change]

Inclusion criteria:

All mouse models of diabetes-related ulcers and their non-diabetic controls. We therefore exclude publications that do work with in vivo experiments on mice.

Exclusion criteria:

Any combination of >1 model is excluded (e.g diabetes-related ulcer + model for another disease/condition). We exclude all publications that do work with in vivo experiments on mice.

Intervention(s), exposure(s) [1 change]

Inclusion criteria:

No treatment of treatment with a placebo/vehicle are eligible

Exclusion criteria:

Any active treatment

Comparator(s)/control [1 change]

Inclusion criteria:

To be included, the article must use at least two different models of diabetes-related ulcer, or one model and its non- diabetic control.

Exclusion criteria:

Studies with only one group

Other selection criteria or limitations applied

Only article in English are included.

Outcome measure(s) [1 change]

Inclusion criteria:

- Measure of wound healing over time

Exclusion criteria:

- No measure of wound healing

Study selection and data extraction [1 change]

Procedure for study selection

Two investigators will identify eligible studies that meet inclusion criteria. Doublons will be excluded, and titles and abstracts will be screened to identify all studies to be included. Then, a second screening based on the full text will be done by two investigators. Ten percent of the articles are reviewed by the two authors and compared to make sure that the protocol for the selection of articles is applied the same way. Any doubt or disagreements will be discussed and submitted to a third investigator.

Prioritise the exclusion criteria

- 1) Publication is not in english
- 2) Publication do work with *in vivo* experiments on mice
- 3) Models do not only include diabetes-related ulcers
- 4) Wound healing measurement is not reported
- 5) There is no control group (i.e all the animal group show active treatment)
- 6) Any combination of >1 model is excluded (e.g diabetes-related ulcer + model for another disease/condition)

Methods for data extraction

Data extraction will be done by two authors. Ten percent of the articles are reviewed by the two authors and compared to make sure that the protocol for extraction of data is applied in the same way. Any doubt or disagreements will be discussed and submitted to a third author.

Data are extracted from text, table and graphs. In case of missing data authors will not be contacted and we note that the data is missing.

Data to be extracted: study design

Controlled vs crossover, number of experimental groups, number of animals, information for assessment of the risk bias (randomization, blinding, reporting bias, selection bias).

Data to be extracted: animal model

Mice strains, weight, gender, age of the animals, duration of hyperglycemia

Data to be extracted: intervention of interest

Type of ulcer (excisional vs pressure), wound localization, wound size at day 0, method to measure the wound size, wound splinted or not, wound covered or not, treated with vehicle or not.

Data to be extracted: primary outcome(s)

All wound size measurement at different time. If necessaries the data are transformed so that all data are expressed as percentage of ulcer size at day 0. This data

Data to be extracted: secondary outcome(s)

The age of mice and age of diabete are transformed in weeks. The ulcer size at day 0 are transformed so that all data are expressed as mm².

Data to be extracted: other

Authors, journal and year

Risk of bias and/or quality assessment [1 change]

By use of SYRCLE's risk of bias tool.

Risk of bias and study quality of all included studies will be assessed by use of SYRCLE's risk of bias tool. We will use the SYRCLE's Risk of Bias tool to assess selection, performance, detection, attrition, and reporting biases. Each domain will be scored as Yes, No, or Unclear.

The risk of bias and quality assessment protocol is established by three authors. It was then applied by the two authors who did the data extraction. Ten percent of the articles are reviewed by both authors and compared to ensure that the risk of bias and quality assessment protocol is applied in the same manner. Any doubts or disagreements will be discussed and referred to a third author.

Strategy for data synthesis [1 change]

Planned approach

Several meta-analyses will be performed to assess the impact of model choice, rodent and protocol characteristics on wound healing at days 3, 7, 11 and 15.

We will first perform a Bayesian network meta-analysis (NMA) at each time point to compare the different DM models on wound healing.

We will then perform component NMA to assess the increment effect of splint, wound covering and topic moisture on wound healing.

We do not apply minimum thresholds to decide to do our NMA.

Effect measure

Standardized mean difference will be used to synthesize the results.

Effect models

Given the anticipated heterogeneity in included studies random effect models will be used.

Heterogeneity

We will assess network heterogeneity using τ and I^2 statistic.

Other

NA

Analysis of subgroups or subsets

Subgroup analyses

We will explore heterogeneity by performing several subgroup analyses according to sex, wound type.

Sensitivity

Impact of risk of bias on the results will be explored

Publication bias

Funnel plot asymmetry will be explored using Egger's regression test as recommended by Cochrane handbook for systemic reviews of interventions, with $p < 0.05$ suggesting publication bias.

Contact details for further information

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Organisational affiliation of the review

Univ Grenoble Alpes <https://www.univ-grenoble-alpes.fr/>

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Review type

Pre-clinical animal intervention review

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Conflicts of interest Language

English

Country

France

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Animals to Diabetes Complications to Mice to Network Meta-Analysis to Skin Diseases to Ulcer to Vascular Diseases

Date of registration in PROSPERO

13 December 2021

Date of first submission

22 October 2021

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

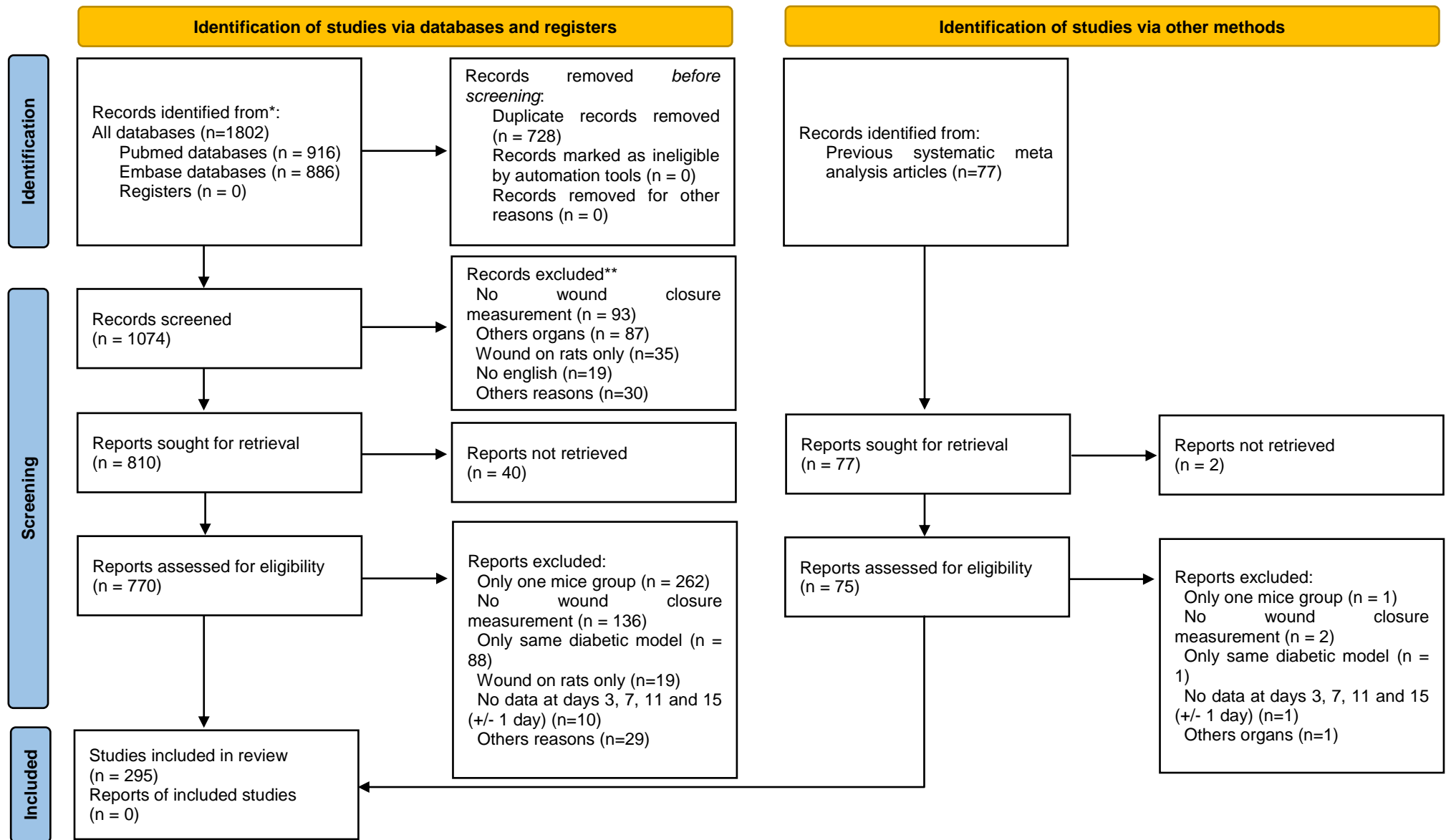
The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

13 December 2021

PRISMA 2020 flow diagram



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;to372:n71. doi: 10.1136/bmj.n71. For more information, visit: <http://www.prisma-statement.org/>