Supplementary Data:

Supplementary Data

Supplementary Table 1. PRISMA-P 2015 checklist

Section/topic	Item #	Checklist item	Reported on page #
ADMINISTRATIVE INFORMATION			
Title			
Identification	1a	Identify the report as a protocol of a systematic review	**1**
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	**N/A**
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number	**6**
Authors			
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	**1**
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	**17**
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	**N/A**
Support			
Sources	5a	Indicate sources of financial or other support for the review	**17**
Sponsor	5b	Provide name for the review funder and/or sponsor	**17**

Section/topic	Item #	Checklist item	Reported on page #
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	**N/A**
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	**5**
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	**5**
METHODS			
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	**6**
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	**6**
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	**6**
Study records			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	**6**
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	**6**

Section/topic	Item #	Checklist item	Reported on page #
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	**6**
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	**6**
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	**6**
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	**6**
Data			
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	**7**
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)	**7**
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	**7**
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	**7**

Section/topic	Item #	Checklist item	Reported on page #
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	**7**
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	**7**

PRISMA-P Preferred Reporting Items for Systematic review and Meta-Analysis Protocols

Supplementary Table *2*. Qualitative assessment tool for examining study quality and reporting.

Section/Topic	Item No.	Checklist Item	Description or Review Authors' Judgement
METHODS			
General			
	1	Provided a statement of ethical practice	Indicated that animal studies complied with institutional or ethical guidelines
Experimental mice			
	2	Indicated sex of included mice	Clear report of which sex of mice was included in the study and numbers of each sex, if applicable
	3	Specified experimental start date	Reported what age the mice were at start of experimental time frame
	3a	Reported the strain and/or sub-strain of mice	Clear report of strain and/or sub-strain of mice
	4	Indicated that calculations were performed to determine appropriate sample sizes	Indicated that power calculations or similar statistical tests were performed to justify the sample sizes used in each animal study
Study design			
	5	Random allocation of mice	Indicates attempts to minimise bias by randomly allocating mice into experimental and control groups
	6	Appropriate inclusion of control mice	Indicated that experimental control mice were littermates, vehicle-treated or heterozygotes, when applicable, of their diabetic/experimental counterparts
	7	Description of primary outcome measurements	Gave a clear explanation of how primary outcomes were measured

	7a	Indicated primary outcome measurements were in a blinded-manner	Demonstrates that measurements of primary outcomes were performed in an unbiased manner
	7b	Indicated repeated measurements of primary outcome measurements	Indicated that examination of primary outcomes were assessed by additional independent observer(s) and thus deemed reproducible
RESULTS			
	8	Inclusion of metabolic parameter data	Presented data concerning metabolic parameters which may be affected during the experimental time-frame, such as such as blood glucose level and body weights
	9	Recorded sample sizes clearly	Exact sample size numbers, not ranges, were provided
	10	Specified the use of SD or SEM	Indicated that error bars in figure were SD or SEM

Scoring:
If Checklist item is; **No = 0**
Unclear, partially or maybe = 0.5
Yes = 1

Supplementary Table 3. Qualitative assessment tool for suitability of studies as a model of diabetes-associated ulceration.

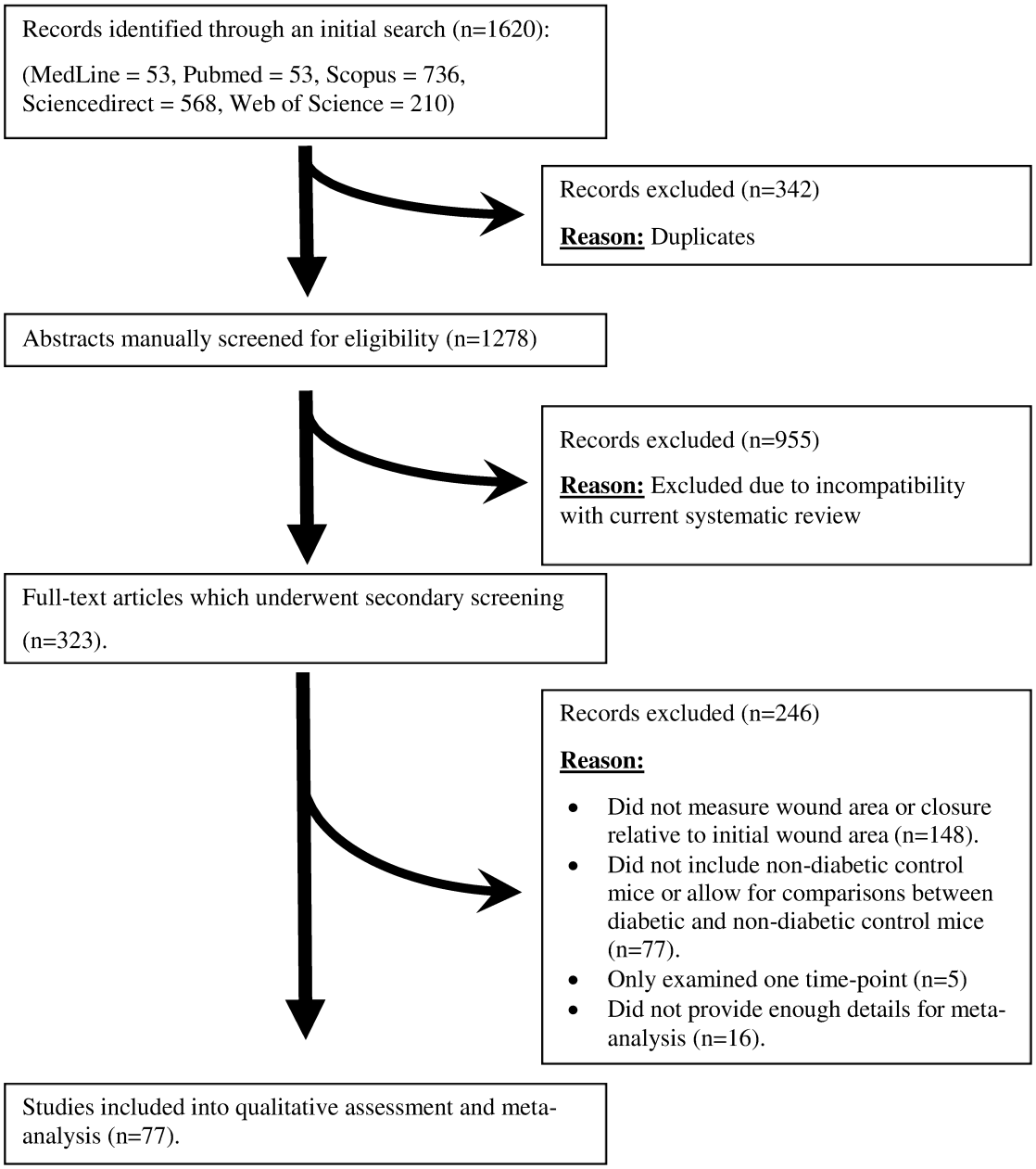
Section/Topic	Item No.	Checklist Item	Description or Review Authors' Judgement
Diagnostic criteria for diabetes			
	1	Inclusion of a diagnostic criterion for diabetes	A clear criteria for diabetes being established in the experimental mice reported
	1b	Confirmation of diabetic status with additional validation techniques	Confirmation of diabetes with an additional experimental test, such as glucose tolerance test, or measurements of glycated haemoglobin or plasma insulin levels.
	2	Acceptable diagnostic criteria	Fasting blood glucose >150mg/dL ≈ 8.3 mmol/L as per recommendations from Diabetic Complications Consortium (DiaComp). In the event fasting blood glucose was not measured, non-fasted blood glucose ≥270mg/dL ≈ 15 mmol/L is considered acceptable.
	3	Reporting of fasting status of blood glucose	Reported that blood glucose measurements were performed on fasted mice
Diabetes-associated wound ulceration			
	4	Reported method of diabetes induction	Provided a clear report of diabetes induction method if diabetes was chemically-induced or the source of genetically-modified diabetic mouse models
	5	Specified date of wound generation	Gave a clear description on the amount of time after diabetes induction wounds were generated
	5a	Adequate duration of hyperglycaemia prior to wound creation	Allowed for a sufficient duration of hyperglycaemia for the development of diabetes-associated injury (0 points for <1 week, 0.5 points for 1 - 6 weeks. 1 point for >6 weeks)
	6	Reported method of wound creation	Clear report of wound creation method

	6a	Wound creation in the periphery of the limb	As the majority of diabetes-associated ulcer occur in the feet of patients. A score of 0.5 given if wound is on the hindlimb.
Outcome measurements			
	7	Direct comparison between non-diabetic and diabetic animals performed	Wound closure measurements were represented in the same figure or statistical analysis was performed between diabetic and non-diabetic mice.
	8	Inclusion of time of complete wound healing	Reported the frequency of complete ulcer healing
	9	Examined parameter associated with ischaemia and/or blood flow in the affected area	Performed experiments to examine blood flow in affected region, i.e. Laser Doppler imaging
	10	Examined parameters associated with neuropathy in mice	Performed tests for the signs of diabetic neuropathy in mice, such as examinations for abnormal sensory symptoms, nerve conductivity velocity deficits and decrease in myelinated fiber and/or intraepidermal nerve fiber densities

Scoring:

If Checklist item is; No = 0

Yes = 1



Supplementary Figure 1. Preferred Reporting Items of Systematic Review and Meta-analyses (PRISMA) flow diagram. A total of 1620 articles were identified from Sciencedirect, Scopus, Web of Science, Pubmed and Medline. Of these, 323 full-text articles were assessed for eligibility and 77 articles were included in the review.

Supplementary Table 4. Characteristics of included studies

Model and duration of diabetes prior to wound creation	Dose of diabetogenic agent (mg/kg body weight)	Mouse strain	Sex	Diagnostic criteria for diabetes (blood glucose mmol/L)	Location of wound	Initial wound diameter (mm)	Primary wound outcome reported	Reference
Streptozotocin-induced diabetes								
Single dose								
4 days	150	C57BL/6	M	>16.7	Back	6	% area	[54]
1 week	150	Swiss albino	M	≥8.3†	Back	15	% area	[38]
2 weeks	60	BALB/c	M	>12.2	Back	8	% closure	[59]
2 weeks	60	BALB/c	M	>12.2	Back	8	% closure	[64]
2 weeks	165	C57BL/6J	M	NR	Back	5	% closure	[71]
3 weeks	180	C57Bl/6	M	>13.9	Back	6	% area	[27]
3 weeks	150	C57BL/6	M	>16	Hindlimb	4	% area	[61]
3 weeks	150	ICR	M	>13.875†	Back	8	% closure	[66]
4 weeks	100	ICR	M	>13.9†	Back	6	% closure	[91]
4 weeks	150	C57BL6	U	>16.7	Hindlimb	4	% area	[37]
4 weeks	150	C57BL/6	U	≥16.7	Hindlimb	4	Ratio of wound area	[51]
4 weeks	180	BALB/c	M	15.8-32.8	Back	6	% area	[58]
5 weeks	200	CD1	M	11.1-22.2	Back	3.5	% area	[30]
6 weeks	150	C57BL/6J	M	>14	Back	6	% area	[62]
6-8 weeks	150	Unknown	M	>13.9	Back	6	% area	[43]
Unknown	65	C57BL/6	U	>13.8	Back	8x8	% closure	[34]
Unknown	60	Swiss Webster	M	NR	Back	5	% area	[41]
Unknown	60	Swiss Webster	M	NR	Back	5	% area	[42]
Unknown	60	Swiss Webster	M	NR	Back	5	% area	[44]
Unknown	60	Swiss Webster	M	NR	Back	5	% area	[48]
Multiple dose								
4 days	50 x 5 days	C57BL/6	M	>16.7	Back	6	% area	[55]
1 week	60 x 5 days	C57BL/6	M	>13.9	Back	4	% closure	[49]
1 week	60 x 5 days	C57BL/6	M	>13.9	Back	6	% closure	[87]
>1 week	50 x 5 days	C57BL/6	M/F	>20	Back	8	% closure	[73]
*>1 week^*	80 x 2 days, non-consecutively	Swiss albino	U	>11.1	Back	8	% closure	[78]
2 weeks	60 x 5 days	BALB/c	M	NR	Back	8	% closure	[85]
2 weeks	Unknown	C57BL/6J	M	>15.6	Back	15	ratio of wound closure	[92]
*>2 weeks^*	50 x 5 days	C57/BL6J	M	>22.2†	Back	10 x 10	% area	[68]
3 weeks	100 x 6 days	C57BL/6	M	>13.9	Back	4	% area	[79]
3 weeks	50 x 5 days	Assumed to be C57BL/6	U	NR	Back	6	% area	[83]
4 weeks	40 x 5 days	CD1	M	>13.8†	Back	4	% closure	[25]
4 weeks	50 x 5 days	C57BL/6	M	>13.9†	Back	6	% closure	[69]
4 weeks	60 x 5 days	C57BL/6	M	≥16.7	Back	6	% closure	[74]
4 weeks	65 x 5 days	C57BL/6J	M	>16.7	Back	4 #	% closure	[75]
4 weeks	50 x 5 days	C57BL/6J	M	>11.1†	Back	6 #	% closure	[76]
5 weeks	50 x 5 days	C57BL/6J	M	>16.7†	Back	8	% area	[65]
6 weeks	50 x 3 days + 200 on final day	C57BL/6J	M	>14	Back	6	% area	[62]
~7 weeks	55 x 6 days	FVB	M	>17†	Back	4	% area	[35]
8 weeks	50 x 5 days	C57BL/6J	M	>13.9	Back	6	% area	[60]
8 weeks	50 x 5 days	C57BL/6	M	>16.7	Back	4	% area	[63]
8 weeks	50 x 5 days	C57BL/6J	M	>13.9†	Back	6	% area	[72]
Alloxan-induced diabetes								
Single dose								
1 week	150	ICR	M	>13.9†	Back	4	Ratio of wound area	[77]
3 weeks	65	Swiss	M	>11.1	Back	10	% closure	[84]
Unknown	150	ICR	F	>13.9†	Back	4	Ratio of wound area	[67]
Multiple dose								
1 week	100 x 3 days	BALB/c	M	>16.7†	Back	4	% closure	[33]
Non-obese diabetic (NOD) mice								
>4 weeks	N/A	NOD	F	>27.8	Flank	8	% area	[26]
Unknown	N/A	C57B6	U	NR ‡	Back	10x10	% area	[20]
High-fat fed mice								
6 weeks	N/A	TALLYHO/JngJ and SWR/J	F	NR	Back	6 #	% closure	[47]
~8 weeks	N/A	C57BL/6J	M	NR	Back	6 #	% closure	[89]
10 weeks	N/A	C57BL/6-129/svev	M	NR	Back	5 #	% area	[57]
10 weeks	N/A	C57/BL6J	M	NR	Back	10 x 10	% area	[68]
ob/ob mice								
8 weeks old	N/A	B6.Vlep ob/J	M	NR	Back	9	Ratio of wound closure	[82]
8-12 weeks old	N/A	B6.VLepob/J	M	>16.7	Back	9	Ratio of wound closure	[81]
db/db mice								
6 weeks old	N/A	C57BLKS-LepR	U	NR	Back	4 #	% closure	[46]
6-8 weeks old	N/A	BKS.Cg-Dock7m+/+Leprdb/J	F	NR	Back	8	% closure	[52]
7 weeks old	N/A	db/db	U	NR	Back	4 #	% closure	[56]

8 weeks old	N/A	C57BL/KsJ-Leprdb	F	NR	Back	8	% area	[31]
8 weeks old	N/A	BKS.Cg-Dock7m+/+Leprdb/J	M	NR	Back	8 #	% closure	[45]
8 weeks old	N/A	BKS(D)-Leprdb/dbJOrlRj	M	NR	Back	6	% area	[86]
8-9 weeks old	N/A	C57Bl/ksOlaHsd-db	M/F	NR	Flank	6	% closure	[23]
8-10 weeks old	N/A	LepRdb/db	M	>17	Back	6	% closure	[93]
8-12 weeks old	N/A	C57BL/KsJ-db/db	F	NR	Back	15x15	% closure	[17]
8-12 weeks old	N/A	C57BL/KsJ-db/db	F	NR	Back	20	% area	[18]
8-12 weeks old	N/A	C57BL/KsJ-db/db	F	NR	Back	15x15	% closure	[19]
8-12 weeks old	N/A	C57BL/KsJ-db/db	F	NR	Back	15x15	% closure	[21]
8-12 weeks old	N/A	C57BL/KsJ-db/db	U	NR	Back	12x12	% closure	[24]
8-12 weeks old	N/A	B6.Cg-m+/+Leprdb/J	M	>16.7	Back	6	% closure	[53]
8-12 weeks old	N/A	BKS.Cg-Dock7m+/+Leprdb/J	M	NR	Back	8	% closure	[90]
8-14 weeks old	N/A	B6.Cgm+/+Leprdb/J	U	NR	Back	20	% area	[28]
10 weeks old	N/A	C57BL/KsJ-db/db	F	NR	Flank	7.5x7.5	% area	[22]
10-12 weeks old	N/A	BKS.Cg-m+/+Leprdb	U	**>19.4***	Back	5 #	% area	[29]
10-12 weeks old	N/A	BKS.Cg-Dock7m+/+Leprdb/Jnju	M	NR	Back	5	% area	[88]
10-14 weeks old	N/A	BKS.Cg-m-/-Leprdb/J	M	>16.7	Back	6	% closure	[36]
12 weeks old	N/A	db/db	M	>22.2†	Back	10 #	% area	[70]
12 weeks old	N/A	B6.BKS(D)-Leprdb/J	M	NR	Back	6 #	% closure	[89]
12-16 weeks old	N/A	db/db	U	NR	Back	8	% closure	[39]
13 weeks old	N/A	BKS.Cg-m+/+Leprdb/J	F	NR	Back	15x15	% closure	[32]
24-28 weeks old	N/A	db/db	U	NR	Back	7	% area	[50]
Unknown	N/A	db/db	U	NR	Back	4 #	% closure	[40]
Unknown	N/A	C57BL/KsJm/Leptdb	U	NR	Back	6	% area	[80]

^responded upon correspondence, *used g/dL, which is likely a reporting error

M = male, U = unknown; F = female; NR = not reported, N/A = not applicable, † = fasting blood glucose measured, ‡ = glycosuria was reported to be measured, # = splint used

Supplementary Table 5. Qualitative assessment of included studies for examining study quality and reporting.

Section/Topic	Item No.	Checklist Item	Description or Review Authors' Judgement	Brown, RL., Breeden, MP., and Greenhalgh, DG. 1994	Matuszewska, B., et al. 1994	Brown, DL., Kao, WW-Y., and Greenhalgh, DG. 1997
METHODS						
General						
	1	Provided a statement of ethical practice	Indicated that animal studies complied with institutional or ethical guidelines	1	1	1
Experimental mice						
	2	Indicated sex of included mice	Clear report of which sex of mice was included in the study and numbers of each sex, if applicable	1	1	0
	3	Specified experimental start date	Reported what age the mice were at start of experimental time frame	0.5	0.5	0.5
	3a	Reported the strain and/or sub-strain of mice	Clear report of strain and/or sub-strain of mice	1	1	1
	4	Indicated that calculations were performed to determine appropriate sample sizes	Indicated that power calculations or similar statistical tests were performed to justify the sample sizes used in each animal study	0	0	0
Study design						
	5	Random allocation of mice	Indicates attempts to minimise bias by randomly allocating mice into experimental and control groups	1	0	0
	6	Appropriate inclusion of control mice	Indicated that experimental control mice were littermates, vehicle-treated or heterozygotes, when applicable, of their diabetic/experimental counterparts	1	1	0.5
	7	Description of primary outcome measurements	Gave a clear explanation of how primary outcomes were measured	1	1	1
	7a	Indicated primary outcome measurements were in a blinded-manner	Demonstrates that measurements of primary outcomes were performed in an unbiased manner	0.5	0	0
	7b	Indicated repeated measurements of primary outcome measurements	Indicated that examination of primary outcomes were assessed by additional independent observer(s) and thus deemed reproducible	0	0.5	0
RESULTS						
	8	Inclusion of metabolic parameter data	Presented data concerning metabolic parameters which may be affected during the experimental time-frame, such as such as blood glucose level and body weights	0	0	0
	9	Recorded sample sizes clearly	Exact sample size numbers, not ranges, were provided	1	1	1
	10	Specified the use of SD or SEM	Indicated that error bars in figure were SD or SEM	1	1	0
				69.2	**61.5**	**38.5**

Darby, IA., et al. 1997	Crowe, MJ., et al. 1999	Hart, J., et al. 2002	Wall, SJ., et al. 2002	Kirchner, LM., et al. 2003	Graiani, G., 2004	Chen, J., et al. 2005	Cianfarani, F., et al. 2006	Mace, KA., et al. 2007	Callaghan, MJ., et al. 2008	Straino, S., et al. 2008	Pietramaggiori, G., et al. 2009	Trousdale, RK., et al. 2009	Abu-Al-Basal, MA. 2010
0	1	1	0.5	1	1	1	0	1	1	1	1	1	1
0	1	1	0.5	0	1	1	1	0	0	1	1	1	1
0	0.5	1	0.5	0.5	1	0.5	1	0.5	0.5	1	1	1	1
0.5	1	1	1	1	0.5	0.5	0.5	1	1	0.5	1	1	0.5
0	0	0	0	0	0	0	0	0	0	0	0	1	0
0	1	1	0	0.5	1	0	0	0	0	0	0	0	1
0.5	0.5	1	0.5	0.5	0	1	0	1	0.5	0	1	1	1
0.5	1	1	1	1	0	1	1	0	1	1	1	1	1
0	1	0	0	0	0	0	1	0	1	0	0	0	0
0	1	0	0	0	0	1	0	0	1	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	1	1
1	0.5	1	1	0.5	1	1	1	1	1	1	1	1	1
1	1	1	1	1	1	1	1	1	1	1	1	0	1
26.9	**73.1**	**69.2**	**46.2**	**46.2**	**50.0**	**61.5**	**50.0**	**42.3**	**61.5**	**50.0**	**61.5**	**69.2**	**73.1**

Fang, Y., et al. 2010	Jacobsen, JN., et al. 2010	Marrotte, EJ., et al. 2010	Albiero, M., et al. 2011	Hegde, VN., et al. 2011	Mirza, R. and Koh, TJ. 2011	Wetterau, M., et al. 2011	Badr, G. 2012	Badr, G., et al. 2012	Loyd, CM., et al. 2012	Mohany, M., et al. 2012	Shin, L. and Peterson, DA.	Steinstraesser, L., et al. 2012	Wagner, IJ., et al. 2012
1	1	1	1	1	1	1	1	1	1	1	1	1	1
0	1	1	0	1	0	0	1	1	1	1	1	0	1
1	1	0.5	1	1	0.5	0	0	0	0	0	1	1	1
0.5	0.5	1	0.5	0.5	0.5	0.5	0.5	0.5	0	0.5	1	1	1
0	0	0	1	0	0	0	0	0	0	0	0	0	1
0	0	0	0	1	0	0	0	0	0	0	0	0	0
1	1	1	0.5	0	1	0	1	1	1	1	0.5	0.5	0.5
1	1	0.5	1	1	0.5	0	1	1	1	1	0.5	1	1
1	0	0	0	0	0	0	0	1	0	0	0	0	0
0	0.5	0	0	0	0	0	0	0	0	0	0	0	0
0	1	0	0	1	0	0	1	1	0	1	1	0	1
0.5	0.5	1	1	1	0.5	0	1	1	0	1	0.5	1	1
1	1	1	1	1	1	1	1	1	1	1	1	1	1
53.8	**65.4**	**53.8**	**53.8**	**65.4**	**38.5**	**19.2**	**57.7**	**65.4**	**38.5**	**57.7**	**57.7**	**50.0**	**73.1**

Badr, G. 2013	Tie, L., et al. 2013	Dhall, S., et al. 2014	Fadini, GP., et al. 2014	Gooyit, M., et al. 2014	Liu, F., et al. 2014	Moura, LIF., et al. 2014 a)	Moura, LIF., et al. 2014 b)	Steinstraesser, L., et al. 2014	Wang, XQ., et al. 2014	Avitabile, S., et al. 2015	Hozzein, WN., et al. 2015	Leal, EC., et al. 2015	Lim, YC., et al. 2015
1	1	1	1	1	1	1	1	1	1	1	1	1	1
1	1	0	0	1	1	1	1	0	1	1	1	1	1
0	0.5	0.5	0.5	0.5	0.5	0	0	1	0	1	1	0.5	1
0.5	0.5	0.5	0.5	1	1	0.5	0.5	0.5	1	0.5	0.5	1	0.5
0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	1	1	1	0	0	0	0	0	0
1	1	0.5	0	0.5	1	0	0	0	1	0	1	0	0
1	0	0	1	1	1	0	0	1	1	1	1	1	0
0	1	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	1	0	0	0	0.5	0	0	0	1	0	1	1	0
1	0.5	1	0	1	1	0	0	1	0	1	1	0	1
1	1	1	1	1	1	1	1	1	1	1	1	1	0
57.7	**57.7**	**34.6**	**30.8**	**53.8**	**69.2**	**34.6**	**34.6**	**42.3**	**53.8**	**50.0**	**65.4**	**50.0**	**34.6**

Rebalka, IA., et al. 2015	Wong, SL., et al. 2015	Badr, G., et al. 2016	Desposito, D., et al. 2016	Dong, MW., et al. 2016	Eo, H., Lee, H-J. and Lim, Y. 2016	Katagiri, S., et al. 2016	Long, M., et al. 2016	Soares, MA., et al. 2016	Tan, JT., et al. 2016	Tellechea, A., et al. 2016	Wu, Y., et al. 2016	Yu, JW., et al. 2016	Agostinho Hunt, AM., et al. 2017
1	1	1	1	1	1	1	1	1	1	1	1	1	1
1	1	1	1	1	1	1	1	1	1	1	0.5	1	1
0.5	1	1	1	1	1	1	1	1	1	1	0.5	1	1
1	0.5	0.5	1	0.5	0.5	1	0.5	0.5	1	1	0.5	0.5	1
0	0.5	0	0	0	0	0	0	0	0	0.5	0	0	0
1	1	1	0	0	0	0	1	0	0	0	1	0	0
0	1	1	1	1	1	0.5	1	0.5	0	1	0	0.5	1
1	1	1	1	1	1	1	1	1	0	1	0	0	0.5
0	0	0	1	0	0	0	0	0	0	0.5	0	0	0
0	0	0	0	0	0	0	0	1	0	0	0	0	1
0.5	1	1	1	0	0.5	0.5	1	0	1	0	0	1	0
0.5	1	1	0	1	0	1	0	1	1	0	1	1	1
1	1	1	1	1	1	1	1	1	1	1	1	1	1
57.7	**76.9**	**73.1**	**69.2**	**57.7**	**53.8**	**61.5**	**65.4**	**61.5**	**53.8**	**61.5**	**42.3**	**53.8**	**65.4**

Shen, TN-Y., et al. 2017	Shin, J., Yang, SJ. and Lim, Y. 2017	Singla, R., et al. 2017	Wang, Y., et al. 2017	Xu, C., et al. 2017	Zhao, H., et al 2017 a)	Zhao, H., et al 2017 b)	Botusan, IR., et al. 2018	Cardoso, SH., et al. 2018	Hozzein, WN., et al. 2018	Jiménez-Jiménez, C., et al. 2018	Shi, Y., et al. 2018	Wang, F., et al. 2018	Yan, J., et al. 2018
1	1	1	1	1	1	1	1	1	1	1	1	1	1
1	1	0	1	0	1	1	0	1	1	1	1	1	1
1	1	0.5	0.5	0	0.5	1	1	0	1	1	0.5	0.5	
1	0.5	0.5	0.5	1	1	1	0	0.5	0.5	1	0.5	1	1
0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	1	0	0	1	1	0	1	0	0	1	1	0
1	1	0	0	1	0.5	0.5	0	1	1	1	1	1	0.5
1	1	1	0	1	1	1	1	1	1	1	0.5	1	0.5
0	0	0	0	0	0	0	1	0	0	0	1	0	0
0	0	0	1	0	0	1	0	0	0	0	0	0	0
0	1	0	0	0	1	1	0	0	0	0	1	1	0
1	1	1	0	1	1	1	0	1	1	1	0	0.5	1
1	1	1	1	1	1	1	1	1	1	1	1	1	1
61.5	**65.4**	**46.2**	**38.5**	**46.2**	**69.2**	**80.8**	**38.5**	**57.7**	**57.7**	**61.5**	**65.4**	**69.2**	**50.0**

Yu, B., et al. 2018	Yuan, Y., Das, SK. and Li, M. 2018	Li, X., et al. 2019	Yang, C-T., et al. 2019
1	1	0	1
1	1	1	1
0.5	1	1	0.5
1	0.5	1	0.5
0	0	0	0
0	0	0	0
1	1	1	1
1	1	0.5	1
0	0	0	0
0	0	0	0
0	1	0	0
0.5	0.5	0	1
1	1	1	1
53.8	**61.5**	**42.3**	**53.8**

Supplementary Table 6. Qualitative assessment of included studies for suitability as a model of diabetes-associated ulceration.

Section/Topic	Item No.	Checklist Item	Description or Review Authors' Judgement	Brown, RL., Breeden, MP., and Greenhalgh, DG. 1994
Diagnostic criteria for diabetes				
	1	Inclusion of a diagnostic criterion for diabetes	A clear criteria for diabetes being established in the experimental mice reported	0
	1b	Confirmation of diabetic status with additional validation techniques	Confirmation of diabetes with an additional experimental test, such as glucose tolerance test, or measurements of glycated haemoglobin or plasma insulin levels.	0
	2	Acceptable diagnostic criteria	Fasting blood glucose >150mg/dL ≈ 8.3 mmol/L as per recommendations from Diabetic Complications Consortium (DiaComp). In the event fasting blood glucose was not measured, non-fasted blood glucose ≥270mg/dL ≈ 15 mmol/L is considered acceptable.	0
	3	Reporting of fasting status of blood glucose	Reported that blood glucose measurements were performed on fasted mice	0
Diabetes-associated wound ulceration				
	4	Reported method of diabetes induction	Provided a clear report of diabetes induction method if diabetes was chemically-induced or the source of genetically-modified diabetic mouse models	1
	5	Specified date of wound generation	Gave a clear description on the amount of time after diabetes induction wounds were generated	0.5
	5a	Adequate duration of hyperglycaemia prior to wound creation	Allowed for a sufficient duration of hyperglycaemia for the development of diabetes-associated injury (0 points for <1 week, 0.5 points for 1 - 6 weeks. 1 point for >6 weeks)	1
	6	Reported method of wound creation	Clear report of wound creation method	1
	6a	Wound creation in the periphery of the limb	As the majority of diabetes-associated ulcer occur in the feet of patients. A score of 0.5 given if wound is on the hindlimb.	0
Outcome measurements				
	7	Direct comparison between non-diabetic and diabetic animals performed	Wound closure measurements were represented in the same figure or statistical analysis was performed between diabetic and non-diabetic mice.	0.5
	8	Inclusion of time of complete wound healing	Reported the frequency of complete ulcer healing	0
	9	Examined parameter associated with ischaemia and/or blood flow in the affected area	Performed experiments to examine blood flow in affected region, i.e. Laser Doppler imaging	0
	10	Examined parameters associated with neuropathy in mice	Performed tests for the signs of diabetic neuropathy in mice, such as examinations for abnormal sensory symptoms, nerve conductivity velocity deficits and decrease in myelinated fiber and/or intraepidermal nerve fiber densities	0
				30.8

Matuszewska, B., et al. 1994	Brown, DL., Kao, WW-Y., and Greenhalgh, DG. 1997	Darby, IA., et al. 1997	Crowe, MJ., et al. 1999	Hart, J., et al. 2002	Wall, SJ., et al. 2002	Kirchner, LM., et al. 2003	Graiani, G., 2004	Chen, J., et al. 2005	Cianfarani, F., et al. 2006	Mace, KA., et al. 2007	Callaghan, MJ., et al. 2008	Straino, S., et al. 2008	Pietramaggiori, G., et al. 2009
1	0	0.5	0	0	0	0	1	1	1	0	1	1	0
0	0	1	0	0	0	0	1	0	0	0	0	0	0
1	0	0.5	0	0	0	0	1	1	0	0	1	0.5	0
1	0	0	0	0	0	0	1	0	0	0	0	0	0
1	1	0	1	1	0	1	1	1	1	1	1	1	1
0.5	0.5	0	0.5	1	0.5	0.5	1	0.5	1	0.5	0.5	1	1
1	1	0	1	1	1	1	0.5	0.5	0.5	1	1	0.5	1
1	1	1	1	1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	1	1	1	1	1	1	1	0	1	0	1	1
1	0.5	0	0.5	0.5	0	0.5	0	0.5	0	0	0.5	0	0
0	0	0	0	0	0	0	0	0	0	0	0.5	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0
65.4	**30.8**	**30.8**	**38.5**	**42.3**	**26.9**	**38.5**	**65.4**	**50.0**	**34.6**	**34.6**	**50.0**	**46.2**	**38.5**

Trousdale, RK., et al. 2009	Abu-Al-Basal, MA. 2010	Fang, Y., et al. 2010	Jacobsen, JN., et al. 2010	Marrotte, EJ., et al. 2010	Albiero, M., et al. 2011	Hegde, VN., et al. 2011	Mirza, R. and Koh, TJ. 2011	Wetterau, M., et al. 2011	Badr, G. 2012	Badr, G., et al. 2012	Loyd, CM., et al. 2012	Mohany, M., et al. 2012	Shin, L. and Peterson, DA.
0	1	1	1	1	1	1	0	0	0	1	1	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	1	0	1	1	1	1	0	0	0	0	0	0	0
1	1	0	1	0	0	1	0	0	0	0	0	0	0
1	1	1	1	1	1	1	1	1	1	1	1	1	1
1	1	0	0.5	0.5	1	0.5	0.5	0	1	1	0.5	1	1
1	0.5	0	1	1	0.5	0.5	1	0	0	0	1	0	1
1	1	1	1	1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0.5	0	0	0	0	0	0	0	0
1	1	1	1	1	1	1	1	0.5	1	1	0.5	1	1
0.5	0	0	0.5	0	0.5	1	0	1	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0
50.0	**57.7**	**30.8**	**61.5**	**50.0**	**57.7**	**61.5**	**34.6**	**26.9**	**30.8**	**38.5**	**38.5**	**30.8**	**38.5**

Steinstraesser, L., et al. 2012	Wagner, IJ., et al. 2012	Badr, G. 2013	Tie, L., et al. 2013	Dhall, S., et al. 2014	Fadini, GP., et al. 2014	Gooyit, M., et al. 2014	Liu, F., et al. 2014	Moura, LIF., et al. 2014 a)	Moura, LIF., et al. 2014 b)	Steinstraesser, L., et al. 2014	Wang, XQ., et al. 2014	Avitabile, S., et al. 2015	Hozzein, WN., et al. 2015
0	0	0	1	0	1	0	1	1	1	0	0	1	1
0	0	0	0	0	0	0	0	0	0	0	1	1	0
0	0	0	0	0	1	0	1	1	1	0	0	1	0
0	0	0	0	0	0	0	0	0	0	0	1	0	0
1	1	1	1	1	1	1	1	1	1	1	1	1	1
1	1	1	0.5	0.5	1	0.5	0.5	1	1	1	1	1	1
1	1	0	0	1	0.5	1	1	0	0	1	1	0.5	0.5
1	1	1	1	1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0.5	0	0	0	0	0	0	0	0
0	1	1	1	1	1	1	1	0	0	0	1	1	1
0	0	0	0	0.5	0	1	0	0	0.5	0	0	0.5	0
0	0	0	1	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0
30.8	**38.5**	**30.8**	**42.3**	**38.5**	**53.8**	**42.3**	**50.0**	**38.5**	**42.3**	**30.8**	**53.8**	**61.5**	**42.3**

Leal, EC., et al. 2015	Lim, YC., et al. 2015	Rebalka, IA., et al. 2015	Wong, SL., et al. 2015	Badr, G., et al. 2016	Desposito, D., et al. 2016	Dong, MW., et al. 2016	Eo, H., Lee, H-J. and Lim, Y. 2016	Katagiri, S., et al. 2016	Long, M., et al. 2016	Soares, MA., et al. 2016	Tan, JT., et al. 2016	Tellechea, A., et al. 2016	Wu, Y., et al. 2016
1	1	0.5	1	1	1	1	1	1	1	1	0	1	1
0	1	0	0	0	0	0	0	0.5	0	0	0	0	0
0	1	0	1	0	1	1	1	1	1	1	0	1	1
0	0	0	0	0	1	1	1	1	1	0	0	1	0
1	1	1	1	1	1	1	1	1	0.5	0.5	1	1	1
1	0.5	1	1	1	1	1	0	0.5	1	1	1	1	0.5
1	0.5	1	1	0.5	0.5	0.5	0	0.5	0.5	1	0.5	1	0.5
1	1	1	1	1	1	1	1	1	1	1	0.5	1	1
0	0.5	0	0	0	0	0	0	0	0	0	0	0	0
1	1	1	1	1	1	1	1	1	1	1	1	1	1
0	0	1	1	0	0.5	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	1	0	1	0	0
0	0	0	0	0	0	0	0	0	0.5	0	0	0	0
46.2	**57.7**	**50.0**	**61.5**	**42.3**	**61.5**	**57.7**	**46.2**	**57.7**	**65.4**	**50.0**	**38.5**	**61.5**	**46.2**

Yu, JW., et al. 2016	Agostinho Hunt, AM., et al. 2017	Nishikai-Yan Shen, T., et al. 2017	Shin, J., Yang, SJ. and Lim, Y. 2017	Singla, R., et al. 2017	Wang, Y., et al. 2017	Xu, C., et al. 2017	Zhao, H., et al 2017 a)	Zhao, H., et al 2017 b)	Botusan, IR., et al. 2018	Cadoso, SH., et al. 2018	Hozzein, WN., et al. 2018	Jiménez-Jiménez, C., et al. 2018	Shi, Y., et al. 2018
1	1	1	1	1	1	0	1	0	0	1	1	0	1
0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	1	1	1	0	0	0	1	0	0	0	0	0	0.5
0	0	1	1	0	0	0	1	1	0	0	0	0	1
1	1	1	1	1	1	1	1	1	0	1	1	1	1
1	1		0	0	1	0	0.5	1	1	1	1	1	1
0.5	0.5	0.5	0.5	0.5	0.5	0	1	1	0.5	0.5	0.5	1	0.5
1	1	1	1	1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	1	1	1	1	1	1	1	1	1	1	1	1	1
0	0	0	0	0	0	1	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	1
0	0	0	0	0	0	0	0	0	0	0	0	0	0
50.0	**50.0**	**57.7**	**50.0**	**34.6**	**42.3**	**30.8**	**57.7**	**46.2**	**26.9**	**42.3**	**42.3**	**38.5**	**61.5**

	Wang, F., et al. 2018	Yan, J., et al. 2018	Yu, B., et al. 2018	Yuan, Y., Das, SK. and Li, M. 2018	Li, X., et al. 2019	Yang, C-T., et al. 2019
	0	0	0	1	1	1
	0	0	0	0	0	0
	0	0	0	1	1	1
	0	0	0	1	0	0
	1	0.5	1	1	0	1
	0.5	0.5	0.5	1	0.5	0.5
	1	0.5	1	0.5	0.5	1
	1	1	1	1	1	1
	0	0	0	0	0	0
	1	1	1	1	1	1
	1	0	0	1	0	0
	0	0	0	0	0	0
	0	0	0	0	0	0
	42.3	**26.9**	**34.6**	**65.4**	**38.5**	**50.0**

Supplementary Table 7. Raw data used for meta-analysis of mouse models of diabetic wound closure (Figure 1a)

Study or Subgroup	Day recorded	Non-diabetic Control Mean	SD	Total	Diabetic Animals Mean	SD	Total	Weight	SMD
2.1.1 Single dose streptozotocin-induced diabetic mice									
Moura, LIF. et al 2014 [54]	**3**	-14.33	8.387032	7	-14	12.80544	7	1.40%	-0.03 [-1.08, 1.02]
Hegde, VN. et al 2011 [38]	**3**	6.64	4.497777	7	1.73	1.005385	7	1.30%	1.41 [0.19, 2.63]
Hozzein, WN. et al 2015 [59]	**3**	19.36	10.53038	10	3.03	10.53038	10	1.40%	1.49 [0.47, 2.50]
Badr, G. et al 2016 [64]	**3**	20	10.87824	10	13.02	9.803061	10	1.50%	0.65 [-0.26, 1.55]
Tan, JT. et al 2016 [71]	**3**	3.326	6.673049	11	3.588	9.863642	11	1.60%	-0.03 [-0.87, 0.81]
Cianfarani, F. et al 2006 [27]	**2**	3.979	7.785	9	7.616	15.924	9	1.50%	-0.28 [-1.21, 0.65]
Lim, YC. et al 2015 [61]	**2**	64.951	6.121	10	26.426	7.651	10	0.80%	5.33 [3.29, 7.37]
Dong, MW. et al 2016 [66]	**3**	32.9	8.230286	6	10.65	6.417663	6	0.90%	2.78 [1.01, 4.55]
Yuan, Y. et al 2018 [91]	**3**	24.451	1.472	15	16.139	1.956	15	1.10%	4.67 [3.22, 6.13]
Albiero, M. et al 2011 [37]	**4**	71.68	4.497199	8	56.11	17.53625	8	1.40%	1.15 [0.07, 2.23]
Fadini, GP. et al 2014 [51]	**3**	72.6	9.486833	10	53	15.81139	10	1.50%	1.44 [0.43, 2.45]
Avitabile, S. et al 2015 [58]	**4**	32.999	6.023	12	0.376	2.387	12	0.70%	6.88 [4.60, 9.15]
Straino, S. et al 2008 [30]	**3**	25.19	21.82384	12	14.44	14.13353	12	1.60%	0.56 [-0.25, 1.38]
Rebalka, IA. et al 2015 [62]	**4**	23.252	15.43508	10	15.284	21.08923	10	1.50%	0.41 [-0.48, 1.30]
Loyd, CM. et al 2012 [43]	**2**	28.782	12.40202	23	19.543	10.95368	23	1.70%	0.78 [0.17, 1.38]
Fang, Y. et al 2010 [34]	**5**	80.442	1.029	5	55.59	2.5	5	0.10%	11.74 [5.02, 18.47]
Badr, G. 2012 [41]	**4**	26.77	19.98559	10	2.41	19.03691	10	1.50%	1.20 [0.23, 2.16]
Badr, G. et al 2012 [42]	**4**	33.994	20.2449	10	6.86	23.13839	10	1.50%	1.20 [0.23, 2.16]
Mohany, M. et al 2012 [44]	**4**	33.819	12.45621	10	5.977	17.05733	10	1.40%	1.79 [0.71, 2.86]
Badr, G. 2013 [48]	**4**	30.53	11.57394	10	13.43	16.41222	10	1.50%	1.15 [0.19, 2.12]
Subtotal (95% CI)				**205**			**205**	**26.10%**	**1.53 [0.96, 2.10]**
Heterogeneity: Tau² = 1.28; Chi² = 106.14, df = 19 (P < 0.00001); I² = 82%									
Test for overall effect: Z = 5.25 (P < 0.00001)									
2.1.2 Multiple dose streptozotocin-induced diabetic mice									
Moura, LIF. et al 2014 [55]	**3**	-8.22	6.708204	5	-0.76	8.429976	5	1.20%	-0.88 [-2.22, 0.45]
Tie, L. et al 2013 [49]	**2**	26.298	15.59401	13	7.268	9.378039	13	1.50%	1.43 [0.55, 2.31]
Shi, Y. et al 2018 [87]	**4**	20.66	11.9588	7	6.94	12.40857	7	1.40%	1.05 [-0.09, 2.20]
Wu, Y. et al 2016 [73]	**3**	37.897	16.30312	7	18.196	7.246713	7	1.30%	1.46 [0.23, 2.69]
Wu, Y. et al 2016 [73]	**3**	37.933	14.10979	7	18.669	7.839361	7	1.30%	1.58 [0.33, 2.83]
Wu, Y. et al 2016 [73]	**3**	49.539	11.72598	12	-6.771	26.11933	12	1.30%	2.69 [1.53, 3.84]
Wu, Y. et al 2016 [73]	**3**	47.411	16.473	9	8.171	25.317	9	1.40%	1.75 [0.62, 2.88]
Singla, R. et al 2017 [78]	**3**	19.36	6.24	3	15.91	3.23	3	1.00%	0.56 [-1.13, 2.24]
Hozzein, WN. et al. 2018 [85]	**3**	23.427	12.04828	10	10.102	8.810106	10	1.50%	1.21 [0.24, 2.18]
Li, X., et al. 2019 [92]	**3**	35.656	10.99698	5	19.947	21.99396	5	1.20%	0.82 [-0.51, 2.14]
Katagiri, S. et al 2016 [68]	**3**	29.871	12.85963	5	20.447	17.85947	5	1.30%	0.55 [-0.73, 1.82]
Wang, Y. et al 2017 [79]	**3**	58.78	5.96	9	38.17	9.01	9	1.20%	2.57 [1.24, 3.89]
Botusan, IR. et al 2018 [83]	**2**	20.377	12.465	9	-3.962	15.324	9	1.40%	1.66 [0.55, 2.77]
Graiani, G. et al 2004 [25]	**3**	46.97	5.281004	10	34.42	5.64	9	1.30%	2.20 [1.00, 3.39]
Long, M., et al 2016 [69]	**3**	14.48	7.714435	5	8.97	4.94171	5	1.20%	0.77 [-0.54, 2.08]
Yu, JW. et al 2016 [74]	**2**	51.38	12.00321	5	28.068	8.237674	5	1.00%	2.05 [0.35, 3.74]
Agostinho Hunt, AM. et al 2017 [75]	**-**	-	-	-	-	-	-	-	Not estimable
Nishikai-Yan Shen, T. et al 2017 [76]	**3**	12.55	5.72	4	3.13	4.68	4	0.90%	1.57 [-0.19, 3.32]
Desposito, D. et al 2016 [65]	**3**	56.164	22.14758	7	35.969	8.098645	7	1.30%	1.13 [-0.03, 2.29]
Rebalka, IA. et al 2015 [62]	**2**	30.523	13.084	4	20.058	10.466	4	1.10%	0.77 [-0.72, 2.25]
Jacobsen, JN. et al 2010 [35]	**3**	68.807	6.408	9	60.609	11.27361	14	1.60%	0.81 [-0.06, 1.69]
Leal, EC. et al 2015 [60]	**3**	-14.093	17.19118	8	-10.043	12.41962	8	1.50%	-0.26 [-1.24, 0.73]
Leal, EC. et al 2015 [60]	**3**	-2.516	13.10976	8	-15.816	10.14557	8	1.40%	1.07 [0.00, 2.14]
Wong, SL. et al 2015 [63]	**3**	20.712	13.10705	7	4.69	13.305	9	1.40%	1.15 [0.06, 2.23]
Tellechea, A. et al 2016 [72]	**3**	17.092	13.06021	10	10.02	15.53311	10	1.50%	0.47 [-0.42, 1.36]
Subtotal (95% CI)				**178**			**184**	**31.20%**	**1.16 [0.84, 1.47]**
Heterogeneity: Tau² = 0.26; Chi² = 40.18, df = 23 (P = 0.01); I² = 43%									
Test for overall effect: Z = 7.12 (P < 0.00001)									
2.1.3 Single dose alloxan-induced diabetic mice									
Shin, J. et al [77]	**3**	43	9.797959	6	27	9.797959	6	1.20%	1.51 [0.16, 2.86]
Eo, H. et al 2016 [67]	**3**	47.503	11.85798	6	28.744	7.049631	6	1.20%	1.78 [0.35, 3.20]
Cardoso, SH. et al 2018 [84]	**3**	5.52	4.69	5	3.73	0.84	5	1.30%	0.48 [-0.79, 1.75]
Subtotal (95% CI)				**17**			**17**	**3.60%**	**1.20 [0.42, 1.99]**
Heterogeneity: Tau² = 0.01; Chi² = 2.06, df = 2 (P = 0.36); I² = 3%									
Test for overall effect: Z = 3.00 (P = 0.003)									
2.1.4 Multiple dose alloxan-induced diabetic mice									
Abu-Al-Basal, MA. 2010 [33]	**3**	22.66	1.959592	6	11.58	1.861612	6	0.50%	5.35 [2.50, 8.20]
Subtotal (95% CI)				**6**			**6**	**0.50%**	**5.35 [2.50, 8.20]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.68 (P = 0.0002)									
2.1.5 Non-obese diabetic mice									
Chen, J. et al 2005 [26]	**3**	50.63	8.887	18	39.061	5.642	14	1.60%	1.47 [0.68, 2.27]
Darby, IA. et al 1997 [20]	**-**	-	-	-	-	-	-	-	Not estimable
Subtotal (95% CI)				**18**			**14**	**1.60%**	**1.47 [0.68, 2.27]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.62 (P = 0.0003)									
2.1.6 High fat fed mice									
Wagner, IJ. et al 2012 [47]	**-**	-	-	-	-	-	-	-	Not estimable
Yan, J. et al 2018 [89]	**3**	37.7	15.142	4	11.471	19.40867	8	1.20%	1.33 [-0.04, 2.69]
Wang, XQ. et al 2014 [57]	**3**	36.322	13.0855	10	35.632	11.27352	10	1.60%	0.05 [-0.82, 0.93]
Katagiri, S. et al 2016 [68]	**3**	21.32	1.891714	5	25.718	6.820007	5	1.20%	-0.79 [-2.11, 0.52]
Subtotal (95% CI)				**19**			**23**	**4.00%**	**0.17 [-0.89, 1.23]**
Heterogeneity: Tau² = 0.51; Chi² = 4.88, df = 2 (P = 0.09); I² = 59%									
Test for overall effect: Z = 0.31 (P = 0.75)									
2.1.7 ob/ob mice									
Zhao, H. et al 2017 [82]	**2**	85	5.196152	3	21	8.660254	3	0.10%	7.17 [0.06, 14.27]
Zhao, H. et al 2017 [81]	**2**	83	4.472136	5	32	24.59675	5	0.90%	2.61 [0.69, 4.53]
Subtotal (95% CI)				**8**			**8**	**1.00%**	**3.55 [-0.07, 7.18]**
Heterogeneity: Tau² = 3.36; Chi² = 1.48, df = 1 (P = 0.22); I² = 32%									
Test for overall effect: Z = 1.92 (P = 0.05)									
2.1.8 db/db diabetic mice									
Steinstraesser, L. et al 2012 [46]	**4**	3.37	3.085774	5	9.22	7.334303	5	1.20%	-0.94 [-2.29, 0.41]
Gooyit, M. et al 2014 [52]	**3**	16.58	21.71	28	13.68	16.71	28	1.80%	0.15 [-0.38, 0.67]
Steinstraesser, L. et al 2014 [56]	**2**	13.148	4.389401	5	4.073	3.740371	6	1.00%	2.05 [0.45, 3.65]
Pietramaggiori, G. et al 2009 [31]	**4**	43.058	18.147	12	4.42	18.492	12	1.40%	2.04 [1.02, 3.05]
Shin, L. and Peterson, DA. 2012 [45]	**3**	3.291	1.201666	10	2.914	1.201666	10	1.50%	0.30 [-0.58, 1.18]
Jiménez-Jiménez, C. et al 2018 [86]	**-**	-	-	-	-	-	-	-	Not estimable
Wall, SJ. et al 2002 [23]	**3**	16.695	12.79774	10	-3.377	8.547637	10	1.40%	1.77 [0.70, 2.83]
Yang, C-T. et al 2019 [93]	**3**	13.039	9.456	6	-6.998	18.688	6	1.20%	1.25 [-0.04, 2.53]
Brown, RL. et al 1994 [17]	**3**	2.079	4.525	8	-13.119	6.101	8	1.10%	2.68 [1.23, 4.12]
Matuszewska, B. et al 1994 [18]	**3**	-9.347	6.33683	6	-15.168	14.22416	8	1.40%	0.47 [-0.61, 1.55]
Brown, DL. et al 1997 [19]	**3**	-1.6	6.172714	6	-5.38	7.519934	6	1.30%	0.51 [-0.65, 1.67]
Crowe, MJ. et al 1999 [21]	**3**	9.386	5.601983	6	2.939	1.998784	6	1.20%	1.41 [0.09, 2.74]
Kirchner, LM. et al 2003 [24]	**5**	23.067	10.79731	7	0	4.836433	7	1.10%	2.58 [1.04, 4.12]
Liu, F. et al 2014 [53]	**2**	10.78	17.99336	10	-8.43	19.41	9	1.50%	0.98 [0.02, 1.95]
Yu, B. et al 2018 [90]	**3**	7.812	4.872	4	6.018	6.664	4	1.20%	0.27 [-1.13, 1.67]
Mace, KA. et al 2007 [28]	**5**	31.22	16.94	6	-6.17	8.47	6	1.00%	2.58 [0.89, 4.27]
Mace, KA. et al 2007 [28]	**5**	32.275	8.291	6	-4.234	3.88	6	0.50%	5.21 [2.42, 7.99]
Hart, J., et al 2002 [22]	**4**	60.22	13.81	10	-4.52	31.57	8	1.20%	2.65 [1.30, 3.99]
Callaghan, MJ. et al 2008 [29]	**2**	8.63	12.34543	6	2.81	12.24745	6	1.30%	0.44 [-0.71, 1.59]
Wang, F. et al 2018 [88]	**3**	5.926	10.668	10	-2.963	12.742	12	1.60%	0.72 [-0.15, 1.59]
Marrotte, EJ. et al 2010 [36]	**4**	40.131	22.64823	10	6.419	9.534267	10	1.40%	1.86 [0.77, 2.95]
Soares, MA. et al 2016 [70]	**-**	-	-	-	-	-	-	-	Not estimable
Yan, J. et al 2018 [89]	**3**	37.7	15.142	4	6.261	11.93879	8	1.00%	2.24 [0.61, 3.86]
Mirza, R. and Koh, TJ. 2011 [39]	**5**	42.77	9.503515	8	14.31	13.20875	8	1.20%	2.34 [0.99, 3.69]
Trousdale, RK. et al 2009 [32]	**5**	31.93	14.01606	11	18.639	11.73128	31	1.70%	1.06 [0.33, 1.78]
Dhall, S. et al 2014 [50]	**5**	6.37	6.688	7	18.143	13.061	7	1.30%	-1.06 [-2.21, 0.08]
Wetterau, M. et al 2011 [40]	**-**	-	-	-	-	-	-	-	Not estimable
Xu, C. et al 2017 [80]	**2**	5.054	12.79254	5	1.963	35.5982	5	1.30%	0.10 [-1.14, 1.35]
Subtotal (95% CI)				**206**			**232**	**32.00%**	**1.18 [0.76, 1.60]**
Heterogeneity: Tau² = 0.77; Chi² = 82.22, df = 24 (P < 0.00001); I² = 71%									
Test for overall effect: Z = 5.46 (P < 0.00001)									
Total (95% CI)				**657**			**689**	**100.00%**	**1.25 [1.01, 1.48]**
Heterogeneity: Tau² = 0.75; Chi² = 260.03, df = 78 (P < 0.00001); I² = 70%									
Test for overall effect: Z = 10.25 (P < 0.00001)									
Test for subgroup differences: Chi² = 15.17, df = 7 (P = 0.03), I² = 53.9%									

Supplementary Table 8. Raw data used for meta-analysis of mouse models of diabetic wound closure (Figure 1b)

Study or Subgroup	Day recorded	Non-diabetic Control Mean	SD	Total	Diabetic Animals Mean	SD	Total	Weight	SMD
2.2.1 Single dose streptozotocin-induced diabetic mice									
Moura, LIF. et al 2014 [54]	**8**	39	11.4561	7	38.67	11.4561	7	1.50%	0.03 [-1.02, 1.07]
Hegde, VN. et al 2011 [38]	**7**	20.14	5.21213	7	8.81	1.852026	7	1.20%	2.71 [1.13, 4.29]
Hozzein, WN. et al 2015 [59]	**6**	55.21	15.30542	10	22.08	13.40806	10	1.40%	2.21 [1.04, 3.37]
Badr, G. et al 2016 [64]	**6**	60.31	10.87824	10	26.2	8.348413	10	1.30%	3.37 [1.91, 4.83]
Tan, JT. et al 2016 [71]	**7**	17.179	11.46557	11	14.802	10.03942	11	1.50%	0.21 [-0.63, 1.05]
Cianfarani, F. et al 2006 [27]	**7**	48.27	24.912	9	34.934	20.913	9	1.50%	0.55 [-0.39, 1.50]
Lim, YC. et al 2015 [61]	**6**	49.555	6.816	10	51.321	10.709	10	1.50%	-0.19 [-1.07, 0.69]
Dong, MW. et al 2016 [66]	**7**	66.36	5.486857	6	25.98	9.626495	6	0.80%	4.76 [2.17, 7.34]
Yuan, Y. et al 2018 [91]	**6**	60.147	1.834	15	25.184	1.838	15	0.30%	18.53 [13.45, 23.61]
Albiero, M. et al 2011 [37]	**7**	100	4.016367	8	83.89	5.996266	8	1.20%	2.98 [1.44, 4.53]
Fadini, GP. et al 2014 [51]	**6**	94.7	12.64911	10	80	9.486833	10	1.50%	1.26 [0.28, 2.24]
Avitabile, S. et al 2015 [58]	**7**	55.709	6.77	12	15.934	3.388	12	0.90%	7.17 [4.81, 9.53]
Straino, S. et al 2008 [30]	**7**	83.89	11.11977	12	73.89	22.58594	12	1.50%	0.54 [-0.28, 1.36]
Rebalka, IA. et al 2015 [62]	**8**	56.096	13.37011	10	45.691	23.657	10	1.50%	0.52 [-0.38, 1.41]
Loyd, CM. et al 2012 [43]	**7**	62.606	12.42604	14	59.771	10.164	16	1.60%	0.24 [-0.48, 0.97]
Fang, Y. et al 2010 [34]	**7**	96.55	1.511	5	64.479	2.808	5	0.20%	12.85 [5.51, 20.19]
Badr, G. 2012 [41]	**7**	52.03	18.05661	10	14.44	24.72901	10	1.50%	1.66 [0.61, 2.71]
Badr, G. et al 2012 [42]	**7**	58.232	16.88024	10	16.51	26.51254	10	1.40%	1.80 [0.72, 2.87]
Mohany, M. et al 2012 [44]	**7**	58.017	17.05733	10	15.889	14.29033	10	1.40%	2.56 [1.32, 3.81]
Badr, G. 2013 [48]	**7**	58.01	17.42415	10	22.14	12.55424	10	1.40%	2.26 [1.09, 3.44]
Subtotal (95% CI)				**196**			**198**	**25.20%**	**2.09 [1.35, 2.84]**
Heterogeneity: Tau² = 2.27; Chi² = 148.95, df = 19 (P < 0.00001); I² = 87%									
Test for overall effect: Z = 5.49 (P < 0.00001)									
2.2.2 Multiple dose streptozotocin-induced diabetic mice									
Moura, LIF. et al 2014 [55]	**8**	32.52	11.29214	5	30.94	9.279682	5	1.40%	0.14 [-1.10, 1.38]
Tie, L. et al 2013 [49]	**6**	67.993	6.861364	13	39.966	19.33657	13	1.50%	1.87 [0.92, 2.82]
Shi, Y. et al 2018 [87]	**6**	52.43	11.48256	7	17.89	13.33459	7	1.20%	2.60 [1.05, 4.14]
Wu, Y. et al 2016 [73]	**7**	82.079	7.246713	7	65.118	8.686002	7	1.30%	1.99 [0.62, 3.35]
Wu, Y. et al 2016 [73]	**7**	82.371	7.037698	7	65.33	9.8078	7	1.30%	1.87 [0.54, 3.20]
Wu, Y. et al 2016 [73]	**7**	67.73	13.2174	5	35.623	18.93055	5	1.20%	1.78 [0.18, 3.37]
Wu, Y. et al 2016 [73]	**7**	81.86	6.948988	12	32.929	22.92196	12	1.40%	2.79 [1.61, 3.97]
Singla, R. et al 2017 [78]	**10**	51.4	13.98	3	41.51	7.32	3	1.20%	0.71 [-1.03, 2.45]
Hozzein, WN. et al. 2018 [85]	**6**	46.124	14.84373	10	19.18	9.259149	10	1.40%	2.09 [0.95, 3.22]
Li, X., et al. 2019 [92]	**7**	53.142	7.949222	5	35.931	11.91824	5	1.30%	1.53 [0.02, 3.05]
Katagiri, S. et al 2016 [68]	**7**	81.295	6.039	9	40.179	15.669	9	1.30%	3.30 [1.77, 4.83]
Wang, Y. et al 2017 [79]	**7**	92.36	3.52	9	78.17	5.19	9	1.30%	3.05 [1.59, 4.50]
Botusan, IR. et al 2018 [83]	**6**	63.396	6.225	9	47.169	18.687	9	1.50%	1.11 [0.10, 2.12]
Graiani, G. et al 2004 [25]	**7**	72.88	3.734234	5	64.29	4.648548	10	1.30%	1.84 [0.52, 3.16]
Long, M., et al 2016 [69]	**7**	54.35	7.401385	5	44	8.653583	5	1.30%	1.16 [-0.24, 2.56]
Yu, JW. et al 2016 [74]	**6**	74.847	7.553438	5	54.756	4.114365	5	1.00%	2.98 [0.90, 5.07]
Agostinho Hunt, AM. et al 2017 [75]	**9**	90.306	3.827	10	56.123	4.981	10	0.80%	7.37 [4.68, 10.07]
Nishikai-Yan Shen, T. et al 2017 [76]	**7**	63.12	9.36	4	21.56	13	4	0.80%	3.19 [0.60, 5.79]
Desposito, D. et al 2016 [65]	**7**	76.86	9.262775	7	67.346	5.074551	7	1.40%	1.19 [0.02, 2.36]
Rebalka, IA. et al 2015 [62]	**8**	57.703	10.76	4	51.599	9.03	4	1.30%	0.53 [-0.90, 1.97]
Jacobsen, JN. et al 2010 [35]	**6**	95.853	5.841	9	93.226	4.224331	14	1.50%	0.52 [-0.34, 1.37]
Leal, EC. et al 2015 [60]	**7**	32.752	12.2584	8	9.588	18.17547	8	1.40%	1.41 [0.28, 2.54]
Leal, EC. et al 2015 [60]	**7**	23.207	15.28199	8	21.181	13.85081	8	1.50%	0.13 [-0.85, 1.11]
Wong, SL. et al 2015 [63]	**7**	50.325	13.45365	7	33.371	16.818	9	1.40%	1.04 [-0.03, 2.11]
Tellechea, A. et al 2016 [72]	**7**	64.44	18.0155	10	34.381	20.58643	10	1.50%	1.49 [0.47, 2.50]
Subtotal (95% CI)				**183**			**195**	**32.60%**	**1.69 [1.27, 2.11]**
Heterogeneity: Tau² = 0.67; Chi² = 62.28, df = 24 (P < 0.0001); I² = 61%									
Test for overall effect: Z = 7.86 (P < 0.00001)									
2.2.3 Single dose alloxan-induced diabetic mice									
Shin, J. et al [77]	**7**	79	4.898979	6	52	9.797959	6	1.10%	3.22 [1.28, 5.15]
Eo, H. et al 2016 [67]	**7**	81.241	11.48811	6	42.511	50.39825	6	1.40%	0.98 [-0.25, 2.21]
Cardoso, SH. et al 2018 [84]	**6**	27.86	5.11	5	13.52	2.09	5	1.00%	3.32 [1.08, 5.56]
Subtotal (95% CI)				**17**			**17**	**3.40%**	**2.32 [0.63, 4.01]**
Heterogeneity: Tau² = 1.41; Chi² = 5.48, df = 2 (P = 0.06); I² = 63%									
Test for overall effect: Z = 2.69 (P = 0.007)									
2.2.4 Multiple dose alloxan-induced diabetic mice									
Abu-Al-Basal, MA. 2010 [33]	**6**	38.13	2.547469	6	21	2.816913	6	0.70%	5.89 [2.80, 8.98]
Subtotal (95% CI)				**6**			**6**	**0.70%**	**5.89 [2.80, 8.98]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.74 (P = 0.0002)									
2.2.5 Non-obese diabetic mice									
Chen, J. et al 2005 [26]	**7**	79.407	4.516	18	54.584	3.385	14	1.20%	5.95 [4.25, 7.66]
Darby, IA. et al 1997 [20]	**7**	78.57	5.03	4	22.3	7.8	4	0.30%	7.46 [2.14, 12.77]
Subtotal (95% CI)				**22**			**18**	**1.50%**	**6.09 [4.47, 7.72]**
Heterogeneity: Tau² = 0.00; Chi² = 0.28, df = 1 (P = 0.60); I² = 0%									
Test for overall effect: Z = 7.35 (P < 0.00001)									
2.2.6 High fat fed mice									
Wagner, IJ. et al 2012 [47]	**7**	50	14.33004	15	41	16.65383	15	1.60%	0.56 [-0.17, 1.30]
Yan, J. et al 2018 [89]	**7**	69.433	24.164	4	42.27	25.41342	8	1.40%	1.00 [-0.29, 2.30]
Wang, XQ. et al 2014 [57]	**7**	94.711	7.643225	10	74.597	9.088386	10	1.40%	2.29 [1.11, 3.48]
Katagiri, S. et al 2016 [68]	**7**	69.71	6.442112	5	56.345	14.66637	5	1.30%	1.07 [-0.31, 2.44]
Subtotal (95% CI)				**34**			**38**	**5.60%**	**1.16 [0.38, 1.95]**
Heterogeneity: Tau² = 0.31; Chi² = 5.96, df = 3 (P = 0.11); I² = 50%									
Test for overall effect: Z = 2.91 (P = 0.004)									
2.2.7 ob/ob mice									
Zhao, H. et al 2017 [82]	**6**	92	5.196152	3	47	6.928203	3	0.30%	5.88 [-0.02, 11.78]
Zhao, H. et al 2017 [81]	**6**	91	2.236068	5	60	8.944272	5	0.80%	4.30 [1.58, 7.01]
Subtotal (95% CI)				**8**			**8**	**1.10%**	**4.57 [2.10, 7.04]**
Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 1 (P = 0.63); I² = 0%									
Test for overall effect: Z = 3.63 (P = 0.0003)									
2.2.8 db/db diabetic mice									
Steinstraesser, L. et al 2012 [46]	**6**	25.46	9.592732	5	17.19	6.998893	5	1.30%	0.89 [-0.45, 2.23]
Gooyit, M. et al 2014 [52]	**7**	64.21	15.13	21	35	21.71	21	1.60%	1.53 [0.84, 2.23]
Steinstraesser, L. et al 2014 [56]	**8**	40.699	6.880381	5	22.519	11.21866	6	1.30%	1.74 [0.25, 3.24]
Pietramaggiori, G. et al 2009 [31]	**7**	70.272	8.742	12	23.234	16.463	12	1.30%	3.45 [2.11, 4.78]
Shin, L. and Peterson, DA. 2012 [45]	**7**	14.557	5.217758	10	9.873	3.690378	10	1.50%	0.99 [0.05, 1.93]
Jiménez-Jiménez, C. et al 2018 [86]	**7**	55.081	10.96392	6	21.139	14.44709	6	1.20%	2.44 [0.80, 4.09]
Wall, SJ. et al 2002 [23]	**7**	56.998	13.34165	10	22.092	9.613324	10	1.30%	2.88 [1.55, 4.20]
Yang, C-T. et al 2019 [93]	**6**	45.234	10.591	6	-29.286	16.666	6	0.80%	4.93 [2.27, 7.58]
Brown, RL. et al 1994 [17]	**7**	61.2	12.11698	8	3.139	19.19088	8	1.20%	3.42 [1.74, 5.10]
Matuszewska, B. et al 1994 [18]	**6**	38.927	14.42994	6	12.923	8.533365	8	1.30%	2.14 [0.73, 3.55]
Brown, DL. et al 1997 [19]	**10**	83.877	21.16359	6	1.45	3.968173	6	0.80%	5.00 [2.31, 7.69]
Crowe, MJ. et al 1999 [21]	**6**	20.099	8.759375	6	4.56	3.625245	6	1.20%	2.14 [0.60, 3.68]
Kirchner, LM. et al 2003 [24]	**10**	65.825	10.79202	7	27.289	3.000282	7	1.00%	4.55 [2.31, 6.80]
Liu, F. et al 2014 [53]	**6**	52.75	22.32568	10	9.61	15.3	9	1.40%	2.13 [0.95, 3.31]
Yu, B. et al 2018 [90]	**7**	41.997	5.378	4	26.889	8.978	4	1.10%	1.78 [-0.07, 3.62]
Mace, KA. et al 2007 [28]	**-**	-	-	-	-	-	-	-	Not estimable
Mace, KA. et al 2007 [28]	**10**	67.195	2.827	6	14.109	2.646	6	0.10%	17.90 [9.09, 26.71]
Hart, J., et al 2002 [22]	**7**	85.96	9.38	10	13.9	21.16	8	1.10%	4.38 [2.51, 6.25]
Callaghan, MJ. et al 2008 [29]	**6**	44.17	16.21562	6	16.41	20.28178	6	1.30%	1.40 [0.07, 2.72]
Wang, F. et al 2018 [88]	**7**	42.37	13.778	10	13.332	9.782	12	1.40%	2.38 [1.23, 3.52]
Marrotte, EJ. et al 2010 [36]	**8**	87.817	8.838566	10	36.289	9.942201	10	1.10%	5.25 [3.23, 7.26]
Soares, MA. et al 2016 [70]	**7**	67.35	3.25	3	47.44	3.72	3	0.40%	4.56 [-0.12, 9.25]
Yan, J. et al 2018 [89]	**7**	69.433	24.164	4	13.544	13.18047	8	1.10%	2.99 [1.10, 4.89]
Mirza, R. and Koh, TJ. 2011 [39]	**10**	88.18	4.129504	8	42.48	10.32376	8	0.90%	5.50 [3.09, 7.90]
Trousdale, RK. et al 2009 [32]	**7**	48.622	15.62462	11	24.313	9.025346	31	1.50%	2.16 [1.32, 3.00]
Dhall, S. et al 2014 [50]	**10**	86.302	7.968	7	20.695	16.56	7	0.90%	4.73 [2.41, 7.04]
Wetterau, M. et al 2011 [40]	**7**	25.587	0.442719	10	5.895	0.966484	12	0.20%	24.42 [16.41, 32.42]
Xu, C. et al 2017 [80]	**6**	46.784	18.67564	5	29.629	17.97128	5	1.30%	0.85 [-0.48, 2.17]
Subtotal (95% CI)				**212**			**240**	**29.80%**	**2.90 [2.29, 3.52]**
Heterogeneity: Tau² = 1.75; Chi² = 107.44, df = 26 (P < 0.00001); I² = 76%									
Test for overall effect: Z = 9.23 (P < 0.00001)									
Total (95% CI)				**678**			**720**	**100.00%**	**2.28 [1.94, 2.62]**
Heterogeneity: Tau² = 1.74; Chi² = 412.53, df = 83 (P < 0.00001); I² = 80%									
Test for overall effect: Z = 13.29 (P < 0.00001)									
Test for subgroup differences: Chi² = 48.48, df = 7 (P < 0.00001), I² = 85.6%									

Supplementary Table 9. Raw data used for meta-analysis of mouse models of diabetic wound closure (Figure 1c)

Study or Subgroup	Day recorded	Non-diabetic Control Mean	SD	Total	Diabetic Animals Mean	SD	Total	Weight	SMD
2.3.1 Single dose streptozotocin-induced diabetic mice									
Moura, LIF. et al 2014 [54]	-	-	-	-	-	-	-	-	Not estimable
Hegde, VN. et al 2011 [38]	13	51.69	7.064156	7	20.41	1.772653	7	1.40%	5.69 [2.99, 8.38]
Hozzein, WN. et al 2015 [59]	12	94.39	16.25411	10	50.82	22.48379	10	2.40%	2.13 [0.98, 3.27]
Badr, G. et al 2016 [64]	12	84.94	22.23081	10	45.58	15.6849	10	2.40%	1.96 [0.85, 3.07]
Tan, JT. et al 2016 [71]	-	-	-	-	-	-	-	-	Not estimable
Cianfarani, F. et al 2006 [27]	11	89.791	13.506	9	61.257	15.903	9	2.40%	1.84 [0.69, 2.99]
Lim, YC. et al 2015 [61]	-	-	-	-	-	-	-	-	Not estimable
Dong, MW. et al 2016 [66]	14	98.51	5.045949	6	53.27	15.52976	6	1.80%	3.62 [1.52, 5.71]
Yuan, Y. et al 2018 [91]	14	95.477	1.589	15	65.403	2.078	15	0.80%	15.82 [11.47, 20.17]
Albiero, M. et al 2011 [37]	-	-	-	-	-	-	-	-	Not estimable
Fadini, GP. et al 2014 [51]	-	-	-	-	-	-	-	-	Not estimable
Avitabile, S. et al 2015 [58]	13	92.471	4.524	12	57.591	8.784	12	2.00%	4.82 [3.13, 6.51]
Straino, S. et al 2008 [30]	-	-	-	-	-	-	-	-	Not estimable
Rebalka, IA. et al 2015 [62]	-	-	-	-	-	-	-	-	Not estimable
Loyd, CM. et al 2012 [43]	-	-	-	-	-	-	-	-	Not estimable
Fang, Y. et al 2010 [34]	14	100	1.74	5	90.18	1.73	5	1.20%	5.11 [1.98, 8.25]
Badr, G. 2012 [41]	13	95.49	3.826356	10	67.37	15.21056	10	2.30%	2.43 [1.21, 3.64]
Badr, G. et al 2012 [42]	13	97.409	12.08939	10	68.291	12.54159	10	2.30%	2.26 [1.09, 3.44]
Mohany, M. et al 2012 [44]	13	97.959	6.47002	10	60.787	14.29033	10	2.20%	3.21 [1.80, 4.62]
Badr, G. 2013 [48]	13	98.015	6.277121	10	61.22	11.57394	10	2.10%	3.79 [2.21, 5.36]
Subtotal (95% CI)				**114**			**114**	**23.30%**	**3.62 [2.60, 4.65]**
Heterogeneity: Tau² = 2.40; Chi² = 56.05, df = 11 (P < 0.00001); I² = 80%									
Test for overall effect: Z = 6.94 (P < 0.00001)									
2.3.2 Multiple dose streptozotocin-induced diabetic mice									
Moura, LIF. et al 2014 [55]	12	90.426	5.565573	5	79.113	5.80036	5	2.10%	1.80 [0.20, 3.40]
Tie, L. et al 2013 [49]	14	96.367	5.029744	13	87.197	6.890208	13	2.50%	1.47 [0.59, 2.36]
Shi, Y. et al 2018 [87]	14	92.52	5.714823	7	73.96	10.66238	7	2.20%	2.03 [0.66, 3.40]
Wu, Y. et al 2016 [73]	-	-	-	-	-	-	-	-	Not estimable
Wu, Y. et al 2016 [73]	-	-	-	-	-	-	-	-	Not estimable
Wu, Y. et al 2016 [73]	-	-	-	-	-	-	-	-	Not estimable
Wu, Y. et al 2016 [73]	-	-	-	-	-	-	-	-	Not estimable
Singla, R. et al 2017 [78]	18	97.85	0.65	3	86.88	2.37	3	0.60%	5.05 [-0.08, 10.18]
Hozzein, WN. et al 2018 [85]	12	91.215	24.53927	10	36.164	16.67469	10	2.30%	2.51 [1.28, 3.75]
Li, X., et al. 2019 [92]	14	87.568	10.08467	5	65.164	17.4145	5	2.20%	1.42 [-0.05, 2.90]
Katagiri, S. et al 2016 [68]	-	-	-	-	-	-	-	-	Not estimable
Wang, Y. et al 2017 [79]	-	-	-	-	-	-	-	-	Not estimable
Botusan, IR. et al 2018 [83]	12	97.54	7.359	9	89.444	6.816	9	2.40%	1.09 [0.08, 2.09]
Graiani, G. et al 2004 [25]	14	78.79	5.769055	5	77.68	3.383637	10	2.40%	0.25 [-0.83, 1.32]
Long, M., et al 2016 [69]	14	97.41	4.671146	5	87.04	5.567809	5	2.10%	1.82 [0.21, 3.43]
Yu, JW. et al 2016 [74]	-	-	-	-	-	-	-	-	Not estimable
Agostinho Hunt, AM. et al 2017 [75]	-	-	-	-	-	-	-	-	Not estimable
Nishikai-Yan Shen, T. et al 2017 [76]	-	-	-	-	-	-	-	-	Not estimable
Desposito, D. et al 2016 [65]	-	-	-	-	-	-	-	-	Not estimable
Rebalka, IA. et al 2015 [62]	-	-	-	-	-	-	-	-	Not estimable
Jacobsen, JN. et al 2010 [35]	-	-	-	-	-	-	-	-	Not estimable
Leal, EC. et al 2015 [60]	-	-	-	-	-	-	-	-	Not estimable
Leal, EC. et al 2015 [60]	-	-	-	-	-	-	-	-	Not estimable
Wong, SL. et al 2015 [63]	11	91.391	6.564109	7	71.317	12.54	9	2.30%	1.82 [0.60, 3.05]
Tellechea, A. et al 2016 [72]	-	-	-	-	-	-	-	-	Not estimable
Subtotal (95% CI)				**69**			**76**	**21.10%**	**1.53 [1.06, 1.99]**
Heterogeneity: Tau² = 0.12; Chi² = 11.42, df = 9 (P = 0.25); I² = 21%									
Test for overall effect: Z = 6.46 (P < 0.00001)									
2.3.3 Single dose alloxan-induced diabetic mice									
Shin, J. et al [77]	13	97	2.44949	6	87	4.898979	6	2.10%	2.38 [0.76, 4.01]
Cardoso, SH. et al 2018 [84]	11	96.41	1.24	5	76.14	6.76	5	1.60%	3.77 [1.31, 6.22]
Eo, H. et al 2016 [67]	12	98.605	0.742195	6	68.532	52.62239	6	2.30%	0.75 [-0.44, 1.93]
Subtotal (95% CI)				**17**			**17**	**6.00%**	**2.05 [0.38, 3.72]**
Heterogeneity: Tau² = 1.40; Chi² = 5.86, df = 2 (P = 0.05); I² = 66%									
Test for overall effect: Z = 2.41 (P = 0.02)									
2.3.4 Multiple dose alloxan-induced diabetic mice									
Abu-Al-Basal, MA. 2010 [33]	15	84.83	3.037367	6	64.25	3.453781	6	1.30%	5.84 [2.77, 8.91]
Subtotal (95% CI)				**6**			**6**	**1.30%**	**5.84 [2.77, 8.91]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 3.73 (P = 0.0002)									
2.3.5 Non-obese diabetic mice									
Chen, J. et al 2005 [26]	-	-	-	-	-	-	-	-	Not estimable
Darby, IA. et al 1997 [20]	14	95.35	0.35	4	70.1	2.1	4	0.20%	14.59 [4.46, 24.71]
Subtotal (95% CI)				**4**			**4**	**0.20%**	**14.59 [4.46, 24.71]**
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.82 (P = 0.005)									
2.3.6 High fat fed mice									
Wagner, IJ. et al 2012 [47]	14	93	7.358668	15	79	11.61895	15	2.50%	1.40 [0.59, 2.21]
Yan, J. et al 2018 [89]	14	96.361	6.696	4	78.431	16.238	8	2.20%	1.18 [-0.15, 2.51]
Wang, XQ. et al 2014 [57]	-	-	-	-	-	-	-		Not estimable
Katagiri, S. et al 2016 [68]	-	-	-	-	-	-	-	-	Not estimable
Subtotal (95% CI)				**19**			**23**	**4.80%**	**1.34 [0.65, 2.03]**
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%									
Test for overall effect: Z = 3.79 (P = 0.0001)									
2.3.7 ob/ob mice									
Zhao, H. et al 2017 [82]	-	-	-	-	-	-	-	-	Not estimable
Zhao, H. et al 2017 [81]	-	-	-	-	-	-	-	-	Not estimable
Subtotal (95% CI)				**0**			**0**		**Not estimable**
Heterogeneity: Not applicable									
Test for overall effect: Not applicable									
2.3.8 db/db diabetic mice									
Steinstraesser, L. et al 2012 [46]	14	95.4	3.421184	5	51.88	6.641122	5	0.80%	7.44 [3.07, 11.81]
Gooyit, M. et al 2014 [52]	14	97.1	1.98	7	73.81	12.63	7	2.20%	2.41 [0.93, 3.90]
Steinstraesser, L. et al 2014 [56]	12	63.497	6.887089	5	42.239	8.438492	6	2.00%	2.50 [0.73, 4.26]
Pietramaggiori, G. et al 2009 [31]	14	86.394	6.048	12	62.881	7.056	12	2.20%	3.45 [2.12, 4.79]
Shin, L. and Peterson, DA. 2012 [45]	14	73	10.11929	10	40	9.803061	10	2.20%	3.17 [1.77, 4.58]
Jiménez-Jiménez, C. et al 2018 [86]	14	92.073	7.468494	6	45.732	9.957176	6	1.50%	4.86 [2.23, 7.49]
Wall, SJ. et al 2002 [23]	-	-	-	-	-	-	-	-	Not estimable
Yang, C-T. et al 2019 [93]	12	86.21	7.658	6	-10.375	17.112	6	1.10%	6.73 [3.25, 10.20]
Brown, RL. et al 1994 [17]	15	92.004	18.35932	8	66.509	30.43105	8	2.40%	0.96 [-0.09, 2.01]
Matuszewska, B. et al 1994 [18]	13	97.845	7.654655	6	67.885	7.011671	8	1.80%	3.85 [1.86, 5.84]
Brown, DL. et al 1997 [19]	15	82.98	4.84999	6	-1.96	14.10906	6	1.00%	7.43 [3.63, 11.23]
Crowe, MJ. et al 1999 [21]	12	67.449	13.90575	6	6.905	8.477684	6	1.50%	4.85 [2.23, 7.48]
Kirchner, LM. et al 2003 [24]	15	89.452	8.96116	7	51.9	14.89029	7	2.10%	2.86 [1.23, 4.49]
Liu, F. et al 2014 [53]	14	98.24	8.759509	10	74.71	8.82	9	2.30%	2.56 [1.27, 3.84]
Yu, B. et al 2018 [90]	14	72.599	11.78	4	37.393	7.174	4	1.50%	3.14 [0.57, 5.70]
Mace, KA. et al 2007 [28]	15	90.651	3.175	6	30.159	3.532	6	0.30%	16.63 [8.43, 24.82]
Mace, KA. et al 2007 [28]	15	90.96	2.26	6	29.41	7.91	6	0.70%	9.77 [4.87, 14.67]
Hart, J., et al 2002 [22]	14	99.78	0.31	9	50.48	18.82	8	2.00%	3.64 [1.95, 5.33]
Callaghan, MJ. et al 2008 [29]	14	85.75	15.16234	6	44.84	16.46057	6	2.10%	2.39 [0.76, 4.01]
Wang, F. et al 2018 [88]	11	81.324	5.187	10	30.962	17.926	12	2.20%	3.53 [2.10, 4.95]
Marrotte, EJ. et al 2010 [36]	12	93.756	20.99752	10	58.123	12.26331	10	2.40%	1.98 [0.87, 3.10]
Soares, MA. et al 2016 [70]	14	90.85	8.53	3	53.02	3.72	3	0.70%	4.60 [-0.12, 9.32]
Yan, J. et al 2018 [89]	14	96.361	6.696	4	48.617	12.76186	8	1.70%	3.90 [1.65, 6.16]
Mirza, R. and Koh, TJ. 2011 [39]	20	97.66	0.367423	6	60.73	4.996959	6	0.70%	9.62 [4.79, 14.45]
Trousdale, RK. et al 2009 [32]	14	88.493	6.474052	11	35.822	8.123368	31	2.00%	6.67 [5.02, 8.32]
Dhall, S. et al 2014 [50]	15	96.165	16.882	7	27.707	24.204	7	2.00%	3.07 [1.37, 4.77]
Wetterau, M. et al 2011 [40]	14	99.33	1.900658	5	26.006	2.248889	7	0.10%	31.98 [16.33, 47.63]
Xu, C. et al 2017 [80]	12	92.071	13.48349	5	54.822	19.35764	5	2.00%	2.02 [0.34, 3.70]
Subtotal (95% CI)				**186**			**215**	**43.40%**	**3.87 [3.11, 4.63]**
Heterogeneity: Tau² = 2.49; Chi² = 98.66, df = 26 (P < 0.00001); I² = 74%									
Test for overall effect: Z = 10.01 (P < 0.00001)									
Total (95% CI)				**415**			**455**	**100.00%**	**3.12 [2.66, 3.59]**
Heterogeneity: Tau² = 2.06; Chi² = 234.08, df = 55 (P < 0.00001); I² = 77%									
Test for overall effect: Z = 13.12 (P < 0.00001)									
Test for subgroup differences: Chi² = 51.27, df = 6 (P < 0.00001), I² = 88.3%									

Supplementary Table 10: Subgroup analyses with pairwise comparison using Bonferroni's correction

		Early stage (2-5 days)	Intermediate stage (6-10 days)	Late stage (11-20 days)
Single dose streptozotocin-induced diabetic mice	**Multiple dose streptozotocin-induced diabetic mice**	p=0.26	p=0.35	**p=0.0003**
	Single dose alloxan-induced diabetic mice	p=0.51	p=0.81	p=0.12
	Multiple dose alloxan-induced diabetic mice	p=0.010	p=0.02	p=0.18
	NOD mice	p=0.91	**p<0.0001**	p=0.03
	High-fat fed mice	p=0.03	p=0.09	**p=0.0003**
	Ob/ob	p=0.28	p=0.06	N/A
	Db/db	p=0.33	p=0.10	p=0.71
Multiple dose streptozotocin-induced diabetic mice	**Single dose alloxan-induced diabetic mice**	p=0.91	p=0.48	p=0.55
	Multiple dose alloxan-induced diabetic mice	p=0.004	p=0.008	p=0.006
	NOD mice	p=0.47	**p<0.00001**	p=0.01
	High-fat fed mice	p=0.08	p=0.25	p=0.66
	Ob/ob	p=0.20	p=0.02	N/A
	Db/db	p=0.93	**p=0.001**	**p<0.00001**
Single dose alloxan-induced diabetic mice	**Multiple dose alloxan-induced diabetic mice**	p=0.006	p=0.05	p=0.03
	NOD mice	p=0.64	p=0.002	p=0.02
	High-fat fed mice	p=0.12	p=0.23	p=0.44
	Ob/ob	p=0.21	p=0.14	N/A
	Db/db	p=0.96	p=0.53	p=0.05
Multiple dose alloxan-induced diabetic mice	**NOD mice**	p=0.01	p=0.91	p=0.11
	High-fat fed mice	**p=0.0008**	p=0.004	p=0.005
	Ob/ob	p=0.44	p=0.51	N/A
	Db/db	p=0.004	p=0.06	p=0.22
NOD mice	**High-fat fed mice**	p=0.05	**p<0.00001**	p=0.01

	Ob/ob	p=0.27	p=0.31	N/A
	Db/db	p=0.52	**p=0.0003**	p=0.04
High-fat fed mice	**Ob/ob**	p=0.08	p=0.010	N/A
	Db/db	p=0.08	**p=0.0006**	**p<0.00001**
Ob/ob	**Db/db**	p=0.20	p=0.20	N/A

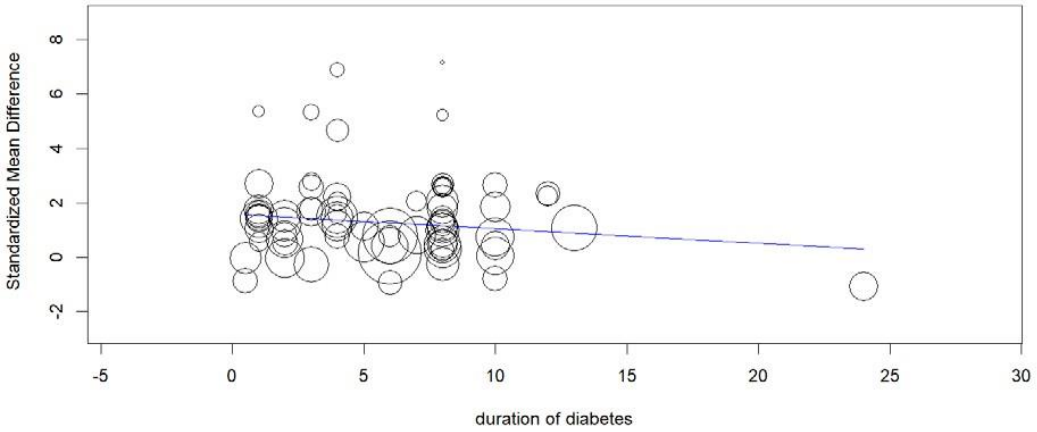
With 28 comparisons being made, a $p<0.0018$ ($p<0.05/28$) is required to reach statistical significance between groups.

a

Meta-Regression
Metric: Standardized Mean Difference
Model Results

	Covariate Coefficients	Lower bound	Upper bound	Std. error	p-Value
Intercept	1.573	1.11	2.036	0.236	<0.001
Duration of diabetes	-0.053	-0.119	0.013	0.034	0.118

Omnibus p-Value
0.118

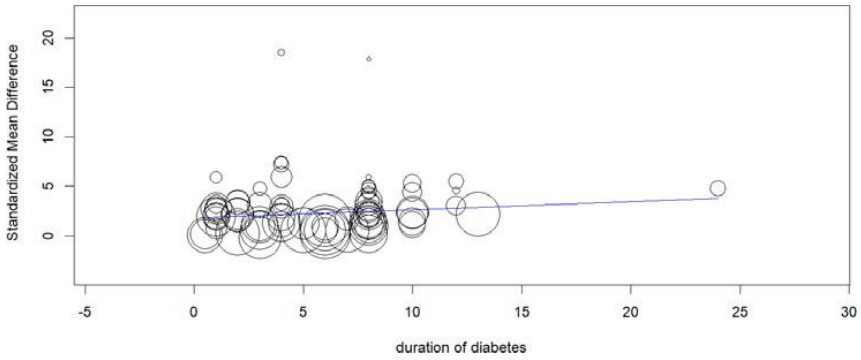


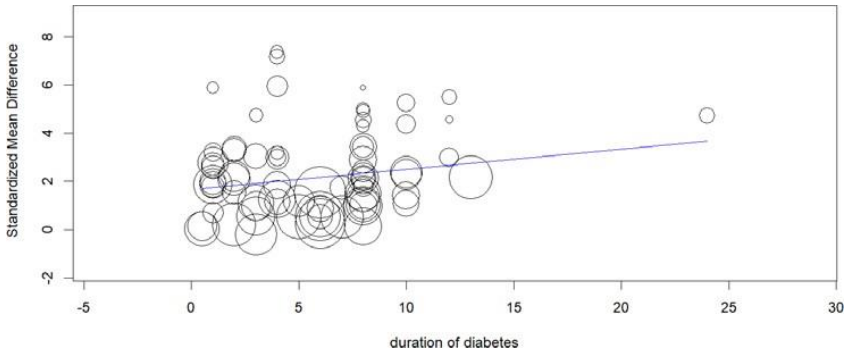
b

Meta-Regression
Metric: Standardized Mean Difference
Model Results

	Covariate Coefficients	Lower bound	Upper bound	Std. error	p-Value
Intercept	1.813→**1.662**	1.134→**1.049**	2.492→**2.275**	0.347→**0.313**	<0.001
Duration of diabetes	0.081→**0.083**	-0.019→**-0.008**	0.181→**0.174**	0.051→**0.046**	0.112→**0.072**

Omnibus p-Value
0.112→0.072



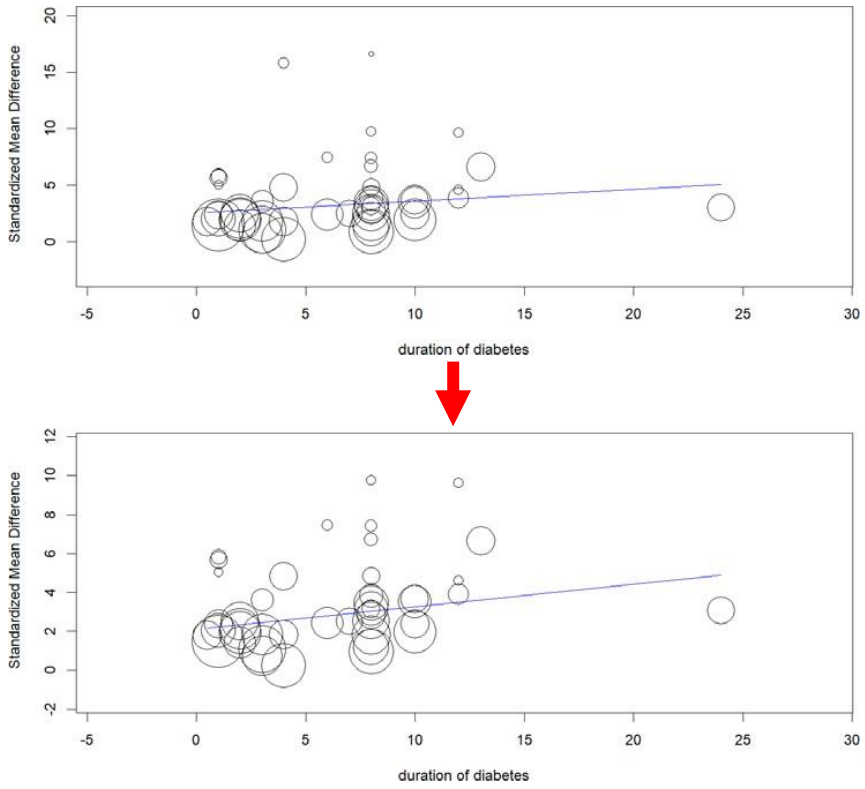


c

Meta-Regression
Metric: Standardized Mean Difference
Model Results

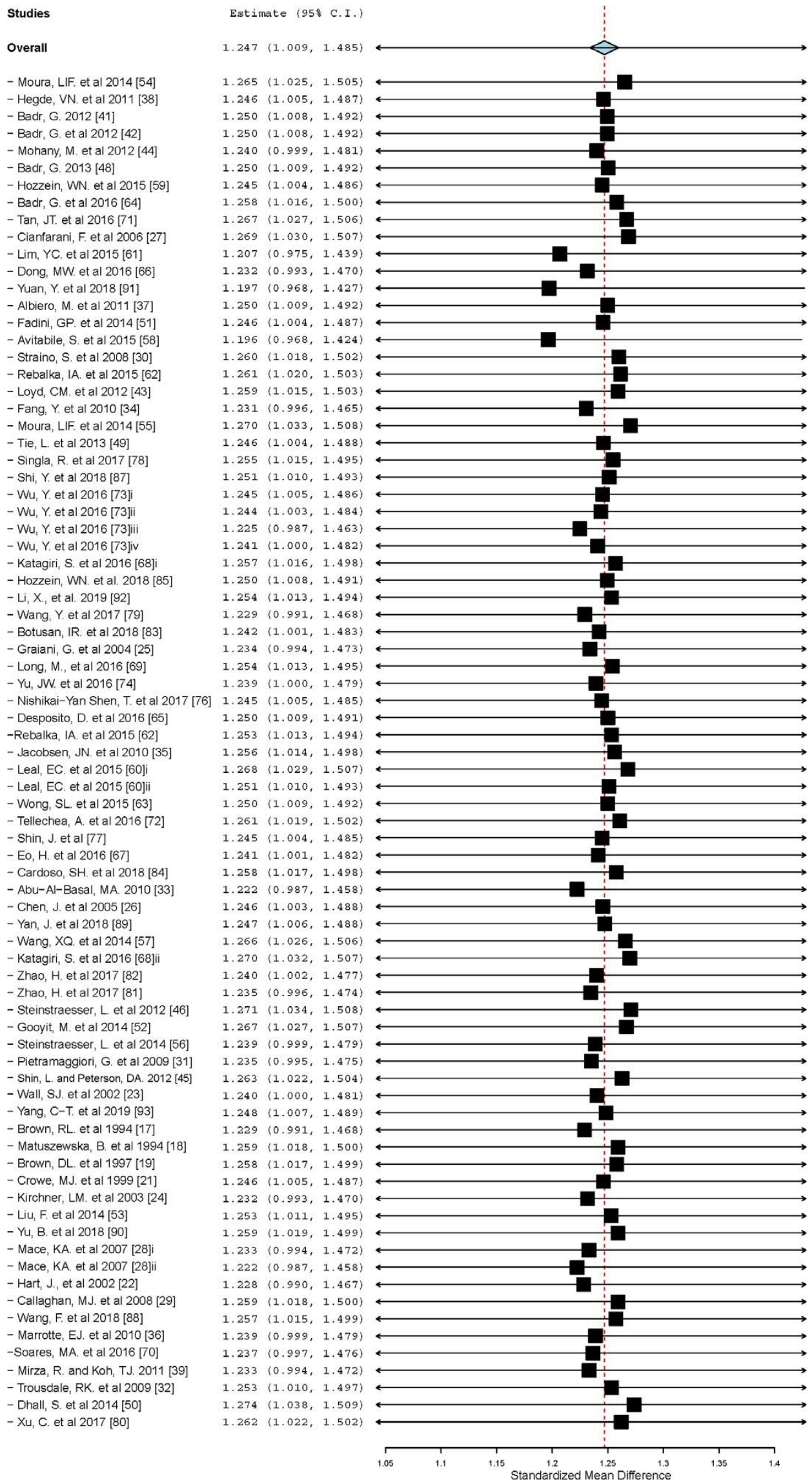
	Covariate Coefficients	Lower bound	Upper bound	Std. error	p-Value
Intercept	2.547→**2.114**	1.559→**1.365**	3.535→**2.864**	0.504→**0.382**	<0.001
Duration of diabetes	0.106→**0.116**	-0.023→**0.018**	0.235→**0.215**	0.066→**0.050**	0.107→**0.021**

Omnibus p-Value
0.107→0.021

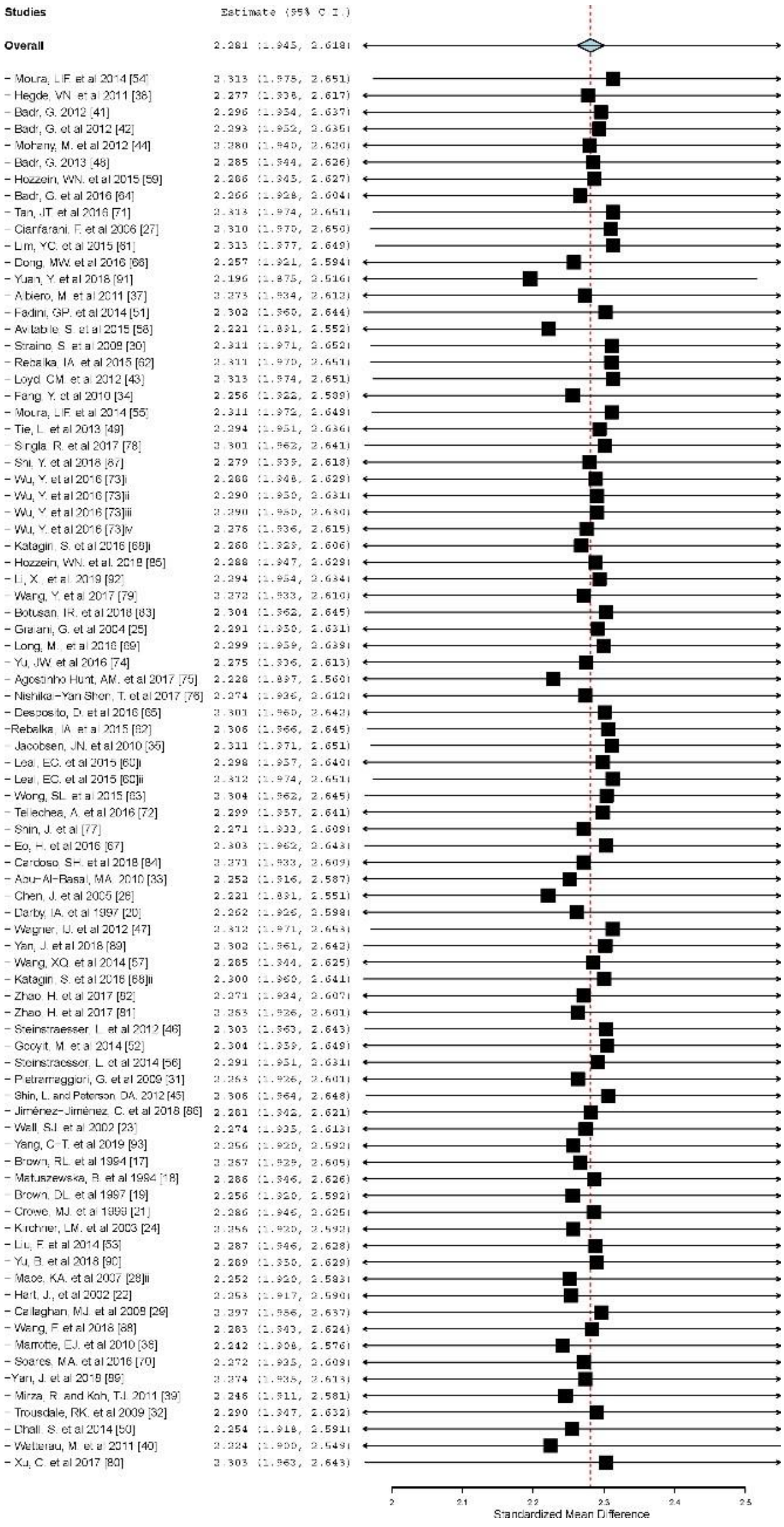


Supplementary Figure *2*. Meta-regression analyses of the effect of diabetes on wound healing impairment versus duration of diabetes prior to wound creation. Meta-regression analyses was performed using OpenMeta-Analyst to represent early (**a**; 2-5 days), intermediate (**b**; 6-10 days) and late stages of wound closure (**c**; 11-20 days). Comparisons were made using standard mean differences and a random effects model. Removal of statistical outliers was performed in **b** and **c**, and highlighted in red

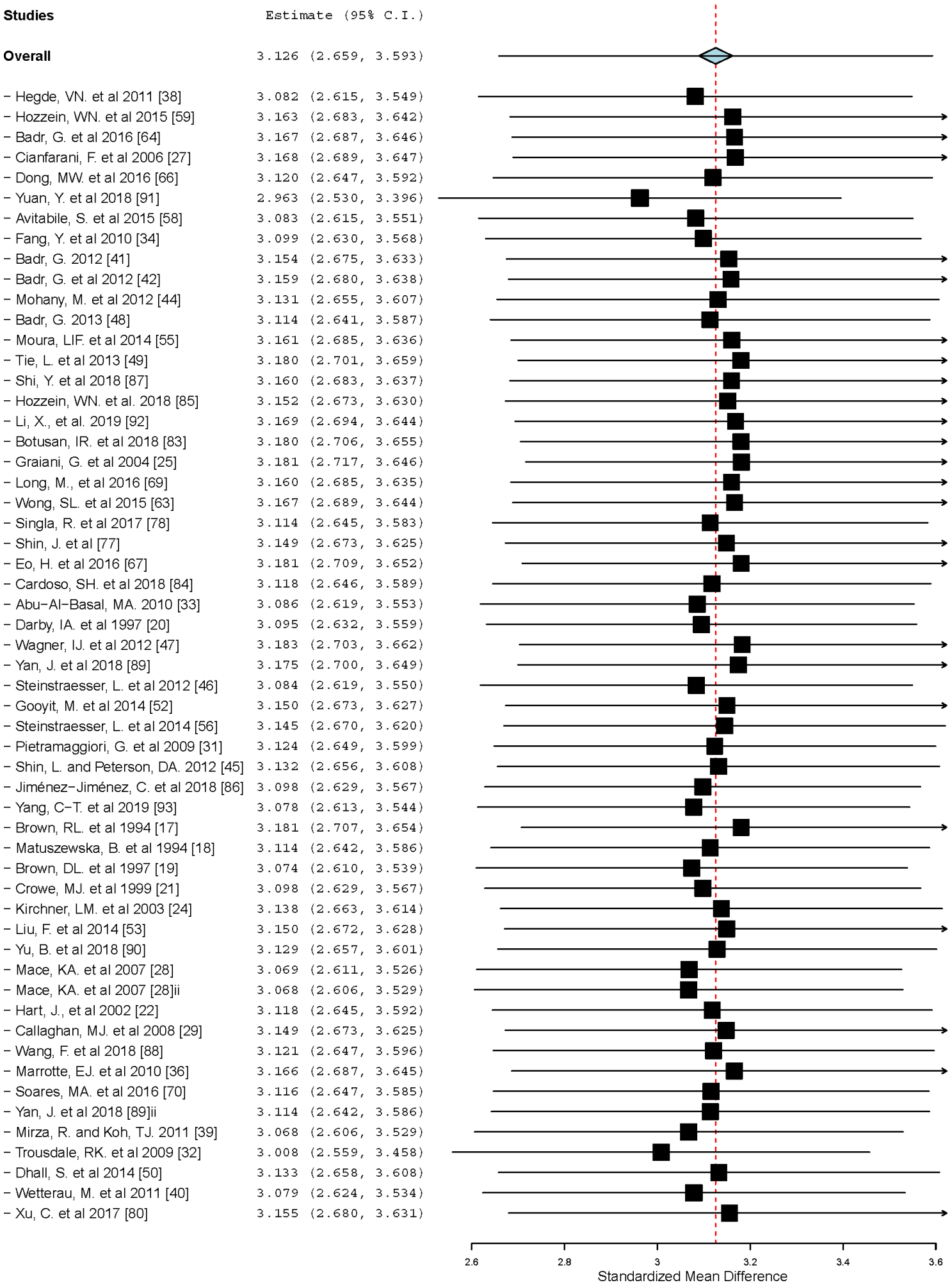
a


Studies
Estimate (95% C.I.)
Overall 1.247 (1.009, 1.485)
- Moura, LIF. et al 2014 [54] 1.265 (1.025, 1.505)
- Hegde, VN. et al 2011 [38] 1.246 (1.005, 1.487)
- Badr, G. 2012 [41] 1.250 (1.008, 1.492)
- Badr, G. et al 2012 [42] 1.250 (1.008, 1.492)
- Mohany, M. et al 2012 [44] 1.240 (0.999, 1.481)
- Badr, G. 2013 [48] 1.250 (1.009, 1.492)
- Hozzein, WN. et al 2015 [59] 1.245 (1.004, 1.486)
- Badr, G. et al 2016 [64] 1.258 (1.016, 1.500)
- Tan, JT. et al 2016 [71] 1.267 (1.027, 1.506)
- Cianfarani, F. et al 2006 [27] 1.269 (1.030, 1.507)
- Lim, YC. et al 2015 [61] 1.207 (0.975, 1.439)
- Dong, MW. et al 2016 [66] 1.232 (0.993, 1.470)
- Yuan, Y. et al 2018 [91] 1.197 (0.968, 1.427)
- Albiero, M. et al 2011 [37] 1.250 (1.009, 1.492)
- Fadini, GP. et al 2014 [51] 1.246 (1.004, 1.487)
- Avitabile, S. et al 2015 [58] 1.196 (0.968, 1.424)
- Straino, S. et al 2008 [30] 1.260 (1.018, 1.502)
- Rebalka, IA. et al 2015 [62] 1.261 (1.020, 1.503)
- Loyd, CM. et al 2012 [43] 1.259 (1.015, 1.503)
- Fang, Y. et al 2010 [34] 1.231 (0.996, 1.465)
- Moura, LIF. et al 2014 [55] 1.270 (1.033, 1.508)
- Tie, L. et al 2013 [49] 1.246 (1.004, 1.488)
- Singla, R. et al 2017 [78] 1.255 (1.015, 1.495)
- Shi, Y. et al 2018 [87] 1.251 (1.010, 1.493)
- Wu, Y. et al 2016 [73]i 1.245 (1.005, 1.486)
- Wu, Y. et al 2016 [73]ii 1.244 (1.003, 1.484)
- Wu, Y. et al 2016 [73]iii 1.225 (0.987, 1.463)
- Wu, Y. et al 2016 [73]iv 1.241 (1.000, 1.482)
- Katagiri, S. et al 2016 [68]i 1.257 (1.016, 1.498)
- Hozzein, WN. et al. 2018 [85] 1.250 (1.008, 1.491)
- Li, X., et al. 2019 [92] 1.254 (1.013, 1.494)
- Wang, Y. et al 2017 [79] 1.229 (0.991, 1.468)
- Botusan, IR. et al 2018 [83] 1.242 (1.001, 1.483)
- Graiani, G. et al 2004 [25] 1.234 (0.994, 1.473)
- Long, M., et al 2016 [69] 1.254 (1.013, 1.495)
- Yu, JW. et al 2016 [74] 1.239 (1.000, 1.479)
- Nishikai-Yan Shen, T. et al 2017 [76] 1.245 (1.005, 1.485)
- Desposito, D. et al 2016 [65] 1.250 (1.009, 1.491)
-Rebalka, IA. et al 2015 [62] 1.253 (1.013, 1.494)
- Jacobsen, JN. et al 2010 [35] 1.256 (1.014, 1.498)
- Leal, EC. et al 2015 [60]i 1.268 (1.029, 1.507)
- Leal, EC. et al 2015 [60]ii 1.251 (1.010, 1.493)
- Wong, SL. et al 2015 [63] 1.250 (1.009, 1.492)
- Tellechea, A. et al 2016 [72] 1.261 (1.019, 1.502)
- Shin, J. et al [77] 1.245 (1.004, 1.485)
- Eo, H. et al 2016 [67] 1.241 (1.001, 1.482)
- Cardoso, SH. et al 2018 [84] 1.258 (1.017, 1.498)
- Abu-Al-Basal, MA. 2010 [33] 1.222 (0.987, 1.458)
- Chen, J. et al 2005 [26] 1.246 (1.003, 1.488)
- Yan, J. et al 2018 [89] 1.247 (1.006, 1.488)
- Wang, XQ. et al 2014 [57] 1.266 (1.026, 1.506)
- Katagiri, S. et al 2016 [68]ii 1.270 (1.032, 1.507)
- Zhao, H. et al 2017 [82] 1.240 (1.002, 1.477)
- Zhao, H. et al 2017 [81] 1.235 (0.996, 1.474)
- Steinstraesser, L. et al 2012 [46] 1.271 (1.034, 1.508)
- Gooyit, M. et al 2014 [52] 1.267 (1.027, 1.507)
- Steinstraesser, L. et al 2014 [56] 1.239 (0.999, 1.479)
- Pietramaggiori, G. et al 2009 [31] 1.235 (0.995, 1.475)
- Shin, L. and Peterson, DA. 2012 [45] 1.263 (1.022, 1.504)
- Wall, SJ. et al 2002 [23] 1.240 (1.000, 1.481)
- Yang, C-T. et al 2019 [93] 1.248 (1.007, 1.489)
- Brown, RL. et al 1994 [17] 1.229 (0.991, 1.468)
- Matuszewska, B. et al 1994 [18] 1.259 (1.018, 1.500)
- Brown, DL. et al 1997 [19] 1.258 (1.017, 1.499)
- Crowe, MJ. et al 1999 [21] 1.246 (1.005, 1.487)
- Kirchner, LM. et al 2003 [24] 1.232 (0.993, 1.470)
- Liu, F. et al 2014 [53] 1.253 (1.011, 1.495)
- Yu, B. et al 2018 [90] 1.259 (1.019, 1.499)
- Mace, KA. et al 2007 [28]i 1.233 (0.994, 1.472)
- Mace, KA. et al 2007 [28]ii 1.222 (0.987, 1.458)
- Hart, J., et al 2002 [22] 1.228 (0.990, 1.467)
- Callaghan, MJ. et al 2008 [29] 1.259 (1.018, 1.500)
- Wang, F. et al 2018 [88] 1.257 (1.015, 1.499)
- Marrotte, EJ. et al 2010 [36] 1.239 (0.999, 1.479)
-Soares, MA. et al 2016 [70] 1.237 (0.997, 1.476)
- Mirza, R. and Koh, TJ. 2011 [39] 1.233 (0.994, 1.472)
- Trousdale, RK. et al 2009 [32] 1.253 (1.010, 1.497)
- Dhall, S. et al 2014 [50] 1.274 (1.038, 1.509)
- Xu, C. et al 2017 [80] 1.262 (1.022, 1.502)
1.05
1.1
1.15
1.2
1.25
1.3
1.35
1.4
Standardized Mean Difference

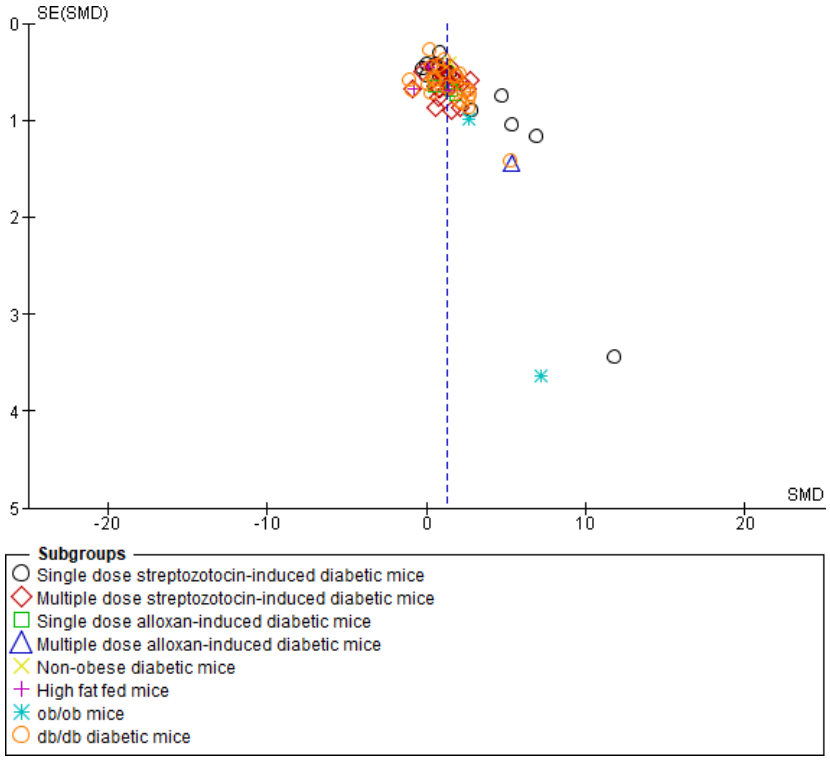
b


Studies
Estimate (95% C.I.)
Overall 2.281 (1.945, 2.618)
Moura, LIF. et al 2014 [54] 2.313 (1.975, 2.651)
Hegde, VN. et al 2011 [38] 2.277 (1.938, 2.617)
Badr, G. 2012 [41] 2.296 (1.954, 2.637)
Badr, G. et al 2012 [42] 2.293 (1.952, 2.635)
Mohany, M. et al 2012 [44] 2.280 (1.940, 2.620)
Badr, G. 2013 [48] 2.285 (1.944, 2.626)
Hozzein, WN. et al 2015 [59] 2.286 (1.945, 2.627)
Badr, G. et al 2016 [64] 2.266 (1.928, 2.604)
Tan, JT. et al 2016 [71] 2.313 (1.974, 2.651)
Cianferani, F. et al 2006 [27] 2.310 (1.970, 2.650)
Lim, YC. et al 2015 [61] 2.313 (1.977, 2.649)
Dong, MW. et al 2016 [66] 2.257 (1.921, 2.594)
Yuan, Y. et al 2018 [91] 2.196 (1.875, 2.516)
Albiero, M. et al 2011 [37] 2.273 (1.934, 2.613)
Fadini, GP. et al 2014 [51] 2.302 (1.960, 2.644)
Available, S. et al 2015 [58] 2.221 (1.891, 2.552)
Straino, S. et al 2008 [30] 2.311 (1.971, 2.652)
Rebalka, IA. et al 2015 [62] 2.311 (1.970, 2.651)
Loyd, CM. et al 2012 [43] 2.313 (1.974, 2.651)
Fang, Y. et al 2010 [34] 2.256 (1.922, 2.589)
Moura, LIF. et al 2014 [55] 2.311 (1.972, 2.649)
Tie, L. et al 2013 [49] 2.294 (1.951, 2.636)
Singla, R. et al 2017 [78] 2.301 (1.962, 2.641)
Shi, Y. et al 2016 [67] 2.279 (1.939, 2.618)
Wu, Y. et al 2016 [73]i 2.268 (1.948, 2.629)
Wu, Y. et al 2016 [73]ii 2.290 (1.950, 2.631)
Wu, Y. et al 2016 [73]iii 2.290 (1.950, 2.630)
Wu, Y. et al 2016 [73]iv 2.276 (1.936, 2.615)
Katagiri, S. et al 2016 [68]i 2.268 (1.928, 2.606)
Hozzein, WN. et al 2018 [85] 2.288 (1.947, 2.629)
Li, X. et al 2019 [92] 2.294 (1.954, 2.634)
Wang, Y. et al 2017 [79] 2.273 (1.933, 2.613)
Botusan, IR. et al 2018 [83] 2.304 (1.962, 2.645)
Graiani, G. et al 2004 [25] 2.291 (1.950, 2.631)
Long, M. et al 2018 [69] 2.299 (1.959, 2.639)
Yu, JW. et al 2016 [74] 2.275 (1.936, 2.613)
Agostinho Hunt, AM. et al 2017 [75] 2.228 (1.897, 2.560)
Nishika-Yan Shen, T. et al 2017 [76] 2.274 (1.936, 2.612)
Desposito, D. et al 2016 [65] 2.303 (1.960, 2.643)
Rebalka, IA. et al 2015 [62] 2.306 (1.966, 2.645)
Jacobsen, JN. et al 2010 [35] 2.311 (1.971, 2.651)
Leal, EC. et al 2015 [60]i 2.298 (1.957, 2.640)
Leal, EC. et al 2015 [60]ii 2.312 (1.974, 2.651)
Wong, SL. et al 2015 [63] 2.304 (1.962, 2.645)
Tellechea, A. et al 2016 [72] 2.299 (1.957, 2.641)
Shin, J. et al [77] 2.271 (1.933, 2.609)
Eo, H. et al 2016 [67] 2.303 (1.962, 2.643)
Cardoso, SH. et al 2018 [84] 2.271 (1.933, 2.609)
Abu-Al-Basal, MA. 2010 [33] 2.252 (1.916, 2.587)
Chen, J. et al 2005 [26] 2.221 (1.891, 2.551)
Darby, IA. et al 1997 [20] 2.262 (1.926, 2.598)
Wegner, IJ. et al 2012 [47] 2.312 (1.971, 2.653)
Yan, J. et al 2018 [89] 2.302 (1.961, 2.642)
Wang, XQ. et al 2014 [57] 2.285 (1.944, 2.625)
Katagiri, S. et al 2016 [68]ii 2.300 (1.960, 2.641)
Zhao, H. et al 2017 [82] 2.271 (1.934, 2.607)
Zhao, H. et al 2017 [81] 2.263 (1.926, 2.601)
Steinstraesser, L. et al 2012 [46] 2.303 (1.963, 2.643)
Goyit, M. et al 2014 [52] 2.304 (1.959, 2.649)
Steinstraesser, L. et al 2014 [56] 2.291 (1.951, 2.631)
Pietramaggiori, G. et al 2009 [31] 2.263 (1.926, 2.601)
Shin, L. and Peterson, DA. 2012 [45] 2.306 (1.964, 2.648)
Jiménez-Jiménez, C. et al 2018 [86] 2.261 (1.942, 2.621)
Wall, SJ. et al 2002 [23] 2.274 (1.935, 2.613)
Yang, C-T. et al 2019 [93] 2.256 (1.920, 2.592)
Brown, RL. et al 1994 [17] 2.267 (1.929, 2.605)
Matuszewska, B. et al 1994 [18] 2.286 (1.946, 2.626)
Brown, DL. et al 1997 [19] 2.256 (1.920, 2.592)
Crowe, MJ. et al 1999 [21] 2.286 (1.946, 2.625)
Kirchner, LM. et al 2003 [24] 2.256 (1.920, 2.592)
Liu, F. et al 2014 [53] 2.287 (1.946, 2.628)
Yu, B. et al 2018 [90] 2.289 (1.950, 2.629)
Mace, KA. et al 2007 [28]ii 2.252 (1.920, 2.583)
Hart, J., et al 2002 [22] 2.253 (1.917, 2.590)
Callaghan, MJ. et al 2009 [29] 2.297 (1.956, 2.637)
Wang, F. et al 2018 [88] 2.283 (1.943, 2.624)
Marrotte, EJ. et al 2010 [36] 2.242 (1.906, 2.576)
Soares, MA. et al 2016 [70] 2.272 (1.935, 2.609)
Yan, J. et al 2019 [99] 2.274 (1.936, 2.613)
Mirza, R. and Koh, T.J. 2011 [39] 2.246 (1.911, 2.581)
Trousdale, RK. et al 2009 [32] 2.290 (1.947, 2.632)
Dhall, S. et al 2014 [50] 2.254 (1.918, 2.591)
Wetterau, M. et al 2011 [40] 2.224 (1.900, 2.549)
Xu, C. et al 2017 [80] 2.303 (1.963, 2.643)
2
2.1
2.2
2.3
2.4
2.5
Standardized Mean Difference

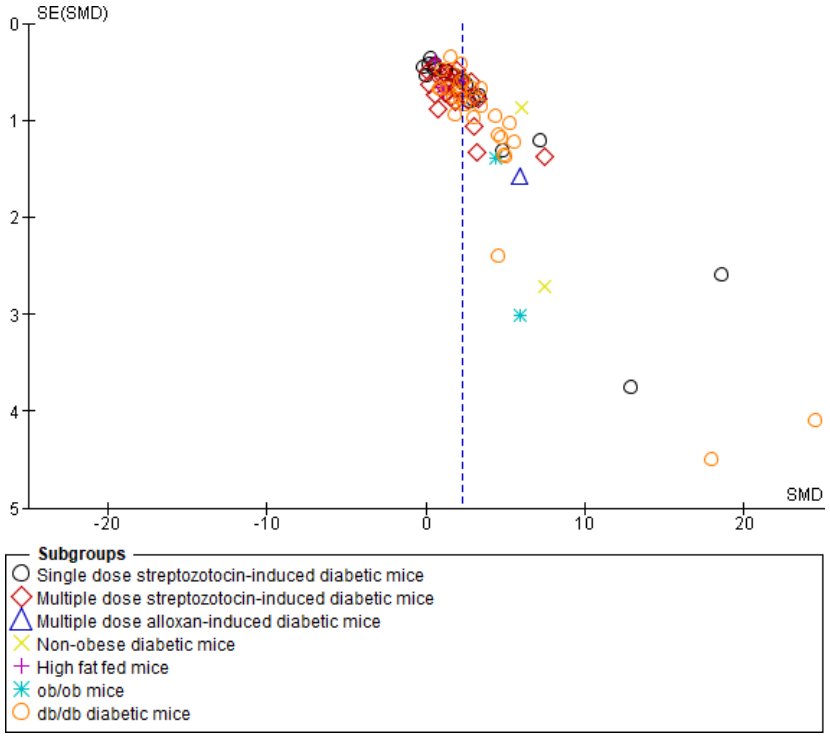
c



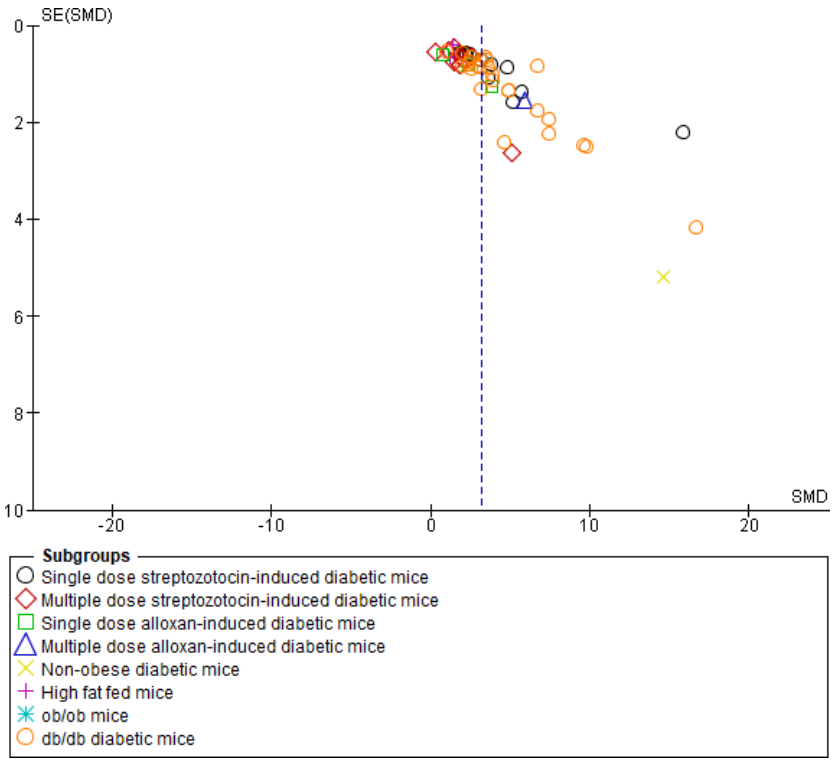
Supplementary Figure 3. Leave-one-out sensitivity analysis. Forest plots generated using OpenMeta-Analyst showing that exclusion of individual studies do not affect the overall SMD at early (**a**; 2-5 days), intermediate (**b**; 6-10 days) and late stages of wound closure (**c**; 11-20 days).


SE(SMD)
0
1
2
3
4
5
-20
-10
0
10
20
SMD
Subgroups
Single dose streptozotocin-induced diabetic mice
Multiple dose streptozotocin-induced diabetic mice
Single dose alloxan-induced diabetic mice
Multiple dose alloxan-induced diabetic mice
Non-obese diabetic mice
High fat fed mice
ob/ob mice
db/db diabetic mice

b


SE(SMD)
0
1
2
3
4
5
-20
-10
0
10
20
SMD
Subgroups
Single dose streptozotocin-induced diabetic mice
Multiple dose streptozotocin-induced diabetic mice
Multiple dose alloxan-induced diabetic mice
Non-obese diabetic mice
High fat fed mice
ob/ob mice
db/db diabetic mice

c



Supplementary Figure 4. Funnel plots for the assessment of publication bias of included studies showing the effect of diabetes on wound closure in different mouse models of diabetes. Meta-analysis was performed on 77 studies, with Funnel plots being generated from Review Manager V5.3 to represent early (**a**; 2-5 days), intermediate (**b**; 6-10 days) and late stages of wound closure (**c**; 11-20 days). Comparisons were made using standard mean differences and a random effects model.

Supplementary Table 11: Key clinical features of diabetes-associated ulcers

Characteristic	Usual clinical findings
Confirmation of diabetes	• Fasting blood glucose of ≥7.0 mmol/L, performed multiple times • Hb1ac blood test result of ≥6.5% (48 mmol/mol)
Average duration of diabetes	~15 years
Site of ulcer	• Neuropathic: plantar surface of foot or pressure point • Ischaemic: toes
Associated findings	• Loss of sensation • Foot deformity e.g. loss of foot arch • Absent foot pulses and gangrene if severe ischemia