

Supplementary Materials

F. A. Meznerics, K. D. Kovács, F. Dembrovszky, P. Fehérvári, L. V. Kemény, D. Csupor, P. Hegyi, A. Bánvölgyi. Platelet-rich plasma in chronic wound management. A systematic review and meta-analysis of randomized clinical trials.

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Table S1. Summary of Findings Table.

Outcomes	№ of wounds [#] (studies)	Certainty of the evidence (GRADE)	Effect		Comments
			Relative effect (95% CI)	Absolute effect (95% CI)	
Primary outcome					
Complete closure (№ of wounds closed) follow-up: 1 to 48 weeks	2198 (33 study groups of 29 RCTs)	⊕⊕⊕○ Moderate	OR 5.32 (3.37; 8.40)	5 fewer per 1000 (from 8 fewer to 3 fewer)	Higher number of completely closed wounds indicates greater improvement
Complete closure (№ of wounds closed) etiology: venous follow-up: 1 to 48 weeks	419 (11 study groups of 9 RCTs)	⊕⊕⊕○ Moderate	OR 8.02 (3.63; 17.71)	8 fewer per 1000 (from 18 fewer to 4 fewer)	
Complete closure (№ of wounds closed) etiology: diabetic follow-up: 1 to 48 weeks	1442 (14 study groups of 14 RCTs)	⊕⊕⊕○ Moderate	OR 2.26 (1.50;3.41)	2 fewer per 1000 (from 3 fewer to 2 fewer)	
Complete closure (№ of wounds closed) application: topical follow-up: 1 to 48 weeks	1920 (28 study groups of 26 RCTs)	⊕⊕⊕○ Moderate	OR 4.74 (2.87; 7.83)	5 fewer per 1000 (from 8 fewer to 3 fewer)	
Complete closure (№ of wounds closed) application: injected follow-up: 1 to 48 weeks	278 (5 study groups of 5 RCTs)	⊕⊕○○ Low	OR 9.42 (3.32;26.76)	9 fewer per 1000 (from 27 fewer to 3 fewer)	
Complete closure (№ of wounds closed) follow-up: <12 weeks	1157 (21 study groups of 18 RCTs)	⊕⊕⊕○ Moderate	OR 6.03 (3.21; 11.33)	6 fewer per 1000 (from 11 fewer to 3 fewer)	
Complete closure (№ of wounds closed) follow-up: 12 to 20 weeks	741 (8 study groups of 8 RCTs)	⊕⊕○○ Low	OR 3.38 (1.15;9.89)	3 fewer per 1000 (from 10 fewer to 1 fewer)	

Outcomes	No of wounds [#] (studies)	Certainty of the evidence (GRADE)	Effect		Comments
			Relative effect (95% CI)	Absolute effect (95% CI)	
Complete closure (No of wounds closed) follow-up: >20 weeks	200 (3 study groups of 2 RCTs)	⊕○○○ Very low	OR 8.24 (1.66; 40.87)	8 fewer per 1000 (from 41 fewer to 2 fewer)	
Reduction of wound area (cm²) follow-up: 1 to 48 weeks	1062 (18 study groups of 16 RCTs)	⊕⊕○○ Low	-	SMD -1.21 cm² lower (CI: -1.74; -0.68)	Lower SMD indicates greater improvement
Reduction of wound area (cm ²) etiology: venous follow-up: 1 to 48 weeks	517 (9 study groups of 7 RCTs)	⊕⊕○○ Low	-	SMD -1.26 cm ² lower (CI: -2.28; -0.24)	
Reduction of wound area (cm ²) etiology: diabetic follow-up: 1 to 48 weeks	201 (4 study groups of 4 RCTs)	⊕○○○ Very low	-	SMD -0.68 cm ² lower (CI: -1.31; -0.66)	
Reduction of wound area (cm ²) application: topical follow-up: 1 to 48 weeks	694 (13 study groups of 13 RCTs)	⊕⊕○○ Low	-	SMD -0.94 cm ² lower (CI: -1.43; -0.46)	
Reduction of wound area (cm ²) application: injected follow-up: 1 to 48 weeks	368 (5 study groups of 5 RCTs)	⊕○○○ Very low	-	SMD -1.03 cm ² lower (CI: -1.79; -0.26)	
Reduction of wound area (cm ²) follow-up: <12 weeks	629 (4 study groups of 4 RCTs)	⊕⊕○○ Low	-	SMD -1.00 cm ² lower (CI: -1.64; -0.35)	
Reduction of wound area (cm ²) follow-up: 12 to 20 weeks	80 (2 study groups of 1 RCT)	⊕○○○ Very low	-	SMD -1.38 cm ² lower (CI: -2.96; 0.19)	
Reduction of wound area (cm ²) follow-up: >20 weeks	353 (5 study groups of 4 RCTs)	⊕○○○ Very low	-	SMD -0.63 cm ² lower (CI: -1.64; 0.37)	

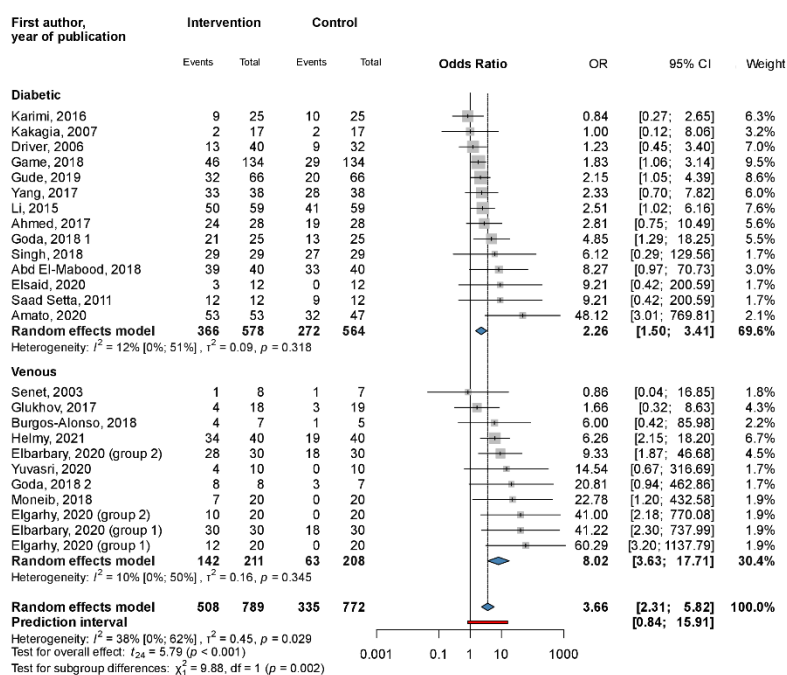
Outcomes	No of wounds [#] (studies)	Certainty of the evidence (GRADE)	Effect		Comments
			Relative effect (95% CI)	Absolute effect (95% CI)	
Healing rate (change of wound size/time interval) follow-up: 1 to 48 weeks	453 (7 study groups of 7 RCTs)	⊕○○○ Very low	not pooled	not pooled	Higher rate indicates greater improvement (see eTable 2)
<i>Secondary outcomes</i>					
Healing time	1198 (16 study groups of 14 RCTs)	⊕○○○ Very low	not pooled	not pooled	see Table 2
Infection	1039 (16 study groups of 14 RCTs)	⊕○○○ Very low	not pooled	not pooled	see Table 2
Pain	953 (11 study groups of 11 RCTs)	⊕○○○ Very low	not pooled	not pooled	see Table 2
Amputation	767 (7 study groups of 7 RCTs)	⊕○○○ Very low	not pooled	not pooled	see Table 2
Adverse event	1100 (15 study groups of 15 RCTs)	⊕○○○ Very low	not pooled	not pooled	see Table 2
CI: confidence interval, RCT: randomized clinical trial, SMD: standardized mean difference, OR: odds ratio					

Table S2. Characteristics of the studies assessing the change of wound size.

First author, year of publication	PRP application	Sample size (intervention)	Sample size (control)	Mean (SD) baseline wound area (cm²)		Time of evaluation	Reduction of wound area				Healing rate		Comlete closure	
							Mean (SD) post-treatment wound area (cm²)		Mean reduction of wound area (%)		Mean (SD) healing rate		Wounds completely closed (% of total)	
				Intervention group	Control group		Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Abd El-Mabood, 2018 [1]	topical	40	40	N/A	N/A	week 2	N/A	N/A	N/A	N/A	0.8 (0.2) cm²/week	0.4 (0.2) cm²/week	33.0%	10.0%
						week 4					0.9 (0.1) cm²/week	0.5 (0.1) cm²/week	47.5%	22.5%
						week 6					0.6 (0.9) cm²/week	0.3 (0.2) cm²/week	7.5%	17.5%
						week 8					0.5 (0.1) cm²/week	0.3 (0.1) cm²/week	5.0%	15.0%
						week 10					0.2 (0.1) cm²/week	0.4 (0.1) cm²/week	2.5%	10.0%
						week 12					0.19 (0.11) cm²/week	0.4 (0.1) cm²/week	2.5%	7.5%
						total					7.3 (0.9) cm²/week	5.8 (0.5) cm²/week	97.5%	82.5%
Ahmed, 2017 [2]	topical	28	28	N/A	N/A	week 2	N/A	N/A	N/A	N/A	0.7 (0.15) cm²/week	0.5 (0.1) cm²/week	28.5%	7.1%
						week 4					0.9 (0.1) cm²/week	0.4 (0.2) cm²/week	39.2%	17.8%
						week 8					0.6 (0.2) cm²/week	0.5 (0.1) cm²/week	14.2%	28.5%
						week 12					0.2 (0.1) cm²/week	0.4 (0.1) cm²/week	3.5%	14.2%
						total					N/A	N/A	85.7%	67.8%
Amato, 2020 [3]	topical	53	47	24.0 (16.0)	22.0 (9.0)	week 1	N/A	N/A	12.0%+	10.0%+	N/A	N/A	N/A	N/A
						week 2			23.0%+	12.0%+			N/A	N/A
						week 3			28.0%+	15.0%+			N/A	N/A
						week 4			35.0%+	19.0%+			N/A	N/A
						week 5			46.0%+	22.0%+			20.7%	4.2%
						week 6			52.0%+	28.0%+			26.4%	2.1%
						week 7			58.0%+	36.0%+			15.0%	6.3%
						week 8			64.0%+	41.0%+			15.0%	6.3%
						week 9			72.0%+	49.0%+			13.2%	10.5%
						week 10			85.0%+	57.0%+			3.7%	14.8%
						week 11			94.0%+	65.0%+			1.8%	13.9%
						week 12			100.0%+	71.0%+			0.0%	18.6%
						total			N/A	N/A			100.0%	68.0%
Anitua, 2008 [4]	topical	7	7	N/A	N/A	week 8	N/A	N/A	72.9%	21.5%	N/A	N/A	N/A	N/A
Burgos-Alonso, 2018 [5]	topical	7	5	N/A	N/A	week 5	N/A	N/A	39.6%	22.9%	N/A	N/A	N/A	N/A
						week 9			82.8%	40.8%			60.0%	20.0%
Cardenosa, 2017 [6]	topical	55	47	13.7 (30.0)	16.7 (23.9)	week 24	10.0 (30.0)	12.1 (19.2)	67.7%	11.2%	N/A	N/A	N/A	N/A
Chandanwale, 2020 [7]	Injected	40	40	23.0 (19.1)	22.6 (17.4)	day 8	N/A	N/A	1.4%	0.2%	N/A	N/A	N/A	N/A
						day 15	21.7	22.4	7.6%	2.4%	N/A	N/A		
						day 20	N/A	N/A	18.6%	8.2%	N/A	N/A		
						day 30	17	20	35.2%	16.2%	N/A	N/A		
						day 60	11.6 (14.0)	17.6 (15.6)	66.2%	29.9%	17.3 mm³/day	8.9 mm³/day		
de Oliveira, 2017 [8]	topical	9	12	7.4 (5.5-10.3)+	16.1 (6.2-47.9)+	week 13	2.7 (1.5-3.7)+	4.9 (2.3-21.3)+	64.0%	70.0%	N/A	N/A	N/A	N/A
Driver, 2006 [9]	topical	40	32	N/A	N/A	week 12	N/A	N/A	N/A	N/A	0.05 cm²/day	0.05 cm²/day	32.5%	28.1%
Elbarbary, 2020 (group I) [10]	topical	30	30	16.5 (8.2)	17.8 (5.4)	week 12	5.8 (2.1)	8.5 (3.3)	65.0%	52.0%	N/A	N/A	33.3%	13.3%
						week 48	1.2 (0.5)	3.8 (1.5)	92.7%	78.6%			66.7%	46.7%
Elbarbary, 2020 (group II) [10]	Injected	30	30	15.7 (7.4)	17.8 (5.4)	week 12	2.5 (1.3)	8.5 (3.3)	84.0%	52.0%	N/A	N/A	46.7%	13.3%
						week 48	1.1 (0.4)	3.8 (1.5)	93.0%	78.6%			80.0%	46.7%
Elgarhy, 2020 (group I) [11]	topical	20	20	33.7 (53.3)	15.0 (8.3)	week 6	8.5 (20.5)	10.1 (6.3)	N/A	N/A	N/A	N/A	60.0%	0.0%
						week 12	3 (7.9)	8.4 (6.6)					N/A	N/A
Elgarhy, 2020 (group II) [11]	Injected	20	20	21.8 (20.2)	15.0 (8.3)	week 6	3.2 (5.4)	10.1 (6.3)	N/A	N/A	N/A	N/A	50.0%	0.0%
						week 12	1.1 (2.3)	8.4 (6.6)					N/A	N/A
Elsaid, 2020 [12]	topical	12	12	N/A	N/A	week 20	N/A	N/A	longitudinal: 43.2%	longitudinal: 4.1%	N/A	N/A	25.0%	0.0%
									horizontal: 42.3%	horizontal: 8.2%				
Game, 2018 [13]	topical	134	134	2.29 (2.1)	2.53 (2.3)	week 20	N/A	N/A	N/A	N/A	N/A	N/A	34.0%	22.0%
Glukhov, 2017 [14]	topical	18	19	17.2 (2.8)	10.3 (5.8)	week 8	N/A	N/A	N/A	N/A	N/A	N/A	22.0%	16.0%
Goda, 2018 1 [15]	topical	25	25	7.3 (1.6)	7.08 (1.3)	week 1	N/A	N/A	N/A	N/A	0.7 cm²/week	0.5 cm²/week	0.0%	0.0%
						week 4							0.0%	0.0%
						week 6							0.0%	0.0%
						week 8							12.0%	0.0%
						week 10							44.0%	4.0%
						week 12							84.0%	52.0%
Goda, 2018 2 (group I) [16]	topical	10	11	<10cm²	<10cm²	week 2	N/A	N/A	53.4%	23.5%	N/A	N/A	N/A	N/A
						week 3			80.2%	47.2%	N/A	N/A	30.0%	0.0%
						week 4			100.0%	62.2%	N/A	N/A	100.0%	9.0%
						week 6			100.0%	100.0%	N/A	N/A	N/A	N/A
Goda, 2018 2 (group II) [16]	topical	8	7	>10cm²	>10cm²	week 2	N/A	N/A	31.1%	14.4%	N/A	N/A	N/A	N/A
						week 3			49.4%	29.1%			0.0%	0.0%
						week 4			64.3%	43.3%			0.0%	0.0%
						week 6			96.3%	71.6%			50.0%	14.3%
						week 7			100.0%	86.8%			100.0%	42.6%
						week 8			100.0%	97.3%			N/A	N/A
Gude, 2019 [17]	topical	66	66	4.1	5.6	week 12	N/A	N/A	N/A	N/A	N/A	N/A	48.2%	30.2%
Helmy, 2021 [18]	Injected	40	40	16.7 (11.1)	20.4 (18.5)	week 12	0.9 (2.2)	3.9 (6.9)	94.8%	80.8%	N/A	N/A	85.0%	42.5%
						week 24	0.8 (2.0)	2.2 (3.8)	95.3%	89.4%			85.0%	62.5%
						week 48	0.8 (2.1)	3.5 (6.5)	95.4%	82.6%			85.0%	47.5%
Hongying, 2020 [19]	injected	20	20	9.55 (0.61)	9.05 (1.19)	2	8.65 (0.93)	9.00 (1.21)	N/A	N/A	N/A	N/A	N/A	N/A
						4	6.85 (1.42)	8.30 (1.75)					N/A	N/A
						6	3.85 (1.89)	7.45 (2.04)					N/A	N/A
						8	1.20 (1.51)	6.65 (2.64)					100.0%	35.0%
Kakagia, 2007 [20]	topical	17	17	28.4 (13.6)	25.8 (15.2)	week 8	N/A	N/A	N/A	N/A	N/A	N/A	11.8%	11.8%
Karimi, 2016 [21]	topical	25	25	7.0 (9.8)	13.2 (9.4)	week 3	2.7 (5.9)	11.9 (13.7)	N/A	N/A	N/A	N/A	36.0%	40.0%
Kulkarni, 2019 [22]	topical	25	25	13.29 (1.3)	13.4 (1.3)	week 3	7.5 (1.0)	11.5 (1.1)	43.4%	14.0%	N/A	N/A	N/A	N/A
Li, 2015 [23]	topical	59	59	4.1 (1.4-11.4)+	2.9 (1.0-10.5)+	week 12	N/A	N/A	N/A	N/A	N/A	N/A	84.8%	69.0%
Milek, 2019 [24]	topical	50	50	3.7 (1.0)	3.7 (1.1)	week 4	0.8 (0.4)	1.7 (0.5)	N/A	N/A	N/A	N/A	56.0%	N/A
Mohammad, 2017 [25]	topical	25	25	12.8 (14.9)	14.2 (8.52)	week 1	7.0 (9.8)	13.2 (9.53)	N/A	N/A	N/A	N/A	N/A	N/A
						week 2	5.1 (8.5)	12.3 (11.0)						
						week 3	2.7 (5.9)	11.9 (13.7)						
Moneib, 2018 [26]	topical	20	20	8.0 (16.9)	2.9	week 6	3.1 (5.9)	2.8 (1.5)	67.6%	13.7%	N/A	N/A	35.0%	0.0%
Obolenskiy, 2014 [27]	topical	44	44	90.2 (14.1)	79.6 (12.3)	week 13	N/A	N/A	N/A	N/A	N/A	N/A	85.0%	12.0%
Obolenskiy, 2017 [28]	topical	50	50	19.2 (3.0)	21.7 (2.5)	N/A	N/A	N/A	N/A	N/A	0.2 cm²/week	N/A	92.0%	60.0%
Pu, 2019 [29]	topical	21	30	6.3 (5.3)	5.2 (5.9)	week 24	3.3 (4.2)	2.6 (8.7)	9.5%	23.3%	N/A	N/A	N/A	N/A
Qin, 2019 [30]	topical	30	30	N/A	N/A	week 12	N/A	N/A	52.1%	21.3%	N/A	N/A	N/A	N/A
	Injected	30	30			93.2%			21.3%					
Rainys, 2019 [31]	topical	35	34	12.9 (16.6)	10.4 (11.3)	week 8	6.2 (6.9)	6.9 (8.8)	52.4%	33.4%	N/A	N/A	25.7%	17.6%

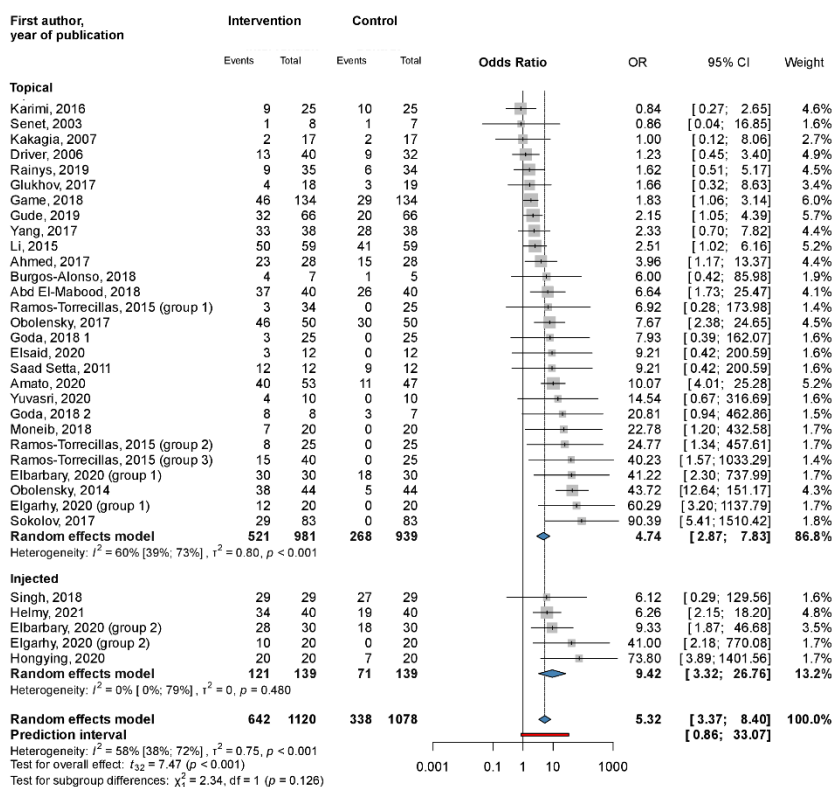
Ramos-Torrecillas, 2015 (group I) [32]	topical PRP (1 dose)	34	25	N/A	N/A	week 5	N/A	N/A	48.3%	10.3%	N/A	N/A	9.0%	0.0%
Ramos-Torrecillas, 2015 (group II) [32]	topical PRP (2 doses)	25	25	N/A	N/A	week 5	N/A	N/A	54.8%	10.3%	N/A	N/A	32.0%	0.0%
Ramos-Torrecillas, 2015 (group III) [32]	topica PRPl+HA	40	25	N/A	N/A	week 5	N/A	N/A	80.4%	10.3%	N/A	N/A	37.5%	0.0%
Saad Setta, 2011 [33]	topical	12	12	10.3 (5-21)	8.5 (4-20)	week 20	N/A	N/A	N/A	N/A	N/A	N/A	100.0%	75.0%
Saha, 2020 [34]	Injected	56	52	5.9 (4.6)	5.6 (3.7)	week 2	3.8 (3.5)	4.9 (3.3)	39.0%	12.5%	N/A	N/A	0.0%	0.0%
						week 4	2.5 (2.6)	3.7 (2.6)	59.6%	33.6%				
						week 6	1.7 (1.8)	2.6 (1.9)	73.3%	54.1%				
						week 8	1.0 (1.1)	1.2 (1.0)	82.6%	79.3%				
						week 10	0.6 (0.7)	1.2 (1.0)	91.1%	79.8%				
Semenić, 2018 [35]	topical	30	30	N/A	N/A	week 24	N/A	N/A	35.0%	90.0%	N/A	N/A	N/A	N/A
Senet, 2003 [36]	topical	8	7	13.8 (7.9)	10.9 (8.4)	week 12	N/A	N/A	26.2%	15.2%	0.0033 (0.0061) cm/day	0.0021 (0.0058) cm/day	12.5%	14.3%
Singh, 2018 [37]	Injected	29	29	N/A	N/A	week 4	N/A	N/A	N/A	N/A	N/A	N/A	100.0%	92.0%
Singh, 2021 [38]	Injected	26	26	37.0	36.4	week 6	N/A	N/A	N/A	N/A	N/A	N/A	0.0%	0.0%
Sokolov, 2017 [39]	topical	83	83	N/A	N/A	week 8	N/A	N/A	N/A	N/A	N/A	N/A	34.9%	0.0%
						week 12							28.9%	8.5%
						total							63.9%	8.5%
Somani, 2017 [40]	topical	9	6	8.1 (5.4)	4.9 (4.7)	week 4	1.7 (3.2)	3.3 (4.4)	85.5%	42.7%	N/A	N/A	0.0%	0.0%
Tsachiridi, 2019 [41]	topical	15	12	0.2 (0.1)	0.5 (0.5)	week 5	0.1 (0.01)	1.5 (1.3)	N/A	N/A	N/A	N/A	0.0%	0.0%
Tsai, 2019 [42]	topical+injected	14	14	N/A	N/A	week 4	N/A	N/A	>75%	50-75%	N/A	N/A	N/A	N/A
Ucar, 2020 [43]	topical	30	30	4.7 (1.8)	4.8 (1.3)	week 8	2.8 (2.4)	5.0 (1.3)	N/A	N/A	N/A	N/A	N/A	N/A
Yang, 2017 [44]	topical	38	38	N/A	N/A	week 4	N/A	N/A	84.6%	77.1%	N/A	N/A	87.5%	75.0%
Yuvasri, 2020 [45]	topical	10	10	4.9 (3.1)	8.3 (6.7)	week 4	0.6 (1.0)	5.0 (1.3)	86.0%	72.0%	N/A	N/A	40.0%	0.0%

SD-standard deviation, PRP-platelet-rich plasma
* median (interquartile range)



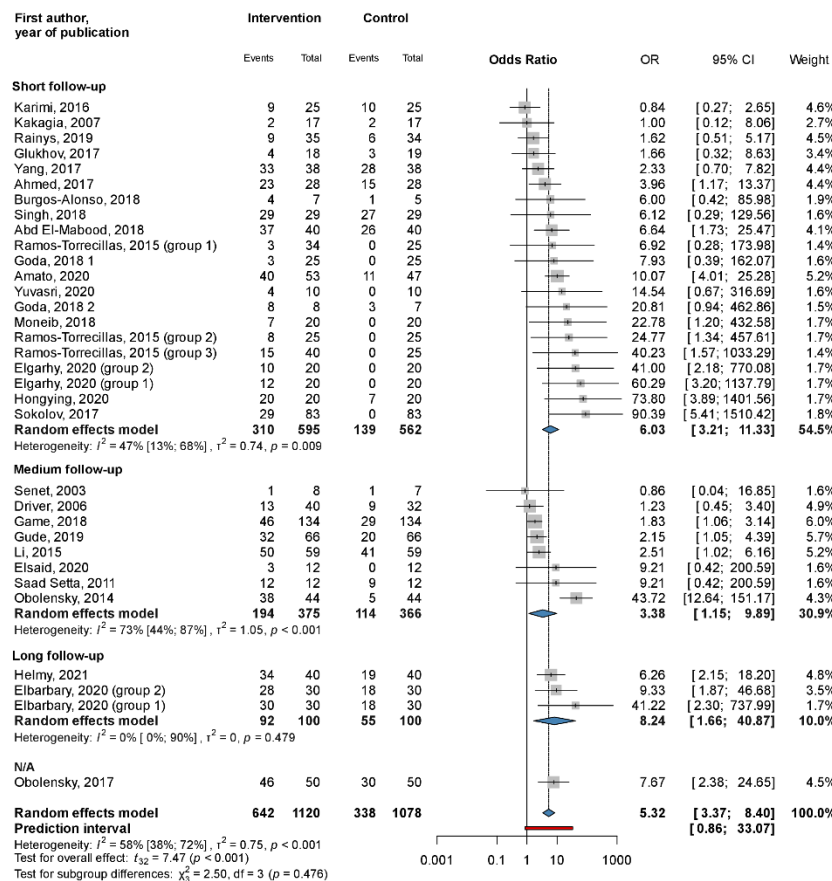
OR-odds ratio; CI-confidence interval

Figure S1. Forest plot for complete closure, subgrouping based on ulcer etiologies.



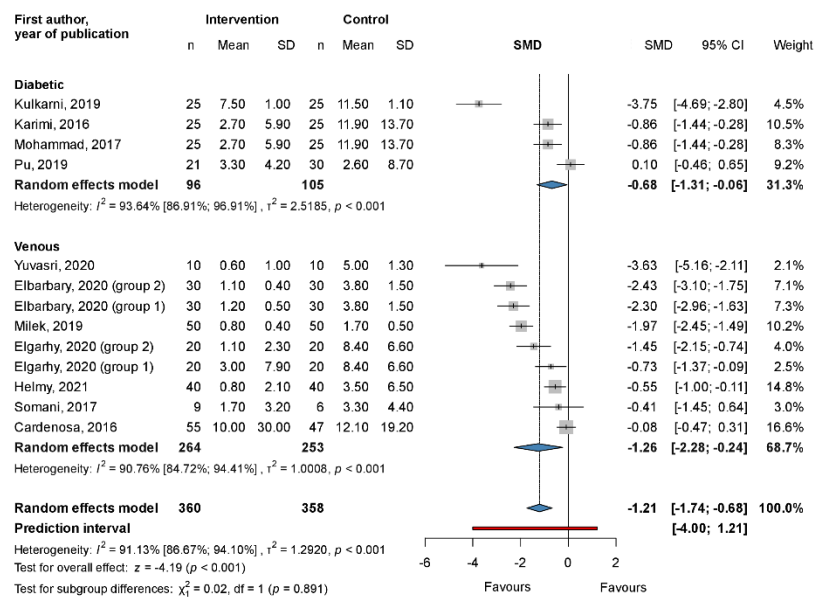
OR-odds ratio; CI-confidence interval

Figure S2. Forest plot for complete closure, subgrouping based on PRP application method.



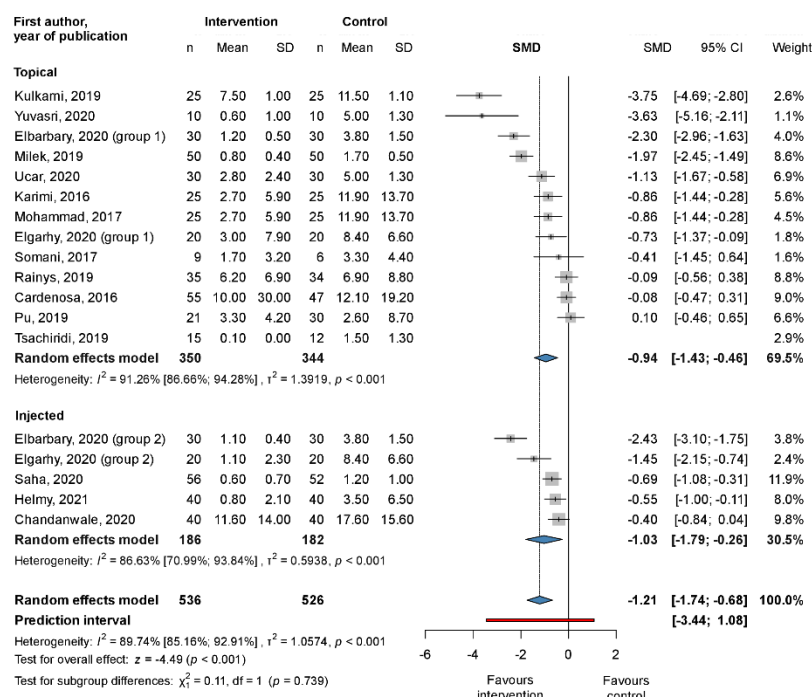
OR-odds ratio; CI-confidence interval

Figure S3. Forest plot for complete closure, subgrouping based on follow-up time.



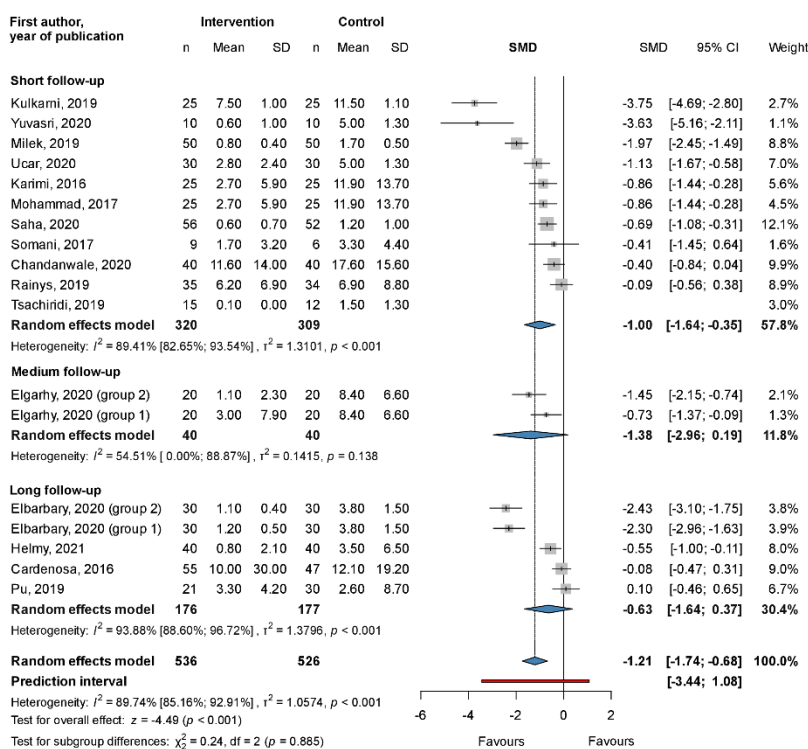
SD-standard deviation; SMD-standardized mean difference; CI-confidence interval

Figure S4. Forest plot for wound area reduction, subgrouping based on ulcer etiologies.



SD-standard deviation; SMD-standardized mean difference; CI-confidence interval

Figure S5. Forest plot for wound area reduction, subgrouping based on PRP application method.



SD-standard deviation; SMD-standardized mean difference; CI-confidence interval

Figure S6. Forest plot for wound area reduction, subgrouping based on follow-up time.

First author, year of publication	Weight	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Abd El Mabood, 2018	1	+	+	+	+	+	+
Ahmed, 2016	1	?	+	+	+	?	!
Amato, 2020	1	?	?	+	+	+	!
Anitua, 2008	1	?	+	?	+	+	!
Burgos-Alonso, 2018	1	?	+	+	+	+	!
Cardenosa, 2017	1	+	+	+	+	+	+
Chandanwale, 2020	1	?	+	+	+	+	!
de Oliveira, 2017	1	+	+	+	+	?	!
Driver, 2006	1	?	+	+	+	+	!
Elbarbary, 2020	1	+	+	+	+	+	+
Elgarhy, 2020	1	+	+	+	+	+	+
Elsaid, 2020	1	+	+	+	+	+	+
Game, 2018	1	+	+	+	+	+	+
Glukhov, 2017	1	?	+	+	+	+	!
Goda, 2018 1	1	+	+	+	+	+	+
Goda, 2018 2	1	+	+	+	+	+	+
Gude, 2019	1	?	?	+	+	?	!
Helmy, 2021	1	?	+	+	+	+	+
Hongying, 2020	1	+	?	+	?	+	!
Kakagia, 2007	1	?	?	+	?	+	!
Karimi, 2016	1	+	+	+	+	+	+
Kulkarni, 2019	1	?	+	+	+	+	+
Li, 2015	1	?	?	+	+	+	!
Milek, 2019	1	?	+	+	+	+	!
Mohammad, 2017	1	?	?	+	?	+	!
Moneib, 2018	1	?	+	+	+	+	+
Obolensky, 2014	1	?	?	+	+	+	!
Obolensky, 2017	1	?	+	+	+	+	!
Pu, 2019	1	+	+	+	+	+	+
Qin, 2019	1	?	?	+	?	+	!
Rainys, 2019	1	+	+	+	+	?	!
Ramos-Torrecillas, 2019	1	?	+	+	+	?	!
Saad Setta, 2011	1	?	?	+	?	+	!
Saha, 2020	1	+	+	+	+	+	+
Semenic, 2018	1	?	+	+	+	+	+
Senet, 2003	1	?	+	+	+	+	!
Singh, 2018	1	?	?	+	+	?	!
Singh, 2021	1	+	+	+	+	+	+
Sokolov, 2017	1	?	+	+	+	+	!
Somani, 2017	1	?	?	+	+	?	!
Tsachiridi, 2019	1	?	+	+	+	+	!
Tsai, 2019	1	?	+	+	+	+	+
Ucar, 2020	1	?	?	+	+	+	!
Yang, 2017	1	?	+	+	+	+	+
Yuvashi, 2020	1	?	+	+	+	?	!

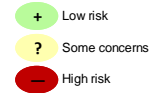


Figure S7. Risk of bias assessment of the included studies assessing the change of wound size [1–6,8–45], using the revised tool for assessing risk of bias in randomized trials (Rob 2).

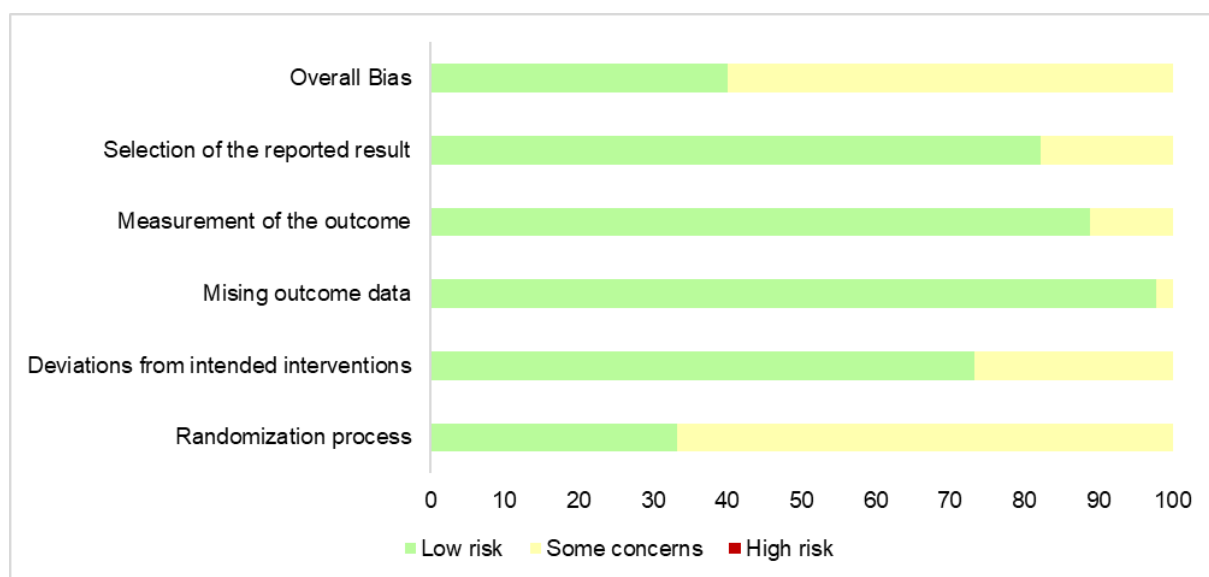


Figure S8. Risk of bias assessment of the included studies assessing the change of wound size [1–6,8–45], broken down to tools, shown in percentage.



Figure S9. Risk of bias assessment of the included studies assessing healing time [9–13,18,22,23,27,28,33,38,44,46], using the revised tool for assessing risk of bias in randomized trials (Rob 2).

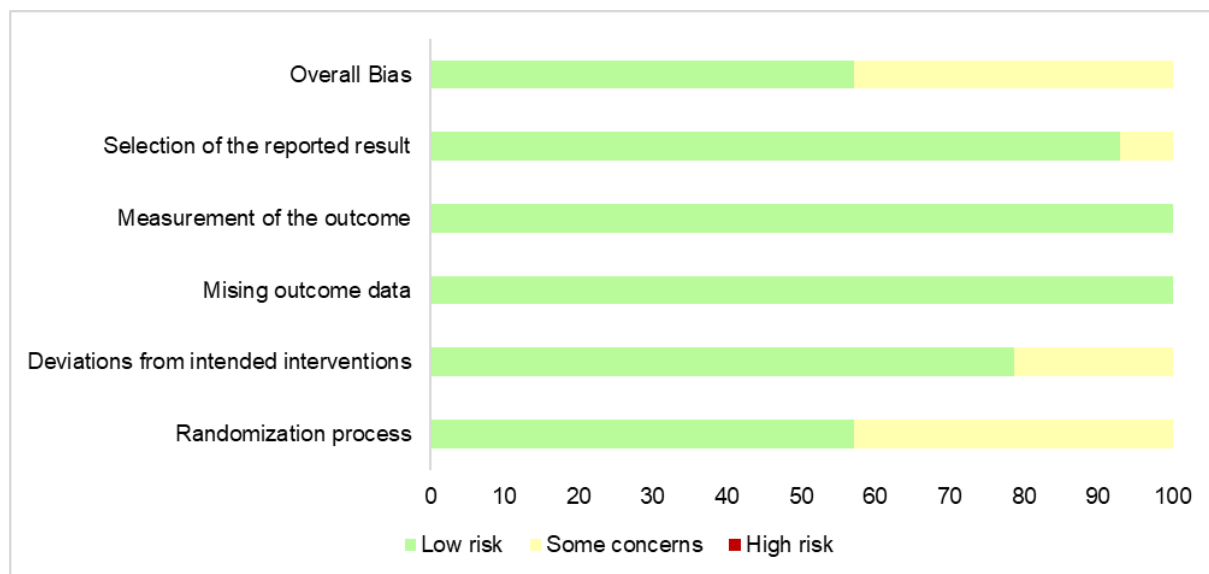


Figure S10. Risk of bias assessment of the included studies assessing healing time [9–13,18,22,23,27,28,33,38,44,46], broken down to tools, shown in percentage.

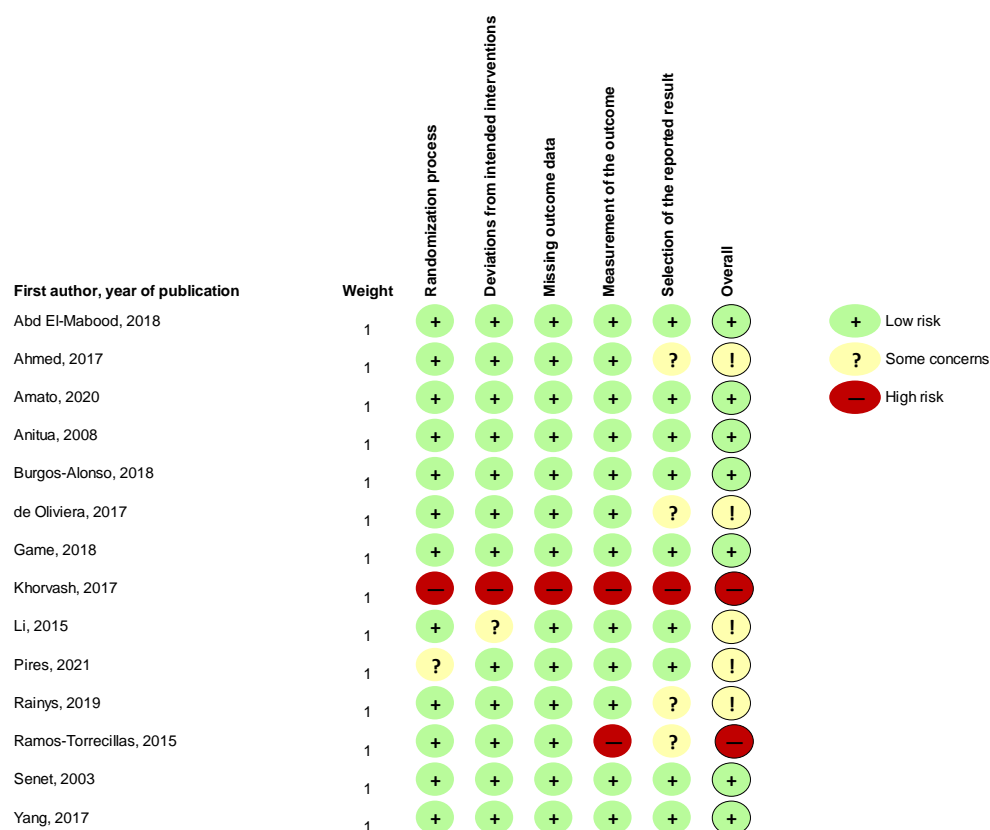


Figure S11. Risk of bias assessment of the included studies assessing infection rates [1–5,8,13,23,31,32,36,44,47,48], using the revised tool for assessing risk of bias in randomized trials (Rob 2).

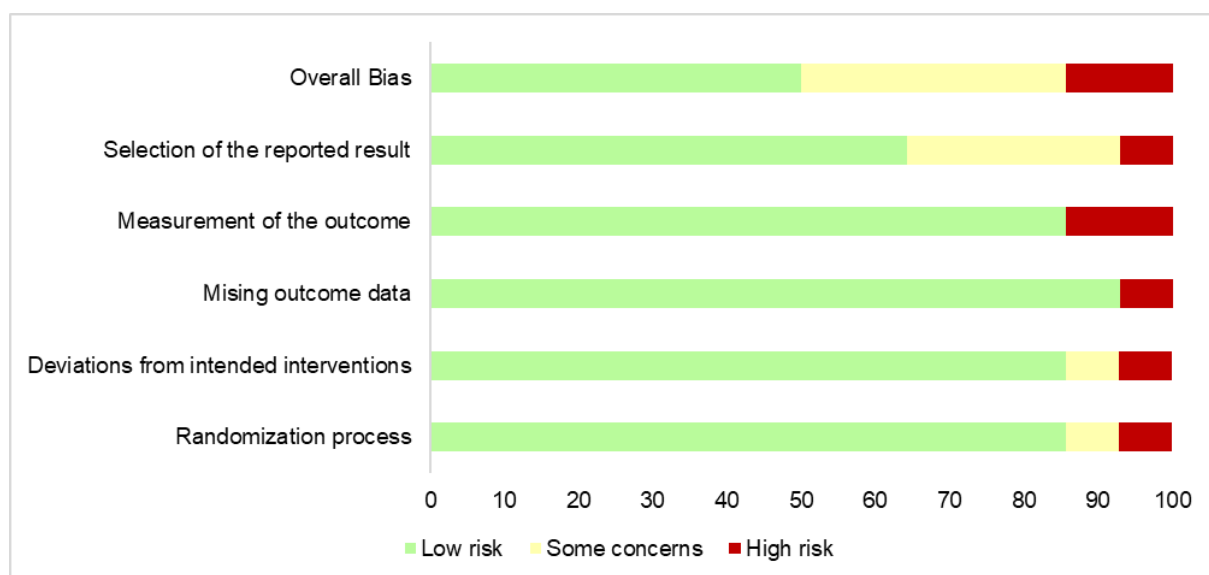


Figure S12. Risk of bias assessment of the included studies assessing infection rates [1–5,8,13,23,31,32,36,44,47,48], broken down to tools, shown in percentage.

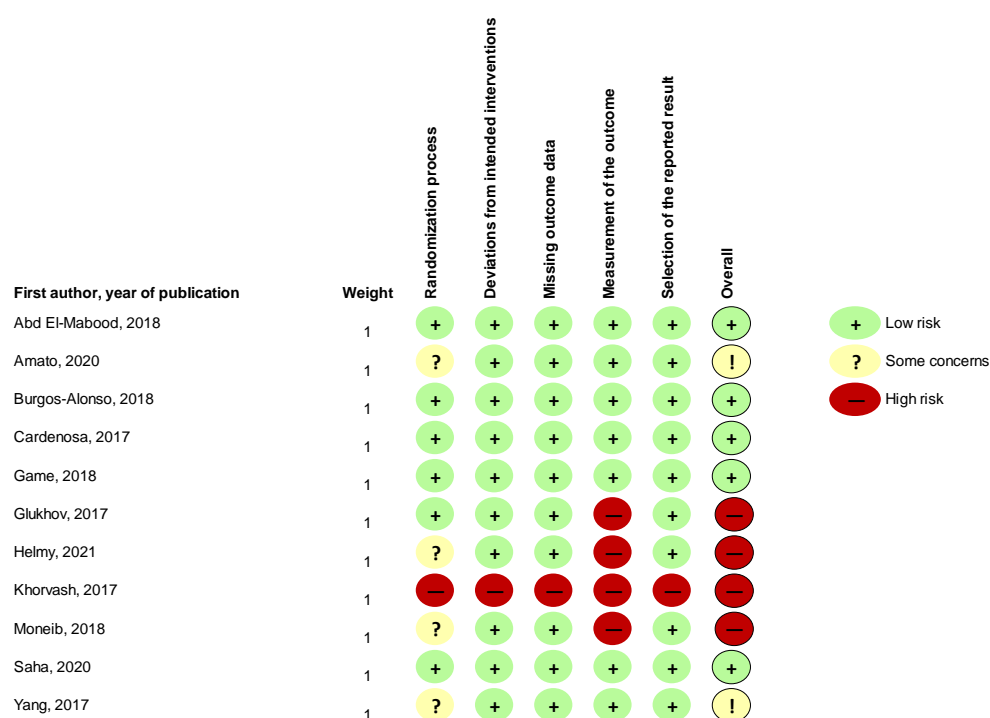


Figure S13. Risk of bias assessment of the included studies assessing pain [1,3,5,6,13,14,18,26,34,44,47], using the revised tool for assessing risk of bias in randomized trials (Rob 2).

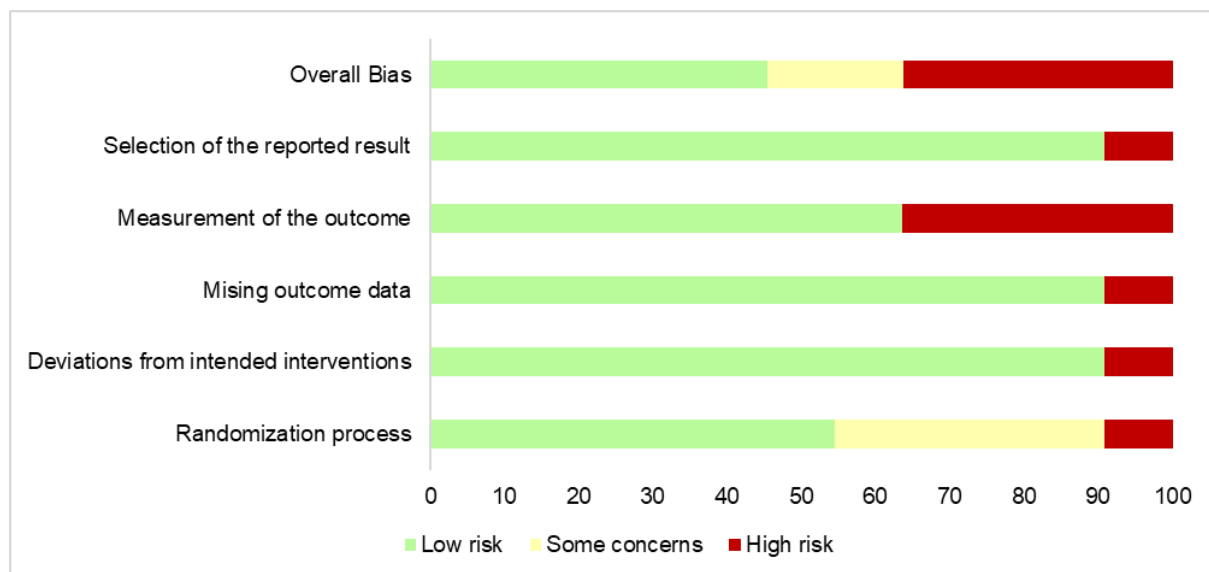


Figure S14. Risk of bias assessment of the included studies assessing pain [1,3,5,6,13,14,18,26,34,44,47], broken down to tools, shown in percentage.

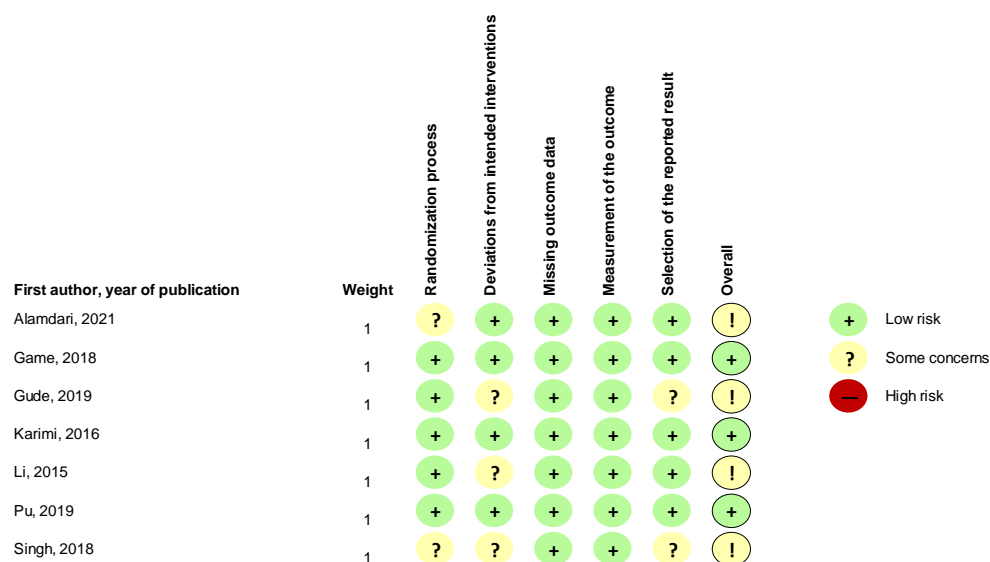


Figure S15. Risk of bias assessment of the included studies assessing amputation rates [13,17,21,23,29,37,46], using the revised tool for assessing risk of bias in randomized trials (Rob 2).

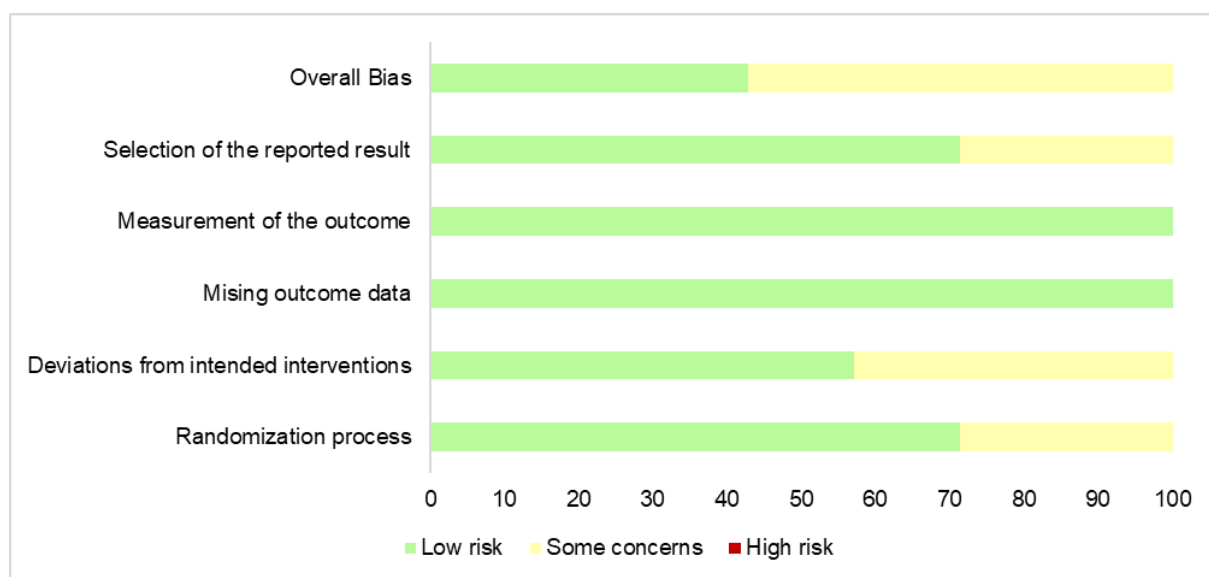


Figure S16. Risk of bias assessment of the included studies assessing amputation rates [13,17,21,23,29,37,46], broken down to tools, shown in percentage.



Figure S17. Risk of bias assessment of the included studies assessing adverse events [5–7,9,13,18,22,23,26,31,35,36,38,44], using the revised tool for assessing risk of bias in randomized trials (Rob 2).

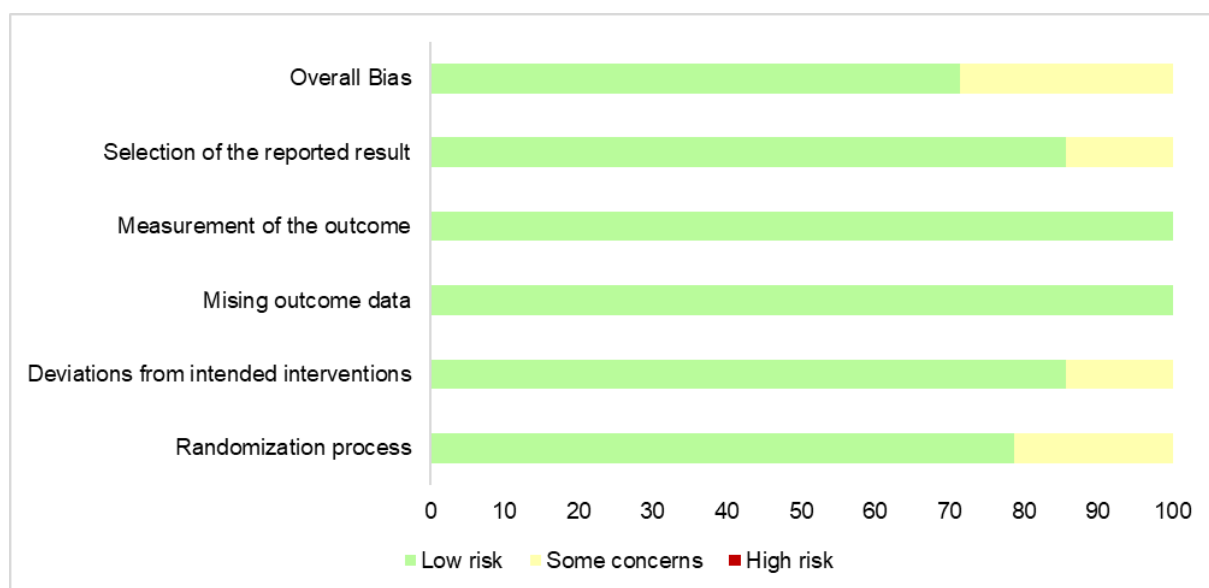


Figure S18. Risk of bias assessment of the included studies assessing adverse events [5–7,9,13,18,22,23,26,31,35,36,38,44], broken down to tools, shown in percentage.

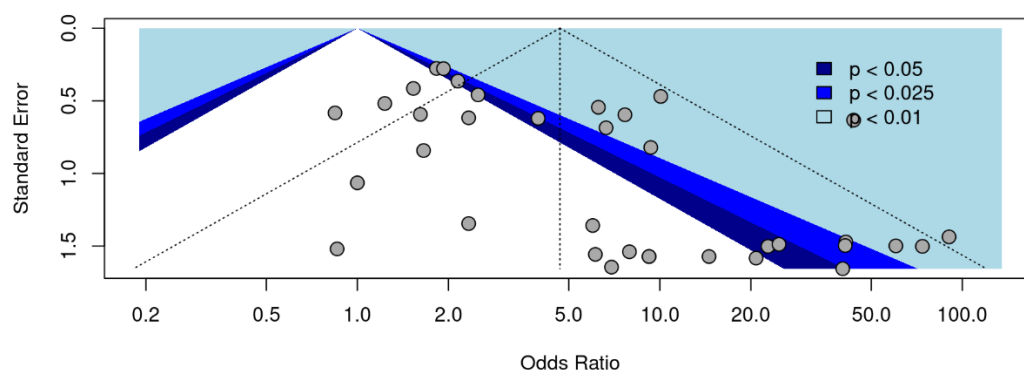


Figure S19. Funnel plot for complete closure.

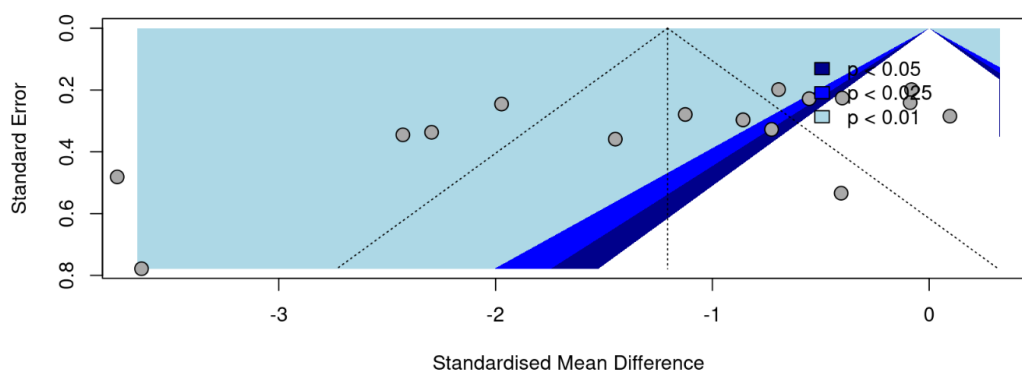


Figure S20. Funnel plot for the reduction of wound area.

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