

Supplementary Data

Calculation of percentage area reduction in 4 weeks (PAR4) healing rate

Randomized controlled trial (RCT) studies describe the absolute area reduction of wounds after treatment with standard wound care (SWC) plus electrostimulation (ES; experimental group) or SWC alone (control group). Comparing studies based up on absolute area reduction is not appropriate because the initial wound size is different. Also, the treatment time in different studies varies. To solve that problem, PAR (percentage area reduction) is a better choice.

When an appropriate treatment strategy is chosen, the wound area should diminish. The clinician evaluates the effectiveness of the intervention up on the PAR during treatment. This is also called the initial healing rate (IHR); the IHR is a strong predictor of the effectiveness of the intervention. On the other side, it might take a couple of weeks before a wound presents the treatment response. In this review, the IHR is expressed as the PAR4, the percentage healing rate in 4 weeks.

This table presents an example with the steps wherein the PAR4 is calculated in RCT study 1.

Electrostimulation group									
No.	Study	n/arms	Weeks	A0 (cm ²)	A1 (cm ²)	A0 - A1	PAR1week	PAR4	
1	Ahmad, 2008	60/2	5	7.1	2.1	5.0	21.67%	62.35%	

The first four columns contain information about the number, the study, number of patients and arms (all studies have two arms; the ES and the control group) and the number of weeks the treatment is applied. The 5th, 6th, and 7th columns present the information about the initial wound size A0, the wound size at the end of the treatment period A1, and the absolute reduction in the wound area. These columns are expressed in cm².

The PAR is expressed as $(1 - A1/A0)$. In our example, $2.1/7.1 = 0.295$; the area reduction = $1 - 0.295 = 0.705$ (= 70.5%). This reduction is realized in 5 weeks (=PAR5). To compare the 20 studies, the PAR4 is calculated. Because the healing rate is an exponential process, raising to a higher power is advisable for the calculation.

First the PAR1 is calculated; this is realized by involution of the PAR by 1/number of weeks treated.

In our example: $1 - (1 - 0.705)^{1/5} = 1 - (1 - 0.705)^{0.2} = 0.2167$ (or: 21.67%).

The last step is to calculate PAR4 from PAR1; the appropriate formula for that is involution of PAR1 by 4. In our example: $1 - (1 - 0.2167)^4 = 0.6235$ (or: 62.35%).

This means that the application of ES in the study of Ahmad realizes in 4 weeks an average PAR of 62.35%; in the control group, where sham ES is applied, the PAR is 20.76%.

Control group									
No.	Study	n/arms	Weeks	A0 (cm ²)	A1 (cm ²)	A0 - A1	PAR1week	PAR4	
3	Ahmad, 2008	60/2	5	7.2	5.4	1.8	5.65%	20.76%	

Adding ES to the standard protocol increases the healing rate by $62.35 - 20.76 = 41.59\%$. Supplementary Table S1 gives the information about PAR4 in ES and control groups for all 15 included studies.

Calculation of standard deviations for the mean PAR4

To produce forest plots from the new calculated PAR4 values, the standard deviations (SDs) of those PAR4 values also need to be present. To calculate the SDs, the method of Altman (DG Altman. *Practical Statistics for Medical Research*, 9th edition (1999), Chapman & Hall/CRC, Boca Raton, ISBN 0-412-27630-5) is applied. On page 161, Altman describes the possibility to calculate the standard error (SE) by considering the group PAR4 values as a binomial distribution. The average wound reduction is the calculated PAR4 and the SE is calculated with the formula

$$SE = \sqrt{((p \times (1 - p)) / n)}$$

In this formula, p is to be replaced by the calculated PAR4. After the calculation of the SE, the SD is determined with the formula

$$SD = SE / (\sqrt{n})$$

For all the studies, the SDs in the experimental and the control groups are calculated and applied to produce the forest plots in the main text of the critical review.

Supplementary Table S1. Percentage area reduction in 4 weeks in the electrostimulation and control groups for all 15 included studies

No.	Study	n/arms	Weeks	ES Group					Control Group				
				A0 (cm ²)	A1 (cm ²)	A0 – A1	PAR1week	PAR4	A0 (cm ²)	A1 (cm ²)	A0 – A1	PAR1week	PAR4
1	Ahmad, 2008	60/2	5	7.1	2.1	5.0	21.67%	62.35%	7.2	5.4	1.8	5.65%	20.76%
2	Baker/Rubayi, 1996	192/2	6	4.7	2.9	1.8	7.78%	27.68%	8.5	4.2	4.4	11.21%	37.84%
3	Baker/Chambers, 1997	114/2	8	n.a.	n.a.	n.a.	22.96%	64.77%	n.a.	n.a.	n.a.	12.65%	41.78%
4	Barczak, 2001	33/2	4	52.0	n.a.	n.a.	n.a.	56.00%	38.0	n.a.	n.a.	n.a.	30.80%
5	Carley, 1985	30/2	5	4.7	0.5	4.2	36.23%	83.46%	3.9	2.2	1.8	11.24%	37.92%
6	Feedar, 1991	50/2	4	14.7	6.4	8.2	18.64%	56.18%	16.9	11.4	5.6	9.47%	32.82%
7	Franek, 2006	55/2	7	18.6	7.2	11.4	12.75%	42.05%	19.3	10.8	8.5	7.97	28.27%
8	Franek, 2012	50/2	6	4.5	0.8	3.8	25.28%	68.83%	4.0	2.7	1.3	6.40	23.24%
9	Houghton, 2003	42/2	4	6.4	n.a.	n.a.	n.a.	44.30%	5.5	n.a.	n.a.	n.a.	16.00%
10	Houghton, 2010	34/2	12	2.7	0.7	2.0	10.92%	37.02%	3.4	2.2	1.2	3.65%	13.83%
11	Jankovic, 2008	42/2	3	6.2	1.1	5.1	43.24%	89.62%	5.9	3.2	2.7	18.75%	56.42%
12	Junger, 2008	40/2	16	5.5	0.8	4.7	11.35%	38.24%	5.4	3.5	2.0	2.77%	10.61%
13	Peters, 2001	40/2	12	1.6	0.1	1.5	18.60%	56.09%	3.5	1.0	2.5	9.92%	34.17%
14	Petrofsky, 2010	20/2	4	n.a.	n.a.	n.a.	23.93%	68.40%	n.a.	n.a.	n.a.	7.93%	30.10%
15	Wood, 1993	74/2	8	2.6	0.4	2.2	20.66%	60.37%	1.9	1.7	0.3	1.74%	6.77%

The healing rate expressed in PAR4. Respectively, described in the columns are the 15 studies with the author name, number of patients (wounds), the treatment period in weeks. A0 is the mean wound area at the start of the study; A1 the mean wound area at the end of the treatment period; A0 – A1 is the absolute reduction in cm²; PAR1week is the percentage area reduction in 1 week of treatment; and PAR4 is the percentage area reduction after 4 weeks of treatment.