National Institute for Health and Care Excellence

Draft for consultation

Acne vulgaris: management

[M] Management of acne vulgaris-associated scarring

NICE guideline number tbc

Evidence review underpinning recommendations 1.8.1 and 1.8.2 and two research recommendations in the NICE guideline

December 2020

Draft for Consultation

These evidence reviews were developed by the National Guideline Alliance which is a part of the Royal College of Obstetricians and Gynaecologists

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Management of acne vulgaris-associated scarring

Review question

What are the most effective treatment options for acne vulgaris-associated scarring?

Introduction

There is a lot of evidence that people with severe acne scarring can suffer life-long psychological problems and their quality of life is reduced. There is also some evidence of stigmatisation and prejudice towards people with acne. Treatments for acne scarring are available in a few NHS centres but there is uncertainty regarding which intervention is the most effective and there is geographical variation in availability of treatments. Therefore, the aim of this review is to determine the most effective treatment options for acne vulgaris-associated scarring.

Summary of the protocol

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol

Population	People with atrophic and/or hypertrophic and/or keloid acne scars as diagnosed by a dermatologist or an experienced investigator
Intervention	Any intervention, or combination of interventions thereof, used to manage different types of acne scars will be considered, for example: **For atrophic scars:** • Chemical peeling • Dermabrasion • Dermal grafting • Laser therapy (e.g. pulsed dye laser) • Microdermabrasion • Needling • Punch techniques • Radiofrequency • Subcision • Surgery • Tissue-augmenting agents **For hypertrophic and keloid scars:** • 5-fluorouracil (5-FU) • Bleomycin • Cryotherapy • Imiquimod • Interferon • Intralesional steroid injection • Laser therapy • Silicone gel • Surgery

Comparison	The following comparisons will be considered: • Any other active intervention for management of acne-related scarring from the list above • No treatment • Placebo or sham treatment (as appropriate) • Waiting list

Outcomes	**Critical**
	• Improvement in scarring at the end of treatment
	  ○ Participant-reported improvement
	  ○ Investigator-assessed improvement
	• Serious adverse events
	Important
	• Participant satisfaction with treatment
	• Skin-related quality of life at the end of treatment (validated tools only, e.g. Dermatology Life Quality Index)
	• Participant's mood at the end of treatment (validated scales only, e.g. score on depression, anxiety scale)
	• Side effects:
	  ○ Local (e.g. hypo- or hyper- pigmentation; scarring)
	  ○ General

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Clinical evidence

Included studies

Overall 30 studies were included in this review. These are divided according to the study design, that is split-face randomised controlled trials (RCTs) and parallel-group RCTs.

Atrophic acne vulgaris scars

Split-face studies

Overall 19 split-face RCTs were included in this review. Five studies were conducted in Egypt (Abdel-Magiod 2019, Galal 2019, Gawdat 2014, Hassan 2019, Osman 2017), 4 in Iran (Faghihi 2015, Fahgihi 2016, Faghihi 2017, Nilforoushzadeh 2017), 3 in Thailand (Khamthara 2018, Manuskiatti 2012, Rongsaard 2014), 2 in Korea (Cho 2010, Lee 2009), 2 in the USA (Sage 2011, Tanzi 2004), 1 in Denmark (Hedelund 2012), 1 in Germany (Reinholz 2015) and 1 in China (Zhang 2013). The sample size of the studies ranged from 8 to 42 participants.

Studies included participants with different severities of atrophic facial acne vulgaris scars: 7 studies included participants with moderate to severe acne scars (Abdel-Maguid 2019, Faghihi 2015, Faghihi 2016, Faghihi 2017, Hassan 2019, Hedelund 2012, Khamthara 2018), 4 studies with mild, moderate or severe acne scars (Cho 2010, Gawdat 2014, Osman 2017, Zhang 2013), 2 with mild to moderate acne scars (Lee 2009, Tanzi 2004); one study included participants with severe acne scars only (Reinholz 2015) and 5 studies did not report the

severity of acne scarring (Galal 2019, Manuskiatti 2012, Nilforoushzadeh 2017, Rongsaard 2014, Sage 2011).

Included studies evaluated the effectiveness of different interventions with carbon dioxide laser (CO2) being the most common intervention:

- ablative fractional CO2 laser with platelet-rich plasma intradermal administration versus CO2 laser with saline intradermal administration (Faghihi 2016, Gawdat 2014) or platelet-rich plasma topical administration (Gawdat 2014), or versus CO2 laser alone (Galal 2019),
- ablative fractional CO2 laser with platelet-rich plasma topical administration versus CO2 with stem cell-conditioned medium topical administration (Abdel-Maguid 2019),
- ablative fractional CO2 laser with stem cell-conditioned medium topical administration versus CO2 laser with saline topical administration (Abdel-Maguid 2019),
- ablative fractional CO2 laser with punch elevation (Faghihi 2015) or subcision (Nilforoushzadeh 2017) versus CO2 laser,
- 2940-nm Er:YAG laser plus silicone gel versus 2940-nm Er:YAG laser plus hydrophilic cream (Khamthara 2018),
- 2940-nm Er:YAG laser versus CO2 laser (Manuskiatti 2012, Reinholz 2015),
- 585-nm pulsed dye laser versus 1064-nm long-pulsed Nd:YAG laser (Lee 2009),
- 1550-nm erbium-doped fractional photothermolysis laser versus ablative fractional CO2 laser (Cho 2010),
- 1320-nm Nd:YAG laser versus 1450-nm diode laser (Tanzi 2004),
- 2940-nm ER:YAG laser versus microneedling (Osman 2017),
- ablative fractional CO2 laser versus no treatment (Hedelund 2012),
- fractional micro-plasma radiofrequency versus ablative fractional CO2 laser (Zhang 2013),
- fractional bipolar radiofrequency versus 1550-nm fractional erbium-doped glass laser (Rongsaard 2014).

The effectiveness of the following interventions not involving laser treatment was also assessed:

- fractionated microneedle frequency plus subcision versus fractionated microneedle frequency (Faghihi 2017),
- subcision plus autologous platelet-rich plasma intradermal administration versus autologous platelet-rich plasma intradermal administration (Hassan 2019),
- subcision versus collagen filler intradermal administration (Sage 2011).

Evidence was identified for the majority of outcomes such as improvement in scarring (investigator or participant reported), participant satisfaction with treatment and side effects.

No evidence was identified for serious adverse events, skin-related quality of life and participant's mood. The included split-face studies are summarised in (Table 2).

Parallel-group studies

Overall 11 parallel-group RCTs were included in this review. One study was conducted in Brazil (Cachafeiro 2016), 5 studies were conducted in Egypt (Ahmed 2014, Leheta 2011, Leheta 2014, Mohammed 2013, Nofal 2014), 1 study was conducted in India (Anupama 2016), 1 study was conducted in Iran (Asilian 2011), 1 study was conducted in Korea (Chae 2015), 1 study was conducted in Turkey (Erbagci 2000), and 1 study was conducted in USA (Bhargava 2019). The sample size of the studies ranged from 28 to 50 participants.

Studies included participants with different severities of atrophic facial acne vulgaris scars. Three studies included participants with mild, moderate, or severe acne scars (Anupama 2016, Erbagci 2000, Nofal 2014); 3 studies included participants with moderate to severe

acne scars (Asilian 2011, Cachafeiro 2016, Mohammed 2013); 1 study included participants with severe acne scars (Bhargava 2019); and 4 studies did not report the severity of acne scarring (Ahmed 2014, Chae 2015, Leheta 2011, Leheta 2014).

Included studies evaluated the effectiveness of different interventions with laser therapy being the most common intervention:

- Trichloroacetic acid (TCA) CROSS 100% versus carbon dioxide (CO_2) laser (Ahmed 2014);
- CO_2 laser with subcision versus CO_2 laser (Anupama 2016);
- 1064 nm Q-switched Nd:YAG laser versus CO2 laser (Asilian 2011);
- 1340 nm non-ablative fraction erbium laser versus microneedling (Cachafeiro 2016);
- 1550 nm Er:Glass fractional laser versus microneedling (Chae 2015);
- 1540 nm fractional photothermolyis versus percutaneous collagen induction (PCI) and TCA 20% versus alternating treatment of both interventions (Leheta 2014);
- CO2 laser and needling versus CO2 laser (Mohammed 2013).

The effectiveness of the following interventions not involving laser treatment was also assessed:

- Subcision and needling and platelet-rich plasma versus subcision and needling (Bhargava 2019);
- Glycolic acid peel versus 15% glycolic acid cream versus placebo (Erbagci 2000);
- PCI versus TCA CROSS 100% (Leheta 2011);
- Intradermal PRP versus TCA CROSS 100% versus needling and topical PRP (Nofal 2014)

Evidence was identified for the majority of outcomes such as improvement in scarring (investigator or participant reported), participant satisfaction with treatment and side effects.

No evidence was identified for serious adverse events, skin-related quality of life and participant's mood. The included parallel-group studies are summarised in (Table 2).

Hypertrophic and keloid acne vulgaris scars

No relevant evidence was identified for hypertrophic or keloid scars.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Split-face RCTs				
Abdel-Maguid 2019 Egypt	N=37, n=33 analysed Group I n=17 (15 females and 2 males)	Group I • CO2 laser + SC-CM topical	Group I • CO2 laser + saline topical	• Overall improvement in scarring – investigator assessed

Study	Population	Intervention	Comparison	Outcomes
	Mean age (SD): 24.8 (4.2) Group II n=16 (9 females and 7 males) Mean age (SD): 25.9 (7.6) Moderate to severe atrophic acne scars	Group II • CO2 laser + PRP topical 3 monthly sessions	Group II • CO2 laser +SC-CM topical 3 monthly sessions	• Improvement by scar type • Participant satisfaction with treatment • Side effects
Cho 2010 Korea	N=8 (males only) Mean age (range): 21.3 (20-23) Mild to severe atrophic acne scars	• 1550-nm erbium-doped fractional photothermolysis laser 1 treatment session	• CO2 laser 1 treatment session	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects
Faghihi 2015 Iran	N=42 (19 females and 23 males) Mean age (SD): 23.4 (2.63) Moderate to severe atrophic acne scars	• CO2 laser + punch elevation 2 treatment sessions	• CO2 laser 2 treatment sessions	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects
Faghihi 2016 Iran	N=16 (12 females and 4 males) Mean age (range): 36.8 (22-52) Moderate to severe atrophic acne scars	• CO2 laser + PRP injection 2 treatment sessions	• CO2 laser + saline injection 2 treatment sessions	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects
Faghihi 2017 Iran	N=25 (16 females and 9 males) Mean age (SD): 30.1 (4.94) Moderate to severe atrophic acne scars	• Fractionated microneedle frequency (FMR) + subcision First, a standard subcision was performed on one side of the face; 2 weeks after subcision, FMR treatment was performed. A second and third FMR treatment session was performed with a	• Fractionated microneedle frequency (FMR) 2 weeks after subcision, FMR treatment was performed on both cheeks of each participant. A second and third FMR treatment session was performed with a 4-week interval.	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects

Study	Population	Intervention	Comparison	Outcomes
		4-week interval.		
Galal 2019 Egypt	N=30 (21 females and 9 males) Mean age (SD): 26.7 (4.7) Severity of atrophic scarring not reported	• CO2 laser + PRP injection 1 treatment session	• CO2 laser 1 treatment session	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects
Gawdat 2014 Egypt	N=30 Group I n=15 (10 females and 5 males) Mean age (SD): 25.2 (5) Group II n=15 (8 females and 7 males) Mean age (SD): 24.3 (3.7) Mild-moderate-severe atrophic acne scars	Group I • CO2 laser + PRP injection Group II • CO2 laser + PRP injection 3 monthly sessions	Group I • CO2 laser + saline injection Group II • CO2 + PRP topical 3 monthly sessions	• Improvement in scar depth – investigator assessed • Side effects
Hassan 2019 Egypt	N=30 (25 females and 5 males), n=25 Mean age (range): 26.1 (5.99) Moderate to severe atrophic acne scars	• Subcision + PRP injection 3 sessions with 1-month interval	• PRP injection 3 sessions with 1-month interval	• Improvement in scarring – investigator
Hedelund 2012 Denmark	N=13 (7 females and 6 males), n=12 analysed at 6 months post-treatment Mean age (range): 33 (22-54) Moderate to severe atrophic acne scars	• CO2 laser 3 treatments at 4- to 5-week intervals	• No treatment	• Improvement in scar skin texture • Improvement in scar skin atrophy
Khamthara 2018 Thailand	N=20 (5 females and 14 males), n=19 analysed Median age (IQR): 25 (23-28) Moderate to severe atrophic acne scars	• 2940-nm Er:YAG laser + silicone gel 3 sessions with 1-month intervals	• 2940-nm Er:YAG laser + hydrophilic cream 3 sessions with 1-month intervals	• Improvement in scarring – participant assessed • Side effects

Study	Population	Intervention	Comparison	Outcomes
Lee 2009 Korea	N=18 (8 females and 10 males) Mean age (range): 23 (21-30) Mild to moderate atrophic acne scars	• 585-nm pulsed dye laser 4 treatment sessions at 2-week intervals	• 1064-nm long-pulsed Nd:YAG laser 4 treatment sessions at 2-week intervals	• Improvement in scarring investigator assessed
Manuskiatti 2012 Thailand	N=24 (12 females and 8 males), n=20 analysed Mean age (range): 33.7 (20-65) Severity of atrophic scarring not reported	• 2940-nm Er:YAG laser 2 treatment sessions	• CO2 laser 2 treatment sessions	• Improvement in scarring – investigator assessed • Side effects
Nilforoushzadeh 2017 Iran	N=30 (22 females and 8 males) Age not reported Severity of atrophic scarring not reported	• 1550-nm fraxel laser + subcision, then CO2 laser 1 combination treatment (subcision + fraxel laser), after 3 weeks 4 sessions of CO2 laser with 3-week interval	• CO2 laser 5 sessions with 3-week interval	• Participant satisfaction with treatment
Osman 2017 Egypt	N=30 (20 females and 10 males) Mean age (SD): 27 (3.75) Mild, moderate and severe atrophic acne scars	• 2940-nm Er:YAG 5 treatment sessions at 1-month intervals	• Microneedling 5 treatment sessions at 1-month intervals	• Participant satisfaction with treatment • Side effects
Reinholz 2015 Germany	N=14 (5 females and 9 males) Mean age (SD): 28.6 (9.2) Severe atrophic acne scars	• 2940-nm Er:YAG laser Treatment was given 4 times every 4 weeks	• CO2 laser Treatment was given 4 times every 4 weeks	• Improvement in scar depth – investigator assessed • Satisfaction with treatment – participant and investigator assessed • Side effects
Rongsaard 2014 Thailand	N=20 (8 females and 12 males), n=19 analysed in the radiofrequency group Age 18-55 years Severity of atrophic scarring not reported	• Fractional bipolar radiofrequency 3 treatment sessions at 4-week intervals	• 1550-nm fractional erbium-doped glass laser 3 treatment sessions at 4-week intervals	• Participant satisfaction with treatment • Side effects

Study	Population	Intervention	Comparison	Outcomes
Sage 2011 USA	N=10 (gender not reported), n=9 analysed at 3-month follow-up visit Mean age (range): 50 (33-65) Severity of atrophic scarring not reported	• Subcision 1 treatment session	• Collagen filler injection 1 treatment session	• Side effects
Tanzi 2004 USA	N=20 (gender not reported) Mean age: 36.7 Mild to moderate atrophic acne scars	• 1320-nm Nd:YAG laser 3 laser treatments at 4-week intervals	• 1450-nm diode laser 3 laser treatments at 4-week intervals	• Side effects
Zhang 2013 China	N=33 (14 females and 19 males) Mean age (SD): 26.4 (3.7) Mild to severe atrophic acne scars	• Fractional micro-plasma radiofrequency 3 treatment sessions at intervals of 6 to 12 (average 8) weeks	• CO2 laser 3 treatment sessions at intervals of 6 to 12 (average 8) weeks	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects
Parallel-group RCTs				
Ahmed 2014 Egypt	N=28 (20 females and 8 males) Mean age (SD): 22.7 (8.4) Severity of atrophic ice-pick acne scarring not reported	• TCA CROSS 100% 4 treatment sessions at 3 weeks intervals	• CO2 laser 4 treatment sessions at 3 weeks intervals	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects
Anupama 2016 India	N=50, n=44 analysed (number of men and women not reported) Mean age (range): 21 (20-25) Randomised to: • subcision followed by CO2 laser n=23 • CO2 laser n=21 Mild to severe atrophic acne scars	• Subcision + CO2 laser 4 sessions at 4-week intervals	• CO2 laser 4 sessions at 4-week intervals	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment
Asilian 2011 Iran	N=64 Randomised to: • Nd:YAG laser n=32; 22 females, 10 males; mean	• 1064-nm Nd:YAG laser 4 treatments at 4-week intervals	• 10600-nm CO2 laser 4 treatments at 4-week intervals	• Improvement in scarring – investigator assessed • Improvement in scarring – participant

Study	Population	Intervention	Comparison	Outcomes
	age (SD): 26.3 (5.5) • CO2 laser n=32; 22 females, 10 males; mean age (SD): 26.9 (5.8) Moderate to severe atrophic acne scars			assessed • Side effects
Bhargava 2019 USA	N=30 Randomised to: • subcision + needling + PRP n=15; 10 females, 5 males; mean age (range): 28.2 (21-35) • subcision + needling n=15; 9 females, 6 males; mean age (range): 27.1 (22-37) Severe atrophic acne scars	• Subcision + needling + PRP 3 treatments at 3-week intervals	• Subcision + needling 3 treatments at 3-week intervals	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment
Cachafeiro 2016 Brazil	N=46, n=42 analysed Randomised to: • microneedling n=20; 10 females, 10 males; mean age (SE): 27.3 (10.72) • laser n=22; 11 females, 11 males; mean age (SE): 25.4 (8.77) Moderate to severe atrophic acne scars	• Microneedling 3 sessions performed monthly	• Non-ablative fractional erbium laser 1,340 nm 3 sessions performed monthly	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects
Chae 2015 Korea	N=40 Randomised to: • laser n=20; 7 females, 13 males; mean age (SD): 25.5 (3.76) • microneedling n=20; 4 females, 16 males; mean age (SD): 28.3 (5.39)	• 1550-nm Er:Glass fractional laser 3 treatments at 4-week interval	• Microneedling 3 treatments at 4-week interval	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects

Study	Population	Intervention	Comparison	Outcomes
	Acne scar severity not reported			
Erbagci 2000 Turkey	N=58 women (age range 18-41) Randomised to: • glycolic acid peel n=23; • glycolic acid cream n=20; • placebo n=15 Mild, moderate and severe atrophic acne scars	• Glycolic acid peel Performed biweekly in a gradual increase in time and concentration • Glycolic acid cream Applied twice daily for 24 weeks	• Placebo Base cream including the same vehicle as the glycolic acid cream, applied twice daily for 24 weeks	• Improvement in scarring – investigator assessed
Leheta 2011 Egypt	N=30, n=27 analysed (14 females and 16 males) Randomised to: • PCI n=15; mean age (SD): 29.7 (7.3) • TCA CROSS n=12; mean age (SD): 23.8 (5.8) Acne scar severity means from 74 to 79 (3 points for deep, 2 points for shallow and 1 point for superficial scars)	• PCI 4 sessions of treatment at 4-week intervals	• 100% TCA CROSS 4 sessions of treatment at 4-week intervals	• Improvement in scarring – investigator assessed • Side effects
Leheta 2014 Egypt	N=39, n=38 analysed Randomised to: • PCI + TCA 20% n=12; 9 females, 4 males; mean age (SD): 31.88 (7.5) • laser n=13; 7 females,6 males; mean age (SD): 32.54 (7.6) • alternating treatment of both n=13; 8 females, 5 males; mean age (SD): 31.23	• PCI + TCA 20% 6 sessions 4 weeks apart • 1540 nm non-ablative fractional laser 6 sessions 4 weeks apart	• Combined alternating sessions of the two modalities 3 sessions of each with 4 weeks in between	• Improvement in scarring – investigator assessed

Study	Population	Intervention	Comparison	Outcomes
	(6.5) Acne scar severity means from 66 to 75 (3 points for deep, 2 points for shallow and 1 point for superficial scars)			
Mohammed 2013 Egypt	N=60 Randomised to: • CO2 laser + needling n=30; age range 19-32 • CO2 laser n=30; age range 19-32 Moderate to severe ice pick acne scars	• CO2 laser + needling 4 sessions at 3-week interval	• CO2 laser 4 sessions at 3-week interval	• Improvement in scarring – investigator assessed • Participant satisfaction with treatment • Side effects
Nofal 2014 Egypt	N=45 Randomised to: • PRP injection n=15; 10 females, 5 males; mean age (SD): 25.1 (3.7) • 100% TCA CROSS n=15; 10 females, 5 males; mean age (SD): 25.5 (5.6) • needling + topical PRP n=15; 11 females, 5 males; mean age (SD): 25.8 (5.3) Mild, moderate and severe atrophic acne scars	• PRP injection • Needling + topical PRP 3 sessions at 2-week interval	• 100% TCA CROSS 3 sessions at 2-week interval	• Improvement in scarring – investigator assessed • Improvement in scarring – participant assessed • Participant satisfaction with treatment

CO2: carbon dioxide laser; CROSS: chemical reconstruction of skin scars; Er:YAG: fractional ablative erbium-doped yttrium aluminum garnet laser; FMR: fractionated microneedle frequency; IQR: interquartile range; N: number of participants randomised; Nd:YAG: long-pulsed neodymium:yttrium-aluminum-garnet laser; PCI: percutaneous collagen induction; PRP: platelet-rich plasma; RCT: randomised controlled trial; SC-CM: topical stem cell-conditioned medium; SD: standard deviation; SE: standard error; TCA: trichloroacetic acid

See the full evidence table in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Quality assessment of included studies in the evidence review

See the evidence profiles in appendix F.

Economic evidence

Included studies

A single economic search was undertaken for all topics included in the scope of this guideline but no economic studies were identified which were applicable to this review question. See the literature search strategy in appendix B and economic study selection flow chart in appendix G.

Excluded studies

Economic studies not included in this review are listed, and reasons for their exclusion are provided, in appendix K.

Economic model

Although this review question was prioritised for economic modelling due to its potentially significant resource implications, no formal economic modelling was possible to undertake, because the available clinical effectiveness data were too limited to inform a meaningful economic analysis of good quality. Instead, a simple cost analysis was carried out to estimate intervention costs of treatments with some evidence of effectiveness, so that clinical effectiveness could be considered alongside intervention costs in a simplistic cost-consequence analysis, to enable the committee to formulate potential recommendations after taking into account both effectiveness and cost considerations.

According to the guideline systematic review, 3 treatments showed some evidence of effectiveness in the management of acne vulgaris-associated scaring: CO_2 laser treatment; punch elevation; and glycolic acid peels. Intervention costs for each treatment option were estimated by combining resource use reported in the RCTs included in the guideline systematic review, modified based on the committee's expert opinion to reflect UK routine practice, with respective national unit costs.

Clinical effectiveness and intervention cost of CO_2 laser treatment

Evidence on the effectiveness of CO_2 laser treatment in the management of acne vulgaris-associated scarring was obtained from Hedelund 2012, which was a split-face trial that compared CO_2 laser treatment with no treatment tested on 13 people. Participants received 3 sessions of laser treatment at 4-5 week intervals. The measure of outcome was the change in the level of scarred skin texture and atrophy. Effect was assessed using numerical scales ranging from 0 (even skin texture without scarring/atrophy) to 10 (worst possible scarring/atrophy). CO_2 laser treatment resulted in higher improvements in both scarred skin texture (MD -1.33, 95% CI -2.35 to -0.31) and scarred skin atrophy (MD -1.33, 95% CI -2.31 to -0.35) compared with no treatment.

The committee advised that, in routine clinical practice, a course of treatment of acne vulgaris-associated scarring with CO_2 laser comprises a range of 1-4 laser sessions (day-case specialist appointments) and 1-2 nurse-led follow-up outpatient visits. Usually, treatment consists of 3 laser sessions and one separate follow-up session, since some follow-up monitoring of a laser treatment session occurs at the same time with the next day-case appointment for laser treatment.

In order to attach appropriate unit costs to the resource use associated with CO_2 laser treatment, the committee advised that CO_2 laser treatment corresponds to 'major skin procedures' Healthcare Resource Group (HRG), as listed in the national schedule of NHS costs. However, it was noted that HRQ 'intermediate skin procedures' had a higher unit cost than 'major skin procedures', and therefore NHS unit costs for both major and intermediate

skin procedures were used in costing, to provide low and high estimates for intervention costs associated with CO2 laser treatment for acne vulgaris-associated scarring.

Table 3 shows the resource use and unit costs relating to a course of CO_2 laser treatment for the management of acne vulgaris-associated scarring, as well as the range of the estimated total intervention cost, depending on the assumptions on the number of CO_2 laser treatment sessions and the number of follow-up outpatient visits required, as well as the related HRG unit cost used. The cost of a course of CO_2 laser treatment is likely to lie between £938 and £4,465. At the usual resource use (3 laser sessions and 1 follow-up visit) the estimated intervention cost is likely to range from £2,619 to £3,300.

Table 3. Estimation of the intervention cost of a course of CO_2 laser treatment for the management of acne vulgaris-associated scarring

Resource use element	Corresponding resource use	Unit cost
Main procedure – CO_2 laser treatment	Major skin procedure – day case Intermediate skin procedure – day case Number of sessions: range1-4; mode 3	£841 per session £1,068 per session
Follow-up / monitoring	Non-consultant (nurse) -led outpatient visit Number of visits: range 1-2; mode 3	£97 per visit
Total estimated cost (2019 prices)	<u>Assuming 'major' skin procedure</u> Range for 1 session + 1 follow-up visit to 4 sessions + 2 follow-up visits Using the mode resource use (3 sessions + 1 follow-up visit) <u>Assuming 'intermediate' skin procedure</u> Range for 1 session + 1 follow-up visit to 4 sessions + 2 follow-up visits Using the mode resource use (3 sessions + 1 follow-up visit)	 £938 to £3,556 £2,619 £1,165 to £4,465 £3,300

Source of unit costs: NHS Improvement. National Schedule of NHS Costs, 2018-19. NHS trusts and NHS foundation trusts. NHS Improvement; 2019. Available from: https://improvement.nhs.uk/resources/national-cost-collection/

Clinical effectiveness and intervention cost of punch elevation

Evidence on the effectiveness of punch elevation in the management of acne vulgaris-associated scarring was obtained from Faghihi 2015, which was a split-face trial that compared punch elevation provided in advance to CO_2 laser treatment versus CO_2 laser treatment alone tested on 42 people. Participants received either 1 session of punch elevation 24 hours prior to 2 sessions of CO_2 laser treatment (which were provided 4 weeks apart) or 2 sessions of CO_2 laser treatment alone. The measure of outcome was the clinician-rated improvement in acne vulgaris-associated scarring, graded as follows: 'excellent' improvement: >75% improvement; 'good' improvement: 51-75% improvement, and 'moderate' improvement: 25-50% improvement. Treatment with punch elevation added on laser treatment produced better effect than laser treatment alone at 4 months after treatment, with a risk ratio for excellent improvement of 6 (95% CI 1.43 to 25.19). However, the risk ratio for either excellent or good improvement was 1.19 (95% CI 0.89 to 1.61).

The committee advised that, in routine clinical practice, in more than 80% of cases, punch elevation is provided as one extra session prior to laser treatment. In 20% of cases, punch elevation may be provided as a separate intervention, in a range of 1-4 sessions (day-case specialist appointments) and 1-2 nurse-led follow-up outpatient visits.

The committee advised that punch elevation corresponds to 'intermediate skin procedures' HRG, as listed in the national schedule of NHS costs. However, because HRQ 'major skin procedures' had a lower unit cost than 'intermediate skin procedures', NHS unit costs for both major and intermediate skin procedures were used in costing, to provide low and high estimates for the intervention cost associated with punch elevation for the management of acne vulgaris-associated scarring.

Table 4 shows the resource use and unit costs relating to a course of punch elevation for the management of acne vulgaris-associated scarring, as well as the range of the estimated total intervention cost, depending on the assumptions on the number of sessions and follow-up outpatient visits required, as well as the related HRG unit cost used. The cost of a course of punch elevation, if provided as a stand-alone intervention (20% of cases), is likely to lie between £938 and £4,465. At the usual resource use (1 session of punch elevation prior to laser treatment – 80% of cases) the estimated intervention cost is likely to range from £841 to £1,068.

Table 4. Estimation of the intervention cost of a course of punch elevation for the management of acne vulgaris-associated scarring

Resource use element	Corresponding resource use	Unit cost
Main procedure – punch elevation	Major skin procedure – day case Intermediate skin procedure – day case Number of sessions: 80% of cases: 1 prior to laser treatment; 20% of cases: stand-alone intervention, range1-4	£841 per session £1,068 per session
Follow-up / monitoring	Non-consultant (nurse) -led outpatient visit Number of visits: 80% of cases: none as follow-up is incorporated into a laser session; 20% of cases: following stand-alone punch elevation, range 1-2	£97 per visit
Total estimated cost (2019 prices)	<u>Assuming 'major' skin procedure</u> 80% of cases: 1 session prior to laser treatment Total cost including laser treatment (comprising 3 sessions + 1 follow-up visit) 20% of cases: stand-alone intervention, range for 1 session + 1 follow-up visit to 4 sessions + 2 follow-up visits <u>Assuming 'intermediate' skin procedure</u> 80% of cases: 1 session prior to laser treatment Total cost including laser treatment (comprising 3 sessions + 1 follow-up visit) 20% of cases: stand-alone intervention, range for 1 session + 1 follow-up visit to 4 sessions + 2 follow-up visits	 £841 £3,459 £938 to £3,556 £1,068 £4,368 £1,165 to £4,465

Source of unit costs: NHS Improvement. National Schedule of NHS Costs, 2018-19. NHS trusts and NHS foundation trusts. NHS Improvement; 2019. Available from: https://improvement.nhs.uk/resources/national-cost-collection/

Clinical effectiveness and intervention cost of glycolic acid peels

Evidence on the effectiveness of glycolic acid peels in the management of acne vulgaris-associated scarring was obtained from Erbagci 2000, which was a parallel group trial that compared glycolic acid peels with glycolic acid cream and with placebo cream tested on 48 people with atrophic acne scars. Peels were applied in 2-weekly intervals. The glycolic acid cream and the placebo cream were applied once or twice daily. Treatment lasted 24 weeks. The measure of outcome was improvement on a 10-point scale, with 'good improvement' being defined as a change of more than 60% from baseline, whereas partial improvement was defined as a change of 30%-60% from baseline. At 24 weeks, glycolic acid peels showed the highest level of good improvement, with a peto odds ratio of 9.64 (95% CI 1.65 to 56.19) versus placebo cream and 12.24 (95% CI 2.15 to 69.74) versus glycolic acid cream. When good and partial improvement were combined, then the peto odds ratio of glycolic acid peels became 12.49 (95% CI 2.80 to 55.73) versus placebo cream and 4.21 (95% CI 0.74 to 24.00) versus glycolic acid cream. The authors concluded that glycolic acid peels were effective for the treatment of atrophic acne scars, but repetitive peels (at least 6 times) with 70% concentration are necessary to obtain evidence of improvement.

The committee advised that, in routine clinical practice, around 6 glycolic acid peels are applied in a course of treatment, in consultant-led, multi-professional outpatient visits, as the presence of a specialist nurse is very helpful. It was noted, though, that in the RCT that provided clinical evidence on the effectiveness of glycolic acid peels these were applied 12 times.

Table 5 shows the resource use and unit costs relating to a course of glycolic acid peels for the management of acne vulgaris-associated scarring, as well as the range of the estimated total intervention cost, depending on the assumptions on the number of sessions required, as well as the related drug ingredient cost. The cost of 6 glycolic acid peels, which represent routine practice, ranges between £845 and £873; the cost of 12 glycolic acid peels, which reflect resource use in the only RCT that provided evidence on the effectiveness of the intervention in the management of acne vulgaris-associated scarring, ranges between £1,672 and £1,728.

Table 5. Estimation of the intervention cost of a course of glycolic acid peels for the management of acne vulgaris-associated scarring

Resource use element	Corresponding resource use	Unit cost
Drug ingredient cost	10ml of acid per application 6 applications (routine practice) to 12 applications (available evidence)	£2 to £7 per 10 ml Over the counter cost: £6 to £20 per 30 ml [higher concentrations closer to £20]
Outpatient contacts	Consultant led, multi-professional	£154 per first contact £136 per follow-up contact
Total estimated cost (2019 prices)	6 sessions 12 sessions	£845 to £873 £1,672 to £1,728

Source of unit costs: drug ingredient cost: market web-based prices; outpatient contacts: NHS Improvement. National Schedule of NHS Costs, 2018-19. NHS trusts and NHS foundation trusts. NHS Improvement; 2019. Available from: https://improvement.nhs.uk/resources/national-cost-collection/

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee agreed that permanent severe acne scarring has a significant and profound life-long impact on the psychological well-being of people affected by it thus investigator-assessed and participant-reported improvement in scarring were prioritised as critical outcomes. Serious adverse events were chosen as a critical outcome and side effects (local and general) as an important outcome because they indicate safety of a particular intervention. Participant satisfaction with treatment, skin-related quality of life and participant's mood were important outcomes as they indicate acceptability of the intervention and its impact on psychological well-being.

The quality of the evidence

Overall, the quality of the evidence from split-face and parallel-group trials ranged from high to very low quality, with most being of very low quality. This was predominately due to risk of bias of individual studies and imprecision in the effect estimates. Many included studies were small in terms of sample size, especially split-face studies, which may have yielded a less reliable or precise effect estimate leading to uncertainty abouth the actual effect size. Most studies also did not clearly describe or carry out any allocation concealment which may have inflated the effects. The process of blinding was also not possible due to the type of scarring treatment used or compared which may have also influenced the subjectively rated outcomes. It was also not possible to meta-analyse the results due to the heterogeneity of the populations, the interventions and the reported outcomes. Therefore the confidence in the evidence base was low.

Benefits and harms

Based on experience and knowledge the committee noted that it is important to talk with the person affected by acne related scarring to explore the impact that acne related scarring has on them and provide information tailored to their needs. The committee discussed that people with acne-related scarring might experience psychological distress, stigmatisation and experience low self-esteem or depression. Treatment options should also be discussed. A common concern of people is to find out what may have caused their scars so that future scarring may be avoided. The committee also noted that the appearance of scars can change over time because tissue remodelling and healing process takes a long time so they recommended that this should also be explained to the person.

Based on their experience and expertise, the committee recommended considering a referral to a dermatology consultant-led team with expertise in scarring management because they noted that some of these treatments could potentially have lasting effects on the skin (such as hyperpigmentation) if used incorrectly. The committee agreed that it is important to not substantially increase the number of referrals for the management of scarring since this is not current practice (and would have a significant resource impact) and therefore restricted this to a specific subgroup of people who would benefit most from such treatment. The committee therefore specified based on the available evidence and clinical expertise that those with persistent severe scarring are likely to have the greatest benefit. The committee discussed that in their experience, tissue remodelling and healing process occurs for up to about a year after the acne has cleared and management of acne scarring should be considered after this timeframe.

There was a considerable amount of evidence that met the inclusion criteria. However, most of the trials compared different types of treatment to each other rather than a treatment to no treatment. Since there is uncertainty about the effectiveness of some of the treatments without this basic knowledge it is difficult to interpret comparisons of one treatment with

another. Despite there being a large number of studies included in this review, it was not possible to meta-analyse the results due to the heterogeneity of the populations, the interventions and the reported outcomes. The pattern of findings was therefore difficult to interpret. Three treatments were recommended based on evidence of effectiveness. These treatment options were glycolic acid peels or CO_2 laser treatment (alone or after a session of punch elevation). The committee recommended these as they demonstrated some evidence of effectiveness for improving atrophic acne-related scarring. In terms of glycolic acid peels the evidence came from a parallel-group RCT that compared the use of glycolic acid peels with glycolic acid cream and with placebo cream. The study showed that after 24 weeks of treatment glycolic acid peels showed the highest level of good improvement in scarring when compared to glycolic acid cream or placebo cream. The evidence on the effectiveness of CO_2 laser treatment came from a split-face RCT that compared CO_2 laser treatment with no treatment, and showed that CO_2 laser treatment was more effective in terms of improvement of scarred skin texture and atrophy when compared to no treatment. The effectiveness of punch elevation on atrophic acne-related scarring was shown in a split-face RCT which compared punch elevation given before CO_2 laser treatment with CO_2 laser treatment only. Since the committee had already established a possible benefit of CO_2 laser treatment (based on the study by Hedelund 2012 comparing CO_2 laser treatment versus no treatment) it made the interpretation of this comparison easier. The combination of punch elevation and CO_2 laser treatment showed a better improvement in scarring than CO_2 laser treatment alone. However, they noted that punch elevation would usually be added only for a particular type of deep scarring which would need to be elevated. The committee stressed that the choice of treatment procedures would depend on the particular types of acne scarring. However, they did not want to be prescriptive about which option to recommend for which particular type of scar because scars can vary between people but also in the same person.

The committee noted that overall the evidence base was small (only 3 studies) for the use of any of these treatments with small participant numbers (13 to 48) and not particularly high level of evidence quality using the GRADE assessment. Although this lowered their confidence in the findings, the committee were aware, from their knowledge and experience, that these interventions show clinical effectiveness for some people with acne-related scarring. They therefore decided the chance of potential benefit outweighs the harm of adverse psycholocal impact.

The committee also discussed that acne scarring treatments are widely available in the private sector but they are rarely, if at all, commissioned in NHS centres. They agreed to make a weak recommendation for the treatment of acne associated scarring which would leave the decision to individual commissioning bodies. Having a stronger recommendation would have a substantial impact on resource and would change clinical practice and the committee decided that the evidence was not strong enough to support such a change.

Due to the small number of participants in the studies and other uncertainties that the systematic review identified (such as the heterogenous patterns of findings), the committee discussed whether the topic should be prioritised for a research recommendation. They decided that the psychological impact of scarring can be significant and therefore justifies this as a topic for further research (see appendix L for details). Since the evidence pointed to the effectiveness of peels and laser treatment the committee decided to make one recommendation for physcial treatments and another for chemical peels.

Cost effectiveness and resource use

No economic evidence was identified for this review question. A simple cost analysis was undertaken to estimate the costs associated with management options for acne-related scarring. The committee considered these costs alongside the limited clinical evidence on the effectiveness of scarring management options versus no treatment and concluded that there is a significant uncertainty around the cost-effectiveness of these interventions. The committee agreed that the clinical experience on such interventions within the NHS is

currently very limited, and therefore scarring management interventions should only be offered within consultant dermatologist-led teams with expertise in scarring management.

The committee considered the benefits of specialist dermatology care for various sub-groups of people with acne-related scarring and agreed that, for people with severe acne-related scarring that persists a year after acne has cleared, referral to a consultant dermatologist-led team with expertise in scarring management is essential for symptom improvement, since in this group non-specialist care has failed to manage scarring effectively (despite of the effective management of acne). The committee was aware that referral to specialist care requires use of additional healthcare resources at extra costs, but decided to make recommendations based on their expertise because they expressed the view that benefits of referral to specialist care are likely to outweigh associated costs for this specific subgroup of people.

Based on the available limited clinical and economic evidence, and considering its uncertainty, the committee decided to make a weak ('consider') recommendation for scarring management interventions (glycolic acid peel or CO_2 laser treatment alone or after a session of punch elevation), delivered within the consultant-led specialist dermatology setting, for people with acne-related scarring that persists a year after acne has cleared. The committee expressed the view that such interventions are likely to be beneficial for this sub-group of people with persistent scarring, with benefits outweighing costs. They also argued that if people with long-term persistent scarring are not offered effective, specialist management for their scarring, they may try other ineffective and potentially harmful treatments outside healthcare settings, which may do harm and increase the need for resource intensive management further down the care pathway.

As the availability of such interventions for the management of acne-related scarring is variable across the NHS, the committee expected that making scarring management interventions available may have some resource impact; however, this is not excepted to be substantive as the recommendation is weak ("consider") and is relevant only to a small sub-group of people, who have acne-related scarring that persists one year after acne has cleared.

The recommendation to provide information to people with severe scarring and discuss their concerns is expected to have only a small impact on resources relating to health professionals' additional time required.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.8.1 and 1.8.2 and research recommendations on the effectivenss of chemical peels and effectiveness of physical modalities in the treatment of acne related scarring in the guideline.

References

Abdel-Maguid 2019

Abdel-Maguid EM, Awad SM, Hassan YS, El-Mokhtar MA, El-Deek HE, Mekkawy MM. Efficacy of Stem cell-conditioned medium vs Platelet-rich plasma as an adjuvant to post-ablative fractional CO2 laser resurfacing for atrophic post-acne scars: a split-face clinical trial. Journal of Dermatological Treatment 2019, 10:1-24

Ahmed 2014

Ahmed R, Mohammed G, Ismail N, Elakhras A. Randomized clinical trial of CO2 LASER pinpoint irradiation technique versus chemical reconstruction of skin scars (CROSS) in treating ice pick acne scars. Journal of Cosmetic and Laser Therapy 2014, 6(1):8-13

Anupama 2016

Anupama YG, Wahab AJ. Effectiveness of CO2 laser with subcision in patients with acne scars. J Cosmet Laser Ther 2016, 18(7):367-371

Asilian 2011

Asilian A, Salimi E, Faghihi G, Dehghani F, Tajmirriahi N, Hosseini SM. Comparison of Q-Switched 1064-nm Nd: YAG laser and fractional CO2 laser efficacies on improvement of atrophic facial acne scar. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences 2011, 16(9):1189

Bhargava 2019

Bhargava S, Kroumpouzos G, Varma K, Kumar U. Combination therapy using subcision, needling, and platelet-rich plasma in the management of grade 4 atrophic acne scars: A pilot study. Journal of cosmetic dermatology 2019, 18(4):1092-1097

Cachafeiro 2016

Cachafeiro T, Escobar G, Maldonado G, Cestari T, Corleta O. Comparison of nonablative fractional erbium laser 1,340 nm and microneedling for the treatment of atrophic acne scars: a randomized clinical trial. Dermatologic Surgery 2016, 42(2):232-41

Chae 2015

Chae WS, Seong JY, Jung HN, Kong SH, Kim MH, Suh HS, Choi YS. Comparative study on efficacy and safety of 1550 nm Er: Glass fractional laser and fractional radiofrequency microneedle device for facial atrophic acne scar. Journal of cosmetic dermatology 2015, 14(2):100-6

Cho 2010

Cho SB, Lee SJ, Cho S, Oh S, Chung WS, Kang JM, Kim YK, Kim DH. Non-ablative 1550-nm erbium-glass and ablative 10 600-nm carbon dioxide fractional lasers for acne scars: a randomized split-face study with blinded response evaluation. Journal of the European Academy of Dermatology and Venereology 2010, 24(8):921-5

Erbağcı 2000

Erbağcı Z, Akçalı C. Biweekly serial glycolic acid peels vs. long-term daily use of topical low-strength glycolic acid in the treatment of atrophic acne scars. International journal of dermatology 2000, 39(10):789-94

Faghihi 2015

Faghihi G, Nouraei S, Asilian A, Keyvan S, Abtahi-Naeini B, Rakhshanpour M, Nilforoushzadeh MA, Hosseini SM. Efficacy of punch elevation combined with fractional carbon dioxide laser resurfacing in facial atrophic acne scarring: a randomized split-face clinical study. Indian journal of dermatology 2015, 60(5):473

Faghihi 2016

Faghihi G, Keyvan S, Asilian A, Nouraei S, Behfar S, Nilforoushzadeh MA. Efficacy of autologous platelet-rich plasma combined with fractional ablative carbon dioxide resurfacing laser in treatment of facial atrophic acne scars: A split-face randomized clinical trial. Indian Journal of Dermatology, Venereology, and Leprology 2016, 82(2):162

Faghihi 2017

Faghihi G, Poostiyan N, Asilian A, Abtahi-Naeini B, Shahbazi M, Iraji F, Fatemi Naeini F, Nilforoushzadeh MA. Efficacy of fractionated microneedle radiofrequency with and without adding subcision for the treatment of atrophic facial acne scars: A randomized split-face clinical study. Journal of cosmetic dermatology 2017, 6(2):223-9

Galal 2019

Galal O, Tawfik AA, Abdalla N, Soliman M. Fractional CO2 laser versus combined platelet-rich plasma and fractional CO2 laser in treatment of acne scars: Image analysis system evaluation. Journal of cosmetic dermatology 2019 [Epub ahead of print]

Gawdat 2014

Gawdat HI, Hegazy RA, Fawzy MM, Fathy M. Autologous platelet rich plasma: topical versus intradermal after fractional ablative carbon dioxide laser treatment of atrophic acne scars. Dermatologic Surgery 2014, 40(2):152-61

Hassan 2019

Hassan AS, El-Hawary MS, Abdel Raheem HM, Abdallah SH, El-Komy MM. Treatment of atrophic acne scars using autologous platelet-rich plasma vs combined subcision and autologous platelet-rich plasma: A split-face comparative study. Journal of cosmetic dermatology 2019, [Epub ahead of print]

Hedelund 2012

Hedelund L, Haak CS, Togsverd-Bo K, Bogh MK, Bjerring P, Hædersdal M. Fractional CO2 laser resurfacing for atrophic acne scars: a randomized controlled trial with blinded response evaluation. Lasers in surgery and medicine 2012, 44(6):447-52

Khamthara 2018

Khamthara J, Kumtornrut C, Pongpairoj K, Asawanonda P. Silicone gel enhances the efficacy of Er: YAG laser treatment for atrophic acne scars: A randomized, split-face, evaluator-blinded, placebo-controlled, comparative trial. Journal of Cosmetic and Laser Therapy 2018, 20(2):96-101

Lee 2009

Lee DH, Choi YS, Min SU, Yoon MY, Suh DH. Comparison of a 585-nm pulsed dye laser and a 1064-nm Nd: YAG laser for the treatment of acne scars: A randomized split-face clinical study. Journal of the American Academy of Dermatology 2009, 60(5):801-7

Leheta 2011

Leheta T, El Tawdy A, Abdel Hay RM., Farid S. Percutaneous collagen induction versus full-concentration trichloroacetic acid in the treatment of atrophic acne scars. Dermatologic Surgery 2011, 37(2):207-16

Leheta 2014

Leheta TM, Abdel Hay RM, Hegazy RA, El Garem YF. Do combined alternating sessions of 1540 nm nonablative fractional laser and percutaneous collagen induction with trichloroacetic acid 20% show better results than each individual modality in the treatment of atrophic acne scars? A randomized controlled trial. Journal of Dermatological Treatment 2014, 25(2):137-41

Manuskiatti 2013

Manuskiatti W, Iamphonrat T, Wanitphakdeedecha R, Eimpunth S. Comparison of fractional erbium-doped yttrium aluminum garnet and carbon dioxide lasers in resurfacing of atrophic acne scars in Asians. Dermatologic Surgery 2013, 39(1pt1):111-20

Mohammed 2013

Mohammed G. Randomized clinical trial of CO2 laser pinpoint irradiation technique with/without needling for ice pick acne scars. J Cosmet Laser Ther 2013, 15(3):177-82

Nilforoushzadeh 2017

Nilforoushzadeh MA, Faghihi G, Jaffary F, Haftbaradaran E, Hoseini SM, Mazaheri N. Fractional carbon dioxide laser and its combination with subcision in improving atrophic acne scars. Advanced biomedical research 2017, 6:20

Nofal 2014

Nofal E, Helmy A, Nofal A, Alakad R, Nasr M. Platelet-rich plasma versus CROSS technique with 100% trichloroacetic acid versus combined skin needling and platelet rich plasma in the treatment of atrophic acne scars: a comparative study. Dermatologic Surgery 2014, 40(8):864-73

Osman 2017

Osman MA, Shokeir HA, Fawzy MM. Fractional erbium-doped yttrium aluminum garnet laser versus microneedling in treatment of atrophic acne scars: a randomized split-face clinical study. Dermatologic Surgery 2017, 43:S47-56

Reinholz 2015

Reinholz M, Schwaiger H, Heppt MV, Poetschke J, Tietze J, Epple A, Ruzicka T, Kaudewitz P, Gauglitz GG. Comparison of two kinds of lasers in the treatment of acne scars. Facial Plastic Surgery 2015, 31(05):523-31

Rongsaard 2014

Rongsaard N, Rummaneethorn P. Comparison of a fractional bipolar radiofrequency device and a fractional erbium-doped glass 1,550-nm device for the treatment of atrophic acne scars: a randomized split-face clinical study. Dermatologic Surgery 2014, 40(1):14-21

Sage 2011

Sage RJ, Lopiccolo MC, Liu A, Mahmoud BH, Tierney EP, Kouba DJ. Subcuticular Incision Versus Naturally Sourced Porcine Collagen Filler for Acne Scars: A Randomized Split-Face Comparison. Dermatologic Surgery 2011, 37(4):426-31

Tanzi 2004

Tanzi EL, Alster TS. Comparison of a 1450-nm diode laser and a 1320-nm Nd: YAG laser in the treatment of atrophic facial scars: a prospective clinical and histologic study. Dermatologic surgery 2004, 30(2):152-7

Zhang 2013

Zhang Z, Fei Y, Chen X, Lu W, Chen J. Comparison of a fractional microplasma radio frequency technology and carbon dioxide fractional laser for the treatment of atrophic acne scars: a randomized split-face clinical study. Dermatologic Surgery 2013, 39(4):559-66

Appendices

Appendix A – Review protocol

Review protocol for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

Table 6: Review protocol for management of acne vulgaris-associated scarring

Field	Content
PROSPERO registration number	CRD42019150489
Review title	Management of acne vulgaris-associated scarring
Review question	What are the most effective treatment options for acne vulgaris-associated scarring?
Objective	The aim of this review is to assess the effectiveness of interventions for managing acne scars
Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • Date: No restriction • Language of publication: English language only • Publication status: Conference abstracts will be excluded because these do not typically provide sufficient information to fully assess risk of bias • Standard exclusions filter (animal studies/low level publication types) will be applied • For each search (including economic searches), the principal database search strategy is quality assured by a second information specialist using an adaption of the PRESS 2015 Guideline Evidence-Based Checklist
Condition or domain being studied	• Acne vulgaris; management of scarring
Population	• Inclusion: People with atrophic and/or hypertrophic and/or keloid acne scars as diagnosed by a dermatologist or an experienced investigator • Exclusion: Neonatal acne
Intervention	Any intervention, or combination of interventions thereof, used to manage different types of acne scars will be considered, for example: **For atrophic scars:** o Chemical peeling o Dermabrasion o Dermal grafting o Laser therapy (for example pulsed dye laser) o Microdermabrasion o Needling o Punch techniques o Radiofrequency o Subcision o Surgery

	○ Tissue-augmenting agents **For hypertrophic and keloid scars:** ○ 5-fluorouracil (5-FU) ○ Bleomycin ○ Cryotherapy ○ Imiquimod ○ Interferon ○ Intralesional steroid injection ○ Laser therapy ○ Silicone gel ○ Surgery Note: Results will be presented separately for atrophic and hypertrophic/keloid scars. One and the same intervention can be used as treatment for acne and as treatment for scarring. Whether an intervention is used to prevent or treat scarring will be determined by the stated aims of the trials (for example prevention or management).
Comparator	The following comparisons will be considered: • Any other active intervention for management of acne-related scarring from the list above • No treatment • Placebo or sham treatment (as appropriate) • Waiting list
Types of study to be included	**Included study designs:** • Systematic reviews of randomised controlled trials • Randomised controlled trials (individual, cluster, or split-face/-body) Note: these types of RCTs will be analysed separately **Excluded study designs:** • Quasi- or non-randomised controlled studies • Case-control studies • Cohort studies • Cross-sectional studies • Epidemiological reviews or reviews on associations • Non-comparative studies Note: For further details, see the algorithm in appendix H, Developing NICE guidelines: the manual.
Other exclusion criteria	• Studies will be excluded if they do not specify in their inclusion criteria that participants must not have been receiving oral isotretinoin treatment for at least 6-months (that is a washout period) before the beginning of the trial. • Studies with an indirect population: where studies with a mixed population [that is including people with acne vulgaris and another condition different to acne vulgaris] are identified, those with <66% of the relevant population will be excluded, unless subgroup analysis for acne vulgaris has been reported
Context	Recommendations will apply to those receiving care in all healthcare settings (for example community, primary, secondary care).
Primary outcomes (critical outcomes)	**Critical outcomes** • Improvement in scarring at the end of treatment ○ Participant-reported improvement ○ Investigator-assessed improvement Note: Improvement in scarring should be assessed using a scar improvement, grading or severity scale but may be reported either as a continuous outcome or a dichotomous outcome. These will be reported separately if there is relevant data. Participant-reported and investigator-assessed improvement in scarring will be reported separately. • Serious adverse events Note: FDA definition is: death; life-threatening, initial or prolonged

	hospitalization; disability or permanent damage; congenital anomaly or birth defect; required intervention to prevent permanent impairment or damage due to use of medical devices; other serious events that may endanger the patient and require medical or surgical intervention to prevent any of the events previously listed.

Secondary outcomes (important outcomes)	**Important outcomes**
	• Participant satisfaction with treatment
	• Skin-related quality of life at the end of treatment (validated tools only, for example Dermatology Life Quality Index)
	• Participant's mood at the end of treatment (validated scales only, for example score on depression, anxiety scale)
	• Side effects:
	  ○ Local (for example hypo- or hyper-pigmentation; scarring)
	  ○ General

Data extraction (selection and coding)	• All references identified by the searches and from other sources will be uploaded into STAR and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. • Dual sifting will be performed on at least 10% of records; 90% agreement is required. • Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary. • Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies including study reference, study characteristics (for example design, type of statistical analysis), participant characteristics (for example age, ethnicity, sex, acne severity, concurrent acne treatment), intervention(s) characteristics (intervention details for example dosage, length, duration, frequency, mode), outcomes, and risk of bias. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Risk of bias of individual studies will be assessed using the Cochrane RoB tool, v.2 as described in Developing NICE guidelines: the manual.
Strategy for data synthesis	• The unit of randomisation in the included RCTs may be either the individual or the side of the face or body. So-called 'split-face' or 'split-body' trials will be meta-analysed separately using the generic inverse variance method. • Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. Where possible, meta-analyses will be conducted using Cochrane's Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios or odds ratios for dichotomous outcomes, and mean differences or standardised mean differences for continuous outcomes. For dichotomous outcomes, intention-to-treat (ITT) data will be used if available; if not then available data will be used. Final and change scores will be pooled and if any study reports both, change scores will be used in preference over final scores. • Sensitivity analysis will be conducted according to risk of bias of individual studies. Missing data will be accounted for in the risk of bias assessment. • Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. I2 values of greater than 50% and 80% will be considered as serious and very serious heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled. • Default MIDs will be used for risk ratios and continuous outcomes only,

	unless the committee pre-specifies published or other MIDs for specific outcomes ○ For risk ratios: 0.8 and 1.25. ○ For continuous outcomes: +/-0.5 times the baseline SD of the control arm. If there are 2 studies, the MID is calculated as +/- 0.5 times the mean of the SDs of the control arms at baseline. If there are 3 or more studies, the MID is calculated as +/- 0.5 times the median of the SDs of the control arms at baseline. If baseline SD is not available, then SD at follow up will be used. • The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/
Analysis of sub-groups	If there is serious or very serious heterogeneity for an outcome, subgroup analysis according to the following criteria will be conducted: • Skin colour (for example fair, dark) If there is serious or very serious heterogeneity for an outcome relating to atrophic scars, subgroup analysis according to the following criteria will be conducted: • Type of atrophic scar (icepick, rolling, boxcar) Note: Recommendations will apply to all people with acne vulgaris unless there is evidence of difference for these subgroups.
Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
Language	English
Country	England
Anticipated or actual start date	11 September 2019
Anticipated completion date	13 January 2021

Stage of review at time of this submission	**Review stage**	**Started**	**Completed**
	Preliminary searches	☑	☑
	Piloting of the study selection process	☐	☐
	Formal screening of search results against eligibility criteria	☑	☑

	Data extraction	☑	☑
	Risk of bias (quality) assessment	☑	☑
	Data analysis	☑	☑
Named contact	**5a. Named contact** National Guideline Alliance **5b Named contact e-mail** AcneManagement@nice.org.uk **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and National Guideline Alliance		
Review team members	National Guideline Alliance		
Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance, which is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists. NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England.		
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/gid-ng10109/documents/committee-member-list		
Other registration details	Not applicable		
Reference/URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=150489		
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE		
Keywords	Acne; atrophic; boxcar scar; hypertrophic; icepick scar; management; scarring; treatment.		
Details of existing	Not applicable		

review of same topic by same authors		
Current review status	☒	Ongoing
	☒	Completed but not published
	☐	Completed and published
	☐	Completed, published and being updated
	☐	Discontinued
Additional information	Not applicable	
Details of final publication	www.nice.org.uk	

GRADE: Grading of Recommendations Assessment, Development and Evaluation; MID: minimally important difference; NHS: National health service; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; SD: standard deviation; SE: standard error; SMD: standard mean difference.

Appendix B – Literature search strategies

Literature search strategy for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

Clinical search

Date of initial search: 01/08/2019

Database(s): Embase Classic+Embase 1947 to 2019 July 31, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to July 31, 2019

Multifile database codes: emczd = Embase Classic+Embase; ppez= MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emczd
3	acne.tw.
4	or/1-3
5	(exp scar formation/ or exp skin scar/ or exp scar/) use emczd
6	exp Cicatrix/ use ppez
7	(cicatri* or scar*1 or scarred or scarring or scarification).tw.
8	or/5-7
9	4 and 8
10	chemexfoliation/
11	(amino acid/ or 2 hydroxyacid/) use emczd
12	(Amino Acids/ or Hydroxy Acids/) use ppez
13	citric acid/
14	glycolic acid/ use emczd
15	Glycolates/ use ppez
16	lactic acid/
17	malic acid/ use emczd
18	mandelic acid/ use emczd
19	Mandelic Acids/ use ppez
20	pyruvic acid/
21	salicylic acid/
22	trichloroacetic acid/
23	(chemical adj1 (exfoliat* or peel* or reconstruct* or resurfac*)).tw.
24	(CROSS adj (method* or technique*)).tw.
25	(chemoexfoliat* or chemexfoliat* or chemo exfoliat*).tw.
26	((amino or citric or glycol* or lactic or lipohydroxy or malic or mandelic or pyruvic or salicylic or trichloroa?cetic or salicylic-mandelic or alpha hydroxy or "amino fruit") adj acid*).tw.
27	((Jessner* or phenol or pheno or resorcinol* or Baker-Gordon) adj (peel* or solution*)).tw.
28	skin surgery/ use emczd
29	Dermatologic Surgical Procedures/ use ppez
30	skin abrasion/ use emczd
31	Dermabrasion/ use ppez
32	(chemabrasion* or derm?abrasion* or derma abrasion* or dermo abrasion* or microderm?abrasion* or micro derm?abrasion* or dermaplaning).tw.
33	((cutis or cutaneous or derm* or epiderm* or skin) adj (abrasion* or abrat* or plane or planing or resurfac* or re-surfac* or surg*)).tw.
34	((punch* or puncture*) adj (elevat* or excis* or method* or technique*)).tw.
35	exp laser/ use emczd
36	exp Laser Therapy/ use ppez
37	Lasers, Dye/ use ppez
38	exp phototherapy/
39	(laser* or phototherap* or pulsed dye* or PDL).tw.
40	(radiofrequency/ or radiofrequency ablation/) use emczd
41	exp Radiofrequency Therapy/ use ppez
42	electrosurgery/
43	(radiofrequenc* or radio frequenc* or electrosurg*).tw.
44	esthetic surgery/ use emczd
45	Cosmetic Techniques/ use ppez
46	exp skin graft/ use emczd
47	Skin Transplantation/ use ppez
48	(dermatoplast* or derm?plast* or ((cutis or cutaneous or derm* or epiderm* or skin*) adj (graft* or surg* or transplant*))).tw.
49	adipose tissue/su use emczd
50	Adipose Tissue/su, tr use ppez

#	Searches
51	injectable implant/ use emczd
52	Dermal Fillers/ use ppez
53	(facial sculpt* or tissue augment*).tw.
54	((adipose or cutis or cutaneous or derm* or epiderm* or inject* or skin or subcutaneous or subderm* or tissue) adj (fill* or implant*)).tw.
55	cosmoplast*.tw.
56	collagen/ad, dl, tp, td use emczd
57	Collagen/ad, tu use ppez
58	hyaluronic acid/
59	methacrylic acid methyl ester/ use emczd
60	"poly(methyl methacrylate)"/ use emczd
61	exp Methylmethacrylates/ use ppez
62	polylactic acid/ use emczd
63	polyacrylamide/ use emczd
64	(collagen* or ((hyaluronic or methacrylic or methylmethacryl* or polymethylmethacry* or poly methyl methacry* or polylactic or poly-l-lactic or poly levo lactic or polyacrylamide or polyalkylimide) adj (acid* or fill*))).tw.
65	microneedle/ use emczd
66	Needles/ use ppez
67	(microneedl* or micro needl* or needl*).tw.
68	subcision*.tw.
69	(intralesional drug administration/ and steroid/) use emczd
70	(Injections, Intralesional/ and Steroids/) use ppez
71	((intralesion* or intra lesion* or subcutaneous) adj2 steroid*).tw.
72	(inject* adj2 steroid*).tw.
73	(silicone gel/ or exp silicone/) use emczd
74	exp Silicones/ use ppez
75	silicon* gel*.tw.
76	exp cryotherapy/
77	Hypothermia, Induced/ use ppez
78	(cold/ or exp low temperature procedures/) use emczd
79	exp Cold Temperature/ use ppez
80	((cold or cool* or ice) adj3 (therap* or treat*)).tw.
81	liquid nitrogen.tw.
82	(cryoablat* or cryopeel* or cryosurg* or cryoslush or cryotherap* or cryogenic therap* or cryogenic treat* or cryotherm* or cryotreat*).tw.
83	imiquimod/
84	(aldara or imiquimod).tw.
85	fluorouracil/
86	(fluorouracil or 5-fluorouracil or 5fluorouracil or 5FU or 5-FU).tw.
87	interferon/ use emczd
88	Interferons/ use ppez
89	interferon*.tw.
90	bleomycin/
91	bleomycin.tw.
92	(combination drug therapy/ or drug combination/) use emczd
93	Drug Therapy, Combination/ use ppez
94	Combined Modality Therapy/ use ppez
95	((combin* or concomitant or multimod* or multi mod*) adj2 (therap* or treatment* or drug* or intervention*)).tw.
96	or/10-95
97	9 and 96
98	Letter/ use ppez
99	letter.pt. or letter/ use emczd
100	note.pt.
101	editorial.pt.
102	Editorial/ use ppez
103	News/ use ppez
104	exp Historical Article/ use ppez
105	Anecdotes as Topic/ use ppez
106	Comment/ use ppez
107	Case Report/ use ppez
108	case report/ or case study/ use emczd
109	(letter or comment*).ti.
110	or/98-109
111	randomized controlled trial/ use ppez
112	randomized controlled trial/ use emczd
113	random*.ti,ab.
114	or/111-113
115	110 not 114
116	animals/ not humans/ use ppez
117	animal/ not human/ use emczd
118	nonhuman/ use emczd
119	exp Animals, Laboratory/ use ppez

#	Searches
120	exp Animal Experimentation/ use ppez
121	exp Animal Experiment/ use emczd
122	exp Experimental Animal/ use emczd
123	exp Models, Animal/ use ppez
124	animal model/ use emczd
125	exp Rodentia/ use ppez
126	exp Rodent/ use emczd
127	(rat or rats or mouse or mice).ti.
128	or/115-127
129	97 not 128
130	limit 129 to english language

Date of initial search: 01/08/2019

Database(s): The Cochrane Library: Cochrane Database of Systematic Reviews, Issue 8 of 12, August 2019; Cochrane Central Register of Controlled Trials, Issue 8 of 12, August 2019

#	Searches
#1	MeSH descriptor: [Acne Vulgaris] explode all trees
#2	acne:ti,ab
#3	#1 or #2
#4	MeSH descriptor: [Cicatrix] explode all trees
#5	(cicatri* or scar or scars or scarred or scarring or scarification):ti,ab
#6	#4 or #5
#7	#3 and #6
#8	MeSH descriptor: [Chemexfoliation] this term only
#9	MeSH descriptor: [Amino Acids] this term only
#10	MeSH descriptor: [Hydroxy Acids] this term only
#11	MeSH descriptor: [Citric Acid] this term only
#12	MeSH descriptor: [Glycolates] this term only
#13	MeSH descriptor: [Lactic Acid] this term only
#14	MeSH descriptor: [Mandelic Acids] this term only
#15	MeSH descriptor: [Pyruvic Acid] this term only
#16	MeSH descriptor: [Salicylic Acid] this term only
#17	MeSH descriptor: [Trichloroacetic Acid] this term only
#18	(chemical near (exfoliat* or peel* or reconstruct* or resurfac*)):ti,ab
#19	(CROSS near (method* or technique*)):ti,ab
#20	(chemoexfoliat* or chemexfoliat* or chemo exfoliat*):ti,ab
#21	((amino or citric or glycol* or lactic or lipohydroxy or malic or mandelic or pyruvic or salicylic or trichloroa?cetic or salicylic-mandelic or alpha hydroxy or "amino fruit") next acid*):ti,ab
#22	((Jessner* or phenol or pheno or resorcinol* or Baker-Gordon) next (peel* or solution*)).ti,ab
#23	MeSH descriptor: [Dermatologic Surgical Procedures] this term only
#24	MeSH descriptor: [Dermabrasion] this term only
#25	(chemabrasion* or dermabrasion* or dermoabrasion* or derma abrasion* or dermo abrasion* or microdermabrasion* or microdermoabrasion* or micro dermabrasion* or micro dermoabrasion* or dermaplaning).ti,ab
#26	((cutis or cutaneous or derm* or epiderm* or skin) next (abrasion* or abrat* or plane or planing or resurfac* or re-surfac* or surg*)).ti,ab
#27	((punch* or puncture*) next (elevat* or excis* or method* or technique*)):ti,ab
#28	MeSH descriptor: [Laser Therapy] explode all trees
#29	MeSH descriptor: [Lasers, Dye] this term only
#30	MeSH descriptor: [Phototherapy] explode all trees
#31	(laser* or phototherap* or pulsed dye* or PDL).ti,ab
#32	MeSH descriptor: [Radiofrequency Therapy] explode all trees
#33	MeSH descriptor: [Electrosurgery] this term only
#34	(radiofrequenc* or radio frequenc* or electrosurg*):ti,ab
#35	MeSH descriptor: [Cosmetic Techniques] this term only
#36	MeSH descriptor: [Skin Transplantation] this term only
#37	(dermatoplast* or dermaplast* or dermoplast* or ((cutis or cutaneous or derm* or skin*) adj (graft* or surg* or transplant*))):ti,ab
#38	MeSH descriptor: [Adipose Tissue] explode all trees and with qualifier(s): [surgery - SU, transplantation - TR]
#39	MeSH descriptor: [Dermal Fillers] this term only
#40	(facial sculpt* or tissue augment*):ti,ab
#41	((adipose or cutis or cutaneous or derm* or epiderm* or inject* or skin or subcutaneous or subderm* or tissue) next (fill* or implant*)):ti,ab
#42	cosmoplast*:ti,ab
#43	MeSH descriptor: [Collagen] explode all trees and with qualifier(s): [administration & dosage - AD, therapeutic use - TU]
#44	MeSH descriptor: [Hyaluronic Acid] this term only
#45	MeSH descriptor: [Methylmethacrylates] explode all trees
#46	(collagen* or ((hyaluronic or methacrylic or methylmethacryl* or polymethylmethacry* or poly methyl methacry* or polylactic or poly-l-lactic or poly levo lactic or polyacrylamide or polyalkylimide) next (acid* or fill*))):ti,ab
#47	MeSH descriptor: [Needles] this term only

#	Searches
#48	(microneedl* or micro needl* or needl*):ti,ab
#49	subcision*:ti,ab
#50	((intralesion* or intra lesion*) near/2 (corticosteroid* or steroid*)):ti,ab
#51	(inject* near/2 (corticosteroid* or steroid*)):ti,ab
#52	MeSH descriptor: [Silicones] explode all trees
#53	silicon* gel*:ti,ab
#54	MeSH descriptor: [Cryotherapy] explode all trees
#55	MeSH descriptor: [Hypothermia, Induced] this term only
#56	MeSH descriptor: [Cold Temperature] explode all trees
#57	((cold or cool* or freez* or ice) near/3 (therap* or treat*)):ti,ab
#58	liquid nitrogen:ti,ab
#59	(cryoablat* or cryopeel* or cryosurg* or cryoslush or cryotherap* or cryogenic therap* or cryogenic treat* or cryotherm* or cryotreat*):ti,ab
#60	MeSH descriptor: [Imiquimod] this term only
#61	(aldara or imiquimod):ti,ab
#62	MeSH descriptor: [Fluorouracil] explode all trees
#63	(fluorouracil or "5FU" or "5-FU"):ti,ab
#64	MeSH descriptor: [Interferons] explode all trees
#65	interferon:ti,ab
#66	MeSH descriptor: [Bleomycin] this term only
#67	bleomycin:ti,ab
#68	MeSH descriptor: [Drug Therapy, Combination] this term only
#69	((combin*or concomitant or multimod* or multi mod*) near (therap* or treatment* or drug* or intervention*)):ti,ab
#70	{or #8-#69}
#71	#7 and #70

Health Economics search

Date of initial search: 12/12/2018

Date of updated search: 06/05/2020

Database{s): Embase 1980 to 2020 May 05, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 05, 2020

Multifile database codes: emez = Embase; ppez = MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emez
3	acne.tw.
4	or/1-3
5	Economics/
6	Value of life/
7	exp "Costs and Cost Analysis"/
8	exp Economics, Hospital/
9	exp Economics, Medical/
10	Economics, Nursing/
11	Economics, Pharmaceutical/
12	exp "Fees and Charges"/
13	exp Budgets/
14	(or/5-13) use ppez
15	health economics/
16	exp economic evaluation/
17	exp health care cost/
18	exp fee/
19	budget/
20	funding/
21	(or/15-20) use emez
22	budget*.ti,ab.
23	cost*.ti.
24	(economic* or pharmaco?economic*).ti.
25	(price* or pricing*).ti,ab.
26	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
27	(financ* or fee or fees).ti,ab.
28	(value adj2 (money or monetary)).ti,ab.
29	or/22-27
30	14 or 21 or 29
31	4 and 30
32	limit 31 to english language

#	Searches
33	limit 32 to yr="2004 -Current"
34	remove duplicates from 33

Date of initial search: 12/12/2018

Date of updated search: 06/05/2020

Databases(s): NIHR Centre for Reviews and Dissemination: Health Technology Assessment Database (HTA) and the NHS Economic Evaluation Database (NHS EED)

#	Searches
1	MeSH DESCRIPTOR Acne Vulgaris EXPLODE ALL TREES
2	(acne) IN NHSEED, HTA FROM 2004 TO 2018
3	#1 OR #2

Search for health utility values

Date of initial search: 29/01/2019

Date of updated search: 06/05/2020

Database{s): Embase 1980 to 2020 May 05, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 05, 2020

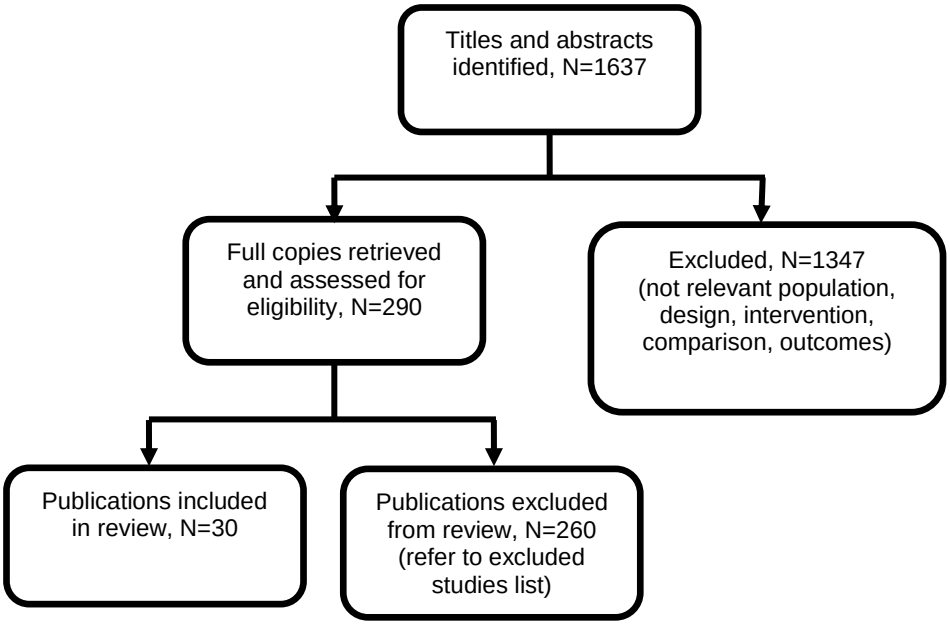
Multifile database codes: emez = Embase; ppez = MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily

#	Searches
1	exp Acne Vulgaris/ use ppez
2	exp acne/ use emez
3	acne.tw.
4	or/1-3
5	Quality-Adjusted Life Years/ use ppez
6	Sickness Impact Profile/
7	quality adjusted life year/ use emez
8	"quality of life index"/ use emez
9	(quality adjusted or quality adjusted life year*).tw.
10	(qaly* or qal or qald* or qale* or qtime* or qwb* or daly).tw.
11	(illness state* or health state*).tw.
12	(hui or hui2 or hui3).tw.
13	(multiattibute* or multi attribute*).tw.
14	(utilit* adj3 (score*1 or valu* or health* or cost* or measur* or disease* or mean or gain or gains or index*)).tw.
15	utilities.tw.
16	(eq-5d* or eq5d* or eq-5* or eq5* or euroqual* or euro qual* or euroqual 5d* or euro qual 5d* or euro qol* or euroqol*or euro quol* or euroquol* or euro quol5d* or euroquol5d* or eur qol* or eurqol* or eur qol5d* or eurqol5d* or eur?qul* or eur?qul5d* or euro* quality of life or european qol).tw.
17	(euro* adj3 (5 d* or 5d* or 5 dimension* or 5dimension* or 5 domain* or 5domain*)).tw.
18	(sf36 or sf 36 or sf thirty six or sf thirtysix).tw.
19	(time trade off*1 or time tradeoff*1 or tto or timetradeoff*1).tw.
20	Quality of Life/ and ((quality of life or qol) adj (score*1 or measure*1)).tw.
21	Quality of Life/ and ec.fs.
22	Quality of Life/ and (health adj3 status).tw.
23	(quality of life or qol).tw. and Cost-Benefit Analysis/ use ppez
24	(quality of life or qol).tw. and cost benefit analysis/ use emez
25	((qol or hrqol or quality of life).tw. or *quality of life/) and ((qol or hrqol* or quality of life) adj2 (increas* or decreas* or improv* or declin* or reduc* or high* or low* or effect or effects or worse or score or scores or change*1 or impact*1 or impacted or deteriorat*)).ab.
26	Cost-Benefit Analysis/ use ppez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
27	cost benefit analysis/ use emez and cost-effectiveness ratio*.tw. and (cost-effectiveness ratio* and (perspective* or life expectanc*)).tw.
28	*quality of life/ and (quality of life or qol).ti.
29	quality of life/ and ((quality of life or qol) adj3 (improv* or chang*)).tw.
30	quality of life/ and health-related quality of life.tw.
31	Models, Economic/ use ppez
32	economic model/ use emez
33	or/5-32
34	4 and 33
35	limit 34 to english language
36	limit 35 to yr="2004 -Current"
37	remove duplicates from 36

Appendix C – Clinical evidence study selection

Clinical study selection for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

Figure 1: Study selection flow chart



Appendix D – Evidence tables

Evidence tables for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

Table 7: Evidence table for split-face studies

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Abdel-Maguid, E. M., Awad, S. M., Hassan, Y. S., El-Mokhtar, M. A., El-Deek, H. E., Mekkawy, M. M., Efficacy of stem cell-conditioned medium vs. platelet-rich plasma as an adjuvant to ablative fractional CO₂ laser resurfacing for atrophic post-acne scars: a split-face clinical trial, Journal of Dermatological Treatment, 1-8, 2019 **Ref Id** 1082791 **Country/ies where the study was carried out** Egypt **Study type** split-face RCT **Aim of the study**	**Sample size** N=37 but analysed n=33 **Characteristics** Mean age (years)- mean (SD): group I: 24.8 (4.2), group II: 25.9 (7.6); male: group I: 2/17, group II: 7/16; female: group I: 15/17, group II: 9/16 Skin phototype III: group I: 9/17, group II: 8/16; Skin phototype IV: group I: 8/17, group II: 8/16 Acne scar severity: macular: group I: 0/17, group II: 0/16; mild: group I: 0/17, group II: 0/16; moderate: group I: 5/17, group II: 1/16; severe: group I: 12/17, group II: 15/16 Previous scar treatment: group I: 2/17, group II: 6/16 **Inclusion criteria**	**Interventions** Group I (n=17) Intervention (CO2 laser + SC-CM topical): received fractional ablative CO2 laser plus topical topical stem cell-conditioned medium (SC-CM) on one side. Comparator (CO2 laser + saline topical): received fractional ablative CO2 laser plus topical saline on the other side. All participants had three monthly sessions. Group II (n=16) Intervention (CO2 laser + PRP topical): received fractional CO2 laser plus topical platelet-rich plasma (PRP) on one side. Comparator (CO2 laser + SC-CM topical): received fractional CO2 laser plus SC-CM on the other side. All participants had three monthly sessions. *Prior to the procedure, the face was cleansed with alcohol and a topical anesthetic cream was applied for 45 min before treatment. A fractional ablative CO2 10,600nm laser device (Daeshin Enterprise Co., Ltd. Model: Multixel, Seoul, Korea) was used. A single pass was performed at the following parameters: pulse energy	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Mann–Whitney U-test and Wilcoxon matched-pairs signed-ranks test were used for comparisons of unpaired and paired non-parametric data, respectively. Kruskal–Wallis test was used to compare means for more than two groups. Chi-Square test and Fisher's exact test were used to compare categorical data as appropriate. **Intention-to-treat analysis** Not mentioned.	**Results** **Primary outcomes** **Overall improvement in scarring - investigator assessed** Mean (SD) total ECCA scores* at baseline: Group I (n=17) CO2 laser plus SC-CM: 96.76 (5.3) CO2 laser plus saline: 94.12 (5) Group II (n=16) CO2 laser plus PRP: 115.31 (6.4) CO2 laser plus SC-CM: 117.81 (6.4) Mean (SD) total ECCA scores* after 3rd final treatment session: Group I (n=17) CO2 laser plus SC-CM: 80.94 (5.6) CO2 laser plus saline: 80.94 (4.7) Group II (n=16) CO2 laser plus PRP:	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: some concerns (no sufficient information provided about the randomisation and allocation concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias (although n=37 were randomised but n=33 analysed as 4 participants dropped out for personal reasons) Detection bias: low risk of bias Reporting bias: low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
To assess the efficacy of AFSC-CM and PRP as adjunctive therapies to FCL compared to FCL alone for treatment of atrophic acne scars. **Study dates** December 2015 - July 2017 **Source of funding** Supported by a grant from Assiut University, Faculty of Medicine research grant office.	Participants with: • moderate-to-severe afacial atrophic scars as per Goodman and Baron's acne scar grading scale **Exclusion criteria** Participants with: • history of keloid scarring, • any active infection, • photosensitivity, • isotretinoin intake within the preceding 6 months, • facial skin resurfacing within the preceding 3 months, pregnant and lactating, • medications or blood disorders that affect platelet concentration or function.	42–45mJ, density of 100 spots/cm2, depth level of 1–2 covering an area of 1 cm2. Postoperatively, adjuvant therapy (in the form of PRP or SC-CM) or normal saline was topically applied directly onto fractional laser treated area on one side of the face in relevant participant groups.		85.36 (6.8) CO2 laser plus SC-CM: 103.21 (7.3) Mean (SD) change** in total ECCA scores* between baseline and 3rd final treatment session: Group I (n=17) CO2 laser plus SC-CM: -15.82 (3.86) CO2 laser plus saline: -13.18 (3.44) Group II (n=16) CO2 laser plus PRP: -29.95 (4.68) CO2 laser plus SC-CM: -14.6 (4.92) **Improvement in ICEPICK scars - investigator assessed** Mean (SD) total ECCA scores* at baseline: Group I (n=13) CO2 laser plus SC-CM: 28.85 (2.7) CO2 laser plus saline: 27.69 (1.6) Group II (n=13) CO2 laser plus PRP: 28.24 (2.8) CO2 laser plus SC-CM: 31.88 (2.3) Mean (SD) total ECCA scores* after 3rd final treatment session: Group I (n=13)	Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				CO2 laser plus SC-CM: 20.77 (3.2) CO2 laser plus saline: 23.08 (2.7) Group II (n=13) CO2 laser plus PRP: 18.75 (3.2) CO2 laser plus SC-CM: 26.00 (2.7) Mean (SD) change** in total ECCA scores* between baseline and 3rd final treatment session: Group I (n=13) CO2 laser plus SC-CM: -8.08 (2.14) CO2 laser plus saline: -4.61 (1.84) Group II (n=13) CO2 laser plus PRP: -9.49 (2.15) CO2 laser plus SC-CM: -5.88 (1.81) **Improvement in BOXCAR scars - investigator assessed** Mean (SD) total ECCA scores* at baseline: Group I CO2 laser plus SC-CM: 31.43 (4.0), n=7 CO2 laser plus saline: 30.00 (3.8), n=8 Group II CO2 laser plus PRP: 41.67 (3.9), n=12 CO2 laser plus SC-	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				CM: 38.46 (3.6), n=13 Mean (SD) total ECCA scores* after 3rd final treatment session: Group I CO2 laser plus SC-CM: 26.67 (6.7), n=7 CO2 laser plus saline: 22.86 (5.2), n=8 Group II CO2 laser plus PRP: 22.00 (4.7), n=12 CO2 laser plus SC-CM: 30.91 (4.9), n=13 Mean (SD) change** in total ECCA scores* between baseline and 3rd final treatment session: Group I CO2 laser plus SC-CM: -4.76 (4.55), n=7 CO2 laser plus saline: -7.14 (3.44), n=8 Group II CO2 laser plus PRP: -19.67 (3.13), n=12 CO2 laser plus SC-CM: -7.55 (3.24), n=13 **Improvement in ROLLING scars - investigator assessed** Mean (SD) total ECCA scores* at baseline: Group I (n=17) CO2 laser plus SC-	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				CM: 61.76 (3.8) CO2 laser plus saline: 58.82 (4.3) Group II (n=16) CO2 laser plus PRP: 57.81 (4.4) CO2 laser plus SC-CM: 59.38 (5.0) Mean (SD) total ECCA scores* after 3rd final treatment session: Group I (n=17) CO2 laser plus SC-CM: 53.12 (5.5) CO2 laser plus saline: 53.12 (5.0) Group II (n=16) CO2 laser plus PRP: 48.21 (5.5) CO2 laser plus SC-CM: 55.36 (4.7) Mean (SD) change** in total ECCA scores* between baseline and 3rd final treatment session: Group I (n=17) CO2 laser plus SC-CM: -8.64 (3.65) CO2 laser plus saline: -5.7 (3.35) Group II (n=16) CO2 laser plus PRP: -9.6 (3.65) CO2 laser plus SC-CM: -4.02 (3.44) *Clinical assessment of acne scar severity was done	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				using Echelle d'Evaluation Clinique des Cicatrices d'acnè (ECCA) scale. **calculated by the NGA technical team **Secondary outcomes** <u>Patient satisfaction with the treatment</u> <u>Very satisfied/satisfied:</u> Group I (n=17) CO2 laser plus SC-CM: 13/17 CO2 laser plus saline: 10/17 Group II (n=16) CO2 laser plus PRP: 13/16 CO2 laser plus SC-CM: 10/16 <u>Slightly satisfied:</u> Group I (n=17) CO2 laser plus SC-CM: 3/17 CO2 laser plus saline: 6/17 Group II (n=16) CO2 laser plus PRP: 3/16 CO2 laser plus SC-CM: 6/16 <u>Unsatisfied:</u> Group I (n=17) CO2 laser plus SC-CM: 1/17 CO2 laser plus saline: 1/17 Group II (n=16)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				CO2 laser plus PRP: 0/16 CO2 laser plus SC-CM: 0/16 <u>Side effects: Erythema (participant reported):</u> Group I (n=17) CO2 laser plus SC-CM: 17/17 CO2 laser plus saline: 17/17 Group II (n=16) CO2 laser plus PRP: 16/16 CO2 laser plus SC-CM: 16/16 <u>Edema (participant reported):</u> Group I (n=17) CO2 laser plus SC-CM: 17/17 CO2 laser plus saline: 17/17 Group II (n=16) CO2 laser plus PRP: 16/16 CO2 laser plus SC-CM: 16/16 <u>Crust formation (investigator reported):</u> Group I (n=17) CO2 laser plus SC-CM: 17/17 CO2 laser plus saline: 17/17 Group II (n=16) CO2 laser plus PRP: 16/16	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				CO2 laser plus SC-CM: 16/16 Acne activation (investigator reported): Group I (n=17) CO2 laser plus SC-CM: 6/17 CO2 laser plus saline: 6/17 Group II (n=16) CO2 laser plus PRP: 1/16 CO2 laser plus SC-CM: 2/16 Persistent pixel stamping marks (investigator reported): Group I (n=17) CO2 laser plus SC-CM: 3/17 CO2 laser plus saline: 4/17 Group II (n=16) CO2 laser plus PRP: 0/16 CO2 laser plus SC-CM: 3/16 Post-inflammatory hyperpigmentation (investigator reported): Group I (n=17) CO2 laser plus SC-CM: 1/17 CO2 laser plus saline: 1/17 Group II (n=16) CO2 laser plus PRP: 0	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				CO2 laser plus SC-CM: 0	
Full citation Cho, S. B., Lee, S. J., Cho, S., Oh, S. H., Chung, W. S., Kang, J. M., Kim, Y. K., Kim, D. H., Non-ablative 1550-nm erbium-glass and ablative 10 600-nm carbon dioxide fractional lasers for acne scars: a randomized split-face study with blinded response evaluation, Journal of the European Academy of Dermatology & VenereologyJ Eur Acad Dermatol Venereol, 24, 921-5, 2010 **Ref Id** 868214 **Country/ies where the study was carried out** Korea **Study type** split-face RCT **Aim of the study** To compare the efficacy and safety of single-session treatments using FPS and CO2 FS to eliminate acne scars through a randomised, split-face,	**Sample size** N=8 males **Characteristics** Mean age (years)- mean (range): 21.3 (20-23) **Inclusion criteria** Participants with: • Males with mild-to-severe atrophic acne scars • Fitzpatrick skin type IV **Exclusion criteria** Participants with: • concomitant treatments including skin resurfacing procedures, • chemical reconstruction of skin scars (CROSS) using trichloroacetic acid, • collagen induction	**Interventions** Intervention (FPS laser): 1 side of each participant's face was treated with a single session of non-ablative 1550-nm erbium-doped fractional photothermolysis laser (FPS) using the Fraxel SR1500 (Reliant Technologies, Mountain View, CA, USA). Comparator (CO2 laser): The other side of the facewas treatedwith a single session of CO2 fractional laser systems (CO2 FS) using the 10,600-nm Ultrapulse Encore laser (Lumenis Inc., Santa Clara, CA, USA). *For local anaesthesia, the face was cleansed with a mild soap and 70% alcohol, and topical EMLA cream (eutectic mixture of 2.5% lidocaine HCl and 2.5% prilocaine; AstraZeneca AB, Sodertalje, Sweden) was applied to the entire face under occlusion an hour prior to the laser therapy. An epidermal cooling device (Zimmer MedizinSystems, Irvine, CA, USA) was used during the treatment to relieve pain. Participants were prescribed 10 mg of oral prednisolone for 3 days after treatment. Participants were instructed to use a facial moisturiser (Physiogel^{TM} Cream; Stiefel Laboratories, Sligo, Ireland) several times for a few days after treatment and a broad-spectrum sunscreen Anthelios XL^{R} (SPF 50+), La Roche-Posay, Paris.	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Non-parametric Mann–Whitney U- and Kruskal–Wallis tests were used to compare clinical assessment scores, overall participant satisfaction levels, the characteristics of adverse events associated with FPS and CO2 FS and scar types. The results are statistically significant if p<0.05. **Intention-to-treat analysis** Not mentioned.	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** Mean (SD) grade* of improvement 3 months after treatment FPS = 2.0 (0.5) CO2 = 2.5 (0.8) (p=0.158) *grade 1: < 25% = minimal to no improvement; grade 2: 26% to 50% = moderate improvement; grade 3: 51% to 75% = marked improvement; grade 4: > 75% = near-total improvement. **Secondary outcomes** Participant satisfaction 3 months after treatment Very satisfied: FPS = 0 CO2 = 2/8 (25%) Slightly satisfied: FPS = 5/8 (62.5%) CO2 = 1/8 (12.5%)	**Limitations Cochrance RoB Tool v2.0 add** Selection bias: some concerns (no information about randomisation and allocation concealment was provided) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
evaluator-blinded study. **Study dates** Not reported **Source of funding** None	therapy using a micro-needle therapy system, • FPS and CO2 FS treatments within the previous 6 months, • keloids, • pregnant, • immunosuppressed, • history of isotretinoin.			Satisfied: FPS = 2/8 (25%) CO2 = 4/8 (50%) Unsatisfied: FPS = 1/8 (12.5%) CO2 = 1/8 (12.5%) Side effects 3 Post-therapy hyperpigmentation: FPS = 1/8 (12.5%) CO2 = 1/8 (12.5%) Transient pinpoint bleeding: FPS = 0 CO2 = 1/8 (12.5%) Post-therapy blister formation: FPS = 0 CO2 = 0 Scarring: FPS = 0 CO2 = 0 Hypopigmentation: FPS = 0 CO2 = 0 Secondary bacterial/viral infection: FPS = 0 CO2 = 0 Treatment-associated pain* (mean (SD)): FPS = 3.9 (2.0) CO2 = 7.0 (2.0) *Pain scores associated with the different laser modalities were evaluated using 10-cm visual analogue	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				scales (VAS), with 0 being 'no pain' and 10 being 'extremely painful'.	
Full citation Faghihi, G., Nouraei, S., Asilian, A., Keyvan, S., Abtahi-Naeini, B., Rakhshanpour, M., Nilforoushzadeh, M., Hosseini, S., Efficacy of punch elevation combined with fractional carbon dioxide laser resurfacing in facial atrophic acne scarring: A randomized split-face clinical study, Indian Journal of Dermatology, 60, 473-478, 2015 **Ref Id** 1082893 **Country/ies where the study was carried out** Iran **Study type** split-face RCT **Aim of the study** To compare the clinical effectiveness and side effects of fractional CO2 laser resurfacing combined	**Sample size** N=42 **Characteristics** Mean age (years)- mean (SD): 23.4 (2.63); males = 23, females = 19; Fitzpatrick skin types: type III = 28, type IV = 14 **Inclusion criteria** Participants: • 18-55 years of age, • with Fitzpatrick skin types III to IV, • moderate to severe atrophic acne scars on both cheeks **Exclusion criteria** Participants: • pregnant, lactating, • with active	**Interventions** Intervention (CO2 laser + punch elevation): 1 side side of the face was treated with the same fractional ablative CO2 laser plus punch elevation (2.5 - 3 mm biopsy disposable punches) Comparator (CO2 laser): other side of the participant's face was treated using the 10600nm fractional ablative CO2 laser alone (M×7000/Stamp Type, Daeshin, South Korea) *Initially, punch elevation using 2.5 or 3 mm biopsy punches was performed on one side of the face. Secondly, 24 h after punch elevation, a full face CO2 laser treatment session was performed. Second full face laser treatment session was performed 4 week later. Anaesthetic cream (2.5% lidocaine/prilocaine, XYLA-P Tehran Chemie Pharmaceutical Company, Iran) was applied to the treatment area under occlusion 1 h before laser treatment. Participants received prophylactic antibiotic and antiviral medications 1 day prior to treatment and continued the medications for 1 week. Clinical evaluation was done 1 and 4 months after the second treatment session was completed.	**Details** **Power Analysis** Not mentioned **Statistical Analyses** T-test was used to compare the effectiveness and side effects of the two treatment sides. **Intention-to-treat analysis** Not mentioned	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** Improvement % in scar scores* at 4 months after treatment (N=42): With punch: minimal = 0; moderate = 26.2 (n=11); good = 45.2 (n=19); excellent = 28.6 (n=12) Without punch: minimal = 4.8 (n=2); moderate = 33.3 (n=14); good = 57.1 (n=24); excellent = 4.8 (n=2) (p=0.02 between groups) *Using a grading scale as follows: 1 = < 25% (minimal) improvement; 2 = 25% - 50% (moderate) improvement; 3 = 51% - 75% (good) improvement; 4 = > 75% (excellent) improvement **Secondary**	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: low risk of bias Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
with punch elevation with fractional CO2 laser resurfacing alone in the treatment of atrophic acne scars. **Study dates** Not reported **Source of funding** Skin Diseases and Leishmaniasis Research Center, Isfahan University of Medical Sciences, Isfahan Iran.	inflammatory acne, • immunocompetence, • history of deep chemical peeling or filler injection in the previous 6 months, • history of hypertrophic scars and keloids, • use of isotretinoin in the previous 6 months, • allergy to anesthesia, • active infection in the treatment area, • premalignant or malignant lesions in the treatment area, • bleeding tendencies, • history of herpes simplex or herpes zoster infection on the face.			**outcomes** Participant satisfaction* with treatment (mean (SD)) at 4 months after treatment (N=42): With punch: 7.8 (1.6) Without punch: 6.8 (1.9) (p=0.009 between groups) *Using a visual analog scale (VAS: a rating of 0 = no satisfaction, a rating of 10 = the best possible satisfaction). Side effects (investigator reported, n/N): Erythema: With punch: 42/42 (100%) Without punch: 42/42 (100%) Hypopigmentation: With punch: 0 Without punch: 0 Post treatment burning: With punch: 42/42 (100%) Without punch: 42/42 (100%)	
Full citation Faghihi, G., Keyvan, S., Asilian, A., Nouraei, S.,	**Sample size** N=16	**Interventions** Intervention (CO2 laser + PRP injection): both the cheeks of each participant were treated with the	**Details** **Power Analysis** Not mentioned. **Statistical Analyses**	**Results** **Primary outcomes** **Improvement in scarring -**	**Limitations** **Cochrance RoB Tool v2.0** Selection

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Behfar, S., Nilforoushzadeh, M., Efficacy of autologous platelet-rich plasma combined with fractional ablative carbon dioxide resurfacing laser in treatment of facial atrophic acne scars: A split-face randomized clinical trial, Indian Journal of Dermatology, Venereology and Leprology, 82, 162-168, 2016 **Ref Id** 1047821 **Country/ies where the study was carried out** Iran **Study type** split-face RCT **Aim of the study** To investigate the potential of the combination therapy with autologous platelet-rich plasma and fractional carbon dioxide laser in enhancing the treatment response of facial acne scars and reducing the risk of adverse events. **Study dates** Not reported	**Characteristics** Mean age (years) - mean (range) 36.8 (22-52); male=4, female=12; Fitzpatrcik skin types: II=1/16 III=4/16 IV=11/16 predominantly rolling and boxcar types with fewer than 20% of the icepick type. Acne grade severity 2: laser + PRP=0 laser + saline=1 Acne grade severity 3: laser + PRP=8 laser + saline=9 Acne grade severity 4: laser + PRP=8 laser + saline=6 **Inclusion criteria** Participants: • aged 22-52 years, Fitzpatrick skin types II-IV, • moderate to severe facial atrophic acne scars **Exclusion criteria** Participants: • with a history of keloid	ablative CO2 fractional laser (Q-ray, Diosis Inc., Seoul, Korea). Parameters used: laser power, 25; dot cycle (duration), 3; energy, 30mj, pixel pitch, 1 and ablation depth, 600 µm. After the laser treatment, one side of the face received autologous platelet-rich plasma (PRP). Injection sites were located within 2 cm intervals to receive 0.2 ml platelet-rich plasma. One month after the initial treatment session, all participants received the second treatment session with the same protocol. Comparator (CO2 laser + saline injection): both the cheeks of each participant were treated with the ablative CO2 fractional laser (Q-ray, Diosis Inc., Seoul, Korea). Parameters used: laser power, 25; dot cycle (duration), 3; energy, 30mj, pixel pitch, 1 and ablation depth, 600 µm. After the laser treatment, the other side of the face received normal saline. Injection sites were located within 2 cm intervals to receive 0.2 ml normal saline. One month after the initial treatment session, all participants received the second treatment session with the same protocol. *About 60 min before the starting the treatment, the targeted region was treated with topical anesthetic cream (mixture of lidocaine 2.5% and prilocaine 2.5%, Xyla P [Tehran Chemical Pharmaceutical Co., Tehran, Iran]) and icepacks to alleviate the pain followed by gentle cleansing and applicaton of 70% isopropyl alcohol as disinfectant. They were instructed to apply a topical antibiotic	Wilcoxon rank test was used to compare the results of the two methods for the degree of clinical improvement of acne scars and patient satisfaction. The paired t-test was utilized for group comparison of numerical variables. **Intention-to-treat analysis** Not mentioned.	**investigator assessed** Scarring improvement* 4 months after the 2nd treatment session: Excellent improvement (n/N): CO2 laser + platelet-rich plasma: 0/16 CO2 laser + saline: 0/16 Fair/good improvement (n/N): CO2 laser + platelet-rich plasma: 14/16 CO2 laser + saline: 11/16 Poor improvement (n/N): CO2 laser + platelet-rich plasma: 2/16 CO2 laser + saline: 5/16 *A quartile grading scale: poor, <25% improvement; fair, 25-50% improvement; good, 51-75% improvement and excellent, >75% improvement was used by two blinded dermatologists was used to evaluate the overall clinical improvement. **Secondary outcomes**	bias: some concerns (no information provided about allocation concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Supported by a grant from the Isfahan University of Medical Sciences (Grant no. 393020)	formation, • herpes simplex infection, • any active inflammation, • diabetes mellitus, • collagen vascular disease, • oral isotretinoin use within the previous 6 months, • pregnant, • lactating, • ablative or non-ablative laser skin resurfacing in the previous 12 months.	(mupirocin) cream twice daily for 5 days after the treatment session.		**Participant satisfaction with treatment** Satisfaction* 4 months after the 2nd treatment session: Satisfied/very satisfied (n/N): CO2 laser + platelet-rich plasma: 9/16 CO2 laser + saline: 7/16 Slightly satisfied (n/N): CO2 laser + platelet-rich plasma: 7/16 CO2 laser + saline: 5/16 Unsatisfied (n/N): CO2 laser + platelet-rich plasma: 0/16 CO2 laser + saline: 4/16 *Each participant evaluated his/her overall satisfaction with the treatment using a quartile grading system which defines 0 as unsatisfied, 1 as slightly satisfied, 2 as satisfied, or 3 as very satisfied. Side effects (investigator reported): Secondary infection: CO2 laser + platelet-rich plasma: 0/16	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				CO2 laser + saline: 0/16 Acneiform eruption: CO2 laser + platelet-rich plasma: 0/16 CO2 laser + saline: 0/16 Dyschromia: CO2 laser + platelet-rich plasma: 0/16 CO2 laser + saline: 0/16 New scar formation: CO2 laser + platelet-rich plasma: 0/16 CO2 laser + saline: 0/16	
Full citation Faghihi, G., Poostiyan, N., Asilian, A., Abtahi-Naeini, B., Shahbazi, M., Iraji, F., Fatemi Naeini, F., Nilforoushzadeh, M. A., Efficacy of fractionated microneedle radiofrequency with and without adding subcision for the treatment of atrophic facial acne scars: A randomized split-face clinical study, Journal of Cosmetic DermatologyJ, 16, 223-229, 2017 **Ref Id** 868508 **Country/ies where the study was carried out**	**Sample size** N=25 **Characteristics** Mean age (years) - mean (SD): 30.1 (4.94); males = 9, females = 16; Fitzpatrick skin types: type II = 5, type III = 16, type IV = 4; Acne grading: III = 16, VI = 10 **Inclusion criteria** Participants with: • a diagnosis of II-IV Fitzpatrick skin type • moderate to severe atrophic facial acne	**Interventions** Intervention (fractionated microneedle frequency (FMR) + subcision): initially, standard subcision by use of Nokor needle (1.5 inch, 18-gauge) after local anaesthesia by 1% lidocaine was performed on one side of the face; then, 2 weeks after subcision, FMR treatment was performed. A second and third FMR treatment session was performed with a 4-week interval. Comparison (FMR): 2 weeks after subcision, FMR treatment was performed on both cheeks of each participant. A second and third FMR treatment session was performed with a 4-week interval. *For FMR, topical anesthetic cream (2.5% lidocaine/prilocaine: XYLA-P Tehran Chemie Pharmaceutical Company, Iran) was applied on both	**Details** **Power Analysis** Not mentioned **Statistical Analyses** The Wilcoxon rank test and paired t-test were used to compare the data of the two methods regarding degree of clinical improvement of acne scars and patient satisfaction. **Intention-to-treat analysis** Not mentioned	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** Improvement in scar scores* at the end of the study (n (%)): FMR + subcision: poor = 5/25 (20); fair = 7/25 (28); good = 13/25 (52); excellent = 0/25 FMR: poor = 5/25 (20); fair = 12/25 (48); good = 8/25 (32); excellent = 0/25 (no p-value provided) *Using a grading scale as follows: poor = <	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: some concerns (no information about the allocation concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Iran **Study type** split-face RCT **Aim of the study** To evaluate the therapeutic effects FMR vs FMR combined with subcision for the treatment of atrophic acne scars in a randomized, split-face clinical study. **Study dates** Not reported **Source of funding** Not reported	scars by Goodman and Baron grading scale on both cheeks **Exclusion criteria** Participants: • pregnant; lactating; • with active inflammatory acne lesions; • history of deep chemical peeling or filler injection in the previous 6 months; • history of hypertrophic scars, and keloids formation; • use of isotretinoin in the previous 6 months; • active infection in the treatment area; • bleeding tendencies; • history of herpes simplex or herpes zoster; • infection on the face; • history of pacemaker implantation.	cheeks under occlusion one hour before FMR treatment. The FMR treatment settings were 1.5-3.5 mm microneedle penetrating depth, 6-8 level intensity, and 120-140 ms RF time.		25% improvement; fair = 25% - 50% improvement; good = 51% - 75% improvement; excellent = > 75% improvement **Secondary outcomes** Participant satisfaction* with treatment (mean (SD)) at the end of the study (n=25): FMR + subcision: 6 (2.2) FMR: 5.1 (1.6) (p=0.001 between groups) *Using a visual analog scale (VAS: a rating of 0 = no satisfaction, a rating of 10 = the best possible satisfaction). Side effects (investigator reported): Infection: FMR + subcision: 0 FMR: 0 Persistent facial erythema: FMR + subcision: 0 FMR: 0 Ulceration: FMR + subcision: 0 FMR: 0 Scar formation:	Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				FMR + subcision: 0 FMR: 0 Treansient bilateral submandibular lymphadenopathy: FMR + subcision: 1/25 FMR: 0	
Full citation Galal, O., Tawfik, A. A., Abdalla, N., Soliman, M., Fractional CO2 laser versus combined platelet-rich plasma and fractional CO2 laser in treatment of acne scars: Image analysis system evaluation, Journal of Cosmetic Dermatology., 2019 **Ref Id** 1047861 **Country/ies where the study was carried out** Egypt **Study type** split-face RCT **Aim of the study** 1) To compare the efficacy of fractional CO2 laser therapy versus the combined use of PRP and fractional CO2 in	**Sample size** N=30 **Characteristics** Mean age (years) - mean (SD) 26.7 (4.7); male=9, female=21; Fitzpatrcik skin types IV and V = 70%; Mean number (SD) of scars: 12.6 (5.8); Type of scars: Ice picks scar = 9/30 Boxcar scar = 16/30 Rolling scar = 5/30 **Inclusion criteria** Participants with atrophic acne scar lesions. **Exclusion criteria** Participants with: • with a history of keloid or hypertrophic scar formation,	**Interventions** Intervention (CO_2 laser + PRP injection): one side of the face received fractional ablative CO2 laser therapy followed by intradermal platelet-rich plasma (PRP) injection. Photographs were taken at baseline and 3 months after treatment. One treatment modality. Comparator (CO2 laser): the other side of the face received fractional ablative CO2 laser therapy. Photographs were taken at baseline and 3 months after treatment. One treatment modality. *Local anesthetic cream was applied under occlusion 45 minutes prior to treatment. A SmartXide DOT Fractionated CO2 Laser (DEKA, Florence, Italy) was used, with a smart stack scanning method with a power of 15 W, spacing of 800 mμ, a 600 sμ dwell time, and stack2. Regular photography (using a Samsung 10-megapixel camera) was also done for all participants at baseline and after each session for 3 months.	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** A paired t-test was used for comparison of numerical variables within groups. A Wilcoxon signed-rank test was used for paired (matched) samples. Correlation between various variables was assessed using the Spearman rank correlation equation for non-normal variables. The Mann-Whitney U Test was used to assess the statistical significance of the difference in a non-parametric variable between the 2 groups. The Kruskal-Wallis test was used to assess the difference between more than two groups of ordinal variables. Linear regression was used to estimate the dependence of a quantitative variable	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** Scarring improvement* at baseline (mean (SD): CO2 + PRP group = 5.7 (5.5) CO2 group = 5.7 (5.5) Scarring improvement* 3 months after treatment (mean (SD): CO2 + PRP group = 2.2 (2.4) CO2 group = 3.3 (2.8) Mean (SD) scarring improvement* from baseline to 3 months after treatment: CO2 + PRP group = -3.5 (4.03) CO2 group = -2.4 (3.87) *The quantitative global acne scarring grading	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: some concerns (randomisation was done by tossing a coin; no information provided about allocation concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: high risk of bias (no information provided whether outcome assessors were blinded) Reporting bias: low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
the treatment of facial atrophic acne scars. 2) To evaluate the results of both treatment modalities quantitatively using a skin image analysis system. **Study dates** Not reported **Source of funding** Not reported	• recurrent active facial acne, • isotretinoin intake within the preceding 6 months, • diabetes, collagen or vascular diseases; • pregnant, • with high level of exposure to sunlight or ultraviolet light (tanning).		based on its relationship to one or more independent variable **Intention-to-treat analysis** Not mentioned.	scale adopted by Goodman and Baron was used. This scale is based on evaluation of both the type and number of scars. **Secondary outcomes** **Participant satisfaction with treatment** Satisfaction* 3 months after treatment: Very satisfied (n/N): CO2 + PRP group = 15/30 CO2 group = 1/30 *Participant satisfaction was assessed and graded using a 3-point Likert scale: satisfied, partially satisfied, or dissatisfied. Side effects (not clear if participant or investigator reported) Hyperpigmentation CO2 + PRP group = 0/30 CO2 group = 0/30	Other bias Overall risk of bias: high risk of bias
Full citation Gawdat, H. I., Hegazy, R. A., Fawzy, M. M., Fathy, M.,	**Sample size** N=30 n=15 randomised to CO2 laser + PRP intradermal vs CO2 +	**Interventions** Group 1 (n = 15) underwent split-face therapy: intervention (CO2 laser + PRP	**Details** **Power Analysis** Not mentioned. **Statistical Analyses**	**Results** **Primary outcomes** **Improvement in scarring -**	**Limitations** **Cochrance RoB Tool v2.0** Selection bias:

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments

Autologous platelet rich plasma: Topical versus intradermal after fractional ablative carbon dioxide laser treatment of atrophic acne scars, Dermatologic Surgery, 40, 152-161, 2014
 	
Ref Id
 	
1047868
 	
Country/ies where the study was carried out
 	
Egypt
 	
Study type
split-face RCT
 	
Aim of the study
To compare the efficacy and safety of combining autologous PRP with FCL in the treatment of atrophic acne scars with that of FCL alone. To compare the efficacy of two modes of administration of autologous PRP (intradermal injection and topical application) after FCL in the treatment of atrophic acne scars.
 	
Study dates
Not reported
	saline intradermal
	n=15 randomised to CO2 laser + PRP intradermal vs CO2 + PRP topical
	
	Characteristics
	Mean age (years)- mean (SD): group 1=25.2 (5), group 2=24.3 (3.7)
	group 1: n=5 men; n=10 women; group 2: n=7 men, n=8 women
	Fitzpatrick skin type:
	group 1: III=7; IV=6; V=2;
	group 2: III=6; IV=7; V=2;
	Acne scar severity:
	2: group 1=3, group 2=3;
	3: group 1=8, group 2=9;
	4: group 1=4, group 2=3;
	
	2=mild, 3=moderate, 4=severe
	
	Inclusion criteria
	Participants:
	
	• aged 19–35,
	• with Fitzpatrick skin phototypes III to V,
	• atrophic acne scars
	
	Exclusion criteria
	Participants:
		injection): one cheek was treated with fractional ablative CO2 (FCL) followed by intradermal injection of autologous platelet-rich plasma (PRP) (area A);
		comparator (CO2 laser + saline injection): the other cheek was treated with fractional ablative CO2 followed by intradermal injection of normal saline (area B). Each participant received 3 treatment sessions at monthly intervals.
		Group 2 (n = 15) underwent split-face therapy:
		intervention (CO2 laser + PRP injection): one cheek was treated with fractional CO2 (FCL) followed by intradermal injection of autologous platelet-rich plasma (PRP); the same regimen as area A (area C).
		comparator (CO2 laser + PRP topical): the other cheek was treated with FCL followed by topical application of autologous PRP (area D). Each participant received 3 treatment sessions at monthly intervals.
		*Local anesthetic cream (5% lidocaine) was applied to the area to be treated in both groups and under occlusion for 60 min before the procedure to minimize pain/discomfort. Then the whole face was cleansed using a mild cleanser and dried with sterile gauze. The cheek was then irradiated with FCL (Smartxide DOT, Advanced CO2 Fractional technology, DEKA, Florence, Italy). The treatment parameters were power, 15 W; dwell time, 600 ls; spacing, 700 lm; smart stack, level 2. Ice packs were used to minimize heat and pain during and after the procedure. Afterward, the treated areas were randomly assigned
			Comparison of numerical variables between the study groups was done using the Student t test for independent samples. Within-group comparison of numerical variables was performed using the paired t-test for paired (matched) samples. The-chi square test was used to compare categorical data.
			Intention-to-treat analysis
			Not mentioned.
				investigator assessed
				Mean (SD) of acne scar depth* (µm) at baseline:
				Group I (n=15)
				CO2 + PRP injection: 92.3 (15.1)
				CO2 + saline injection: 92.3 (15.1)
				Group II (n=15)
				CO2 + PRP injection: 92.3 (15.1)
				CO2 + PRP topical: 92.3 (15.1)
				Mean (SD) of acne scar depth* (µm) 3 months after the last treatment session:
				Group I (n=15)
				CO2 + PRP injection: 28.9 (8.3)
				CO2 + saline injection: 48.8 (16.4)
				Group II (n=15)
				CO2 + PRP injection: 28.9 (8.3)
				CO2 + PRP topical: 29.8 (8.3)
				Mean (SD) change** in acne scar depth* (µm) 3 months after the last treatment session:
				Group I (n=15)
				CO2 + PRP injection: -63.4 (10.44)
				CO2 + saline injection: -43.5 (11.2)
				Group II (n=15)
				CO2 + PRP injection:
					some concerns (no sufficient information provided about the randomisation and allocation concealment)
					Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study)
					Attrition bias: low risk of bias
					Detection bias: low risk of bias
					Reporting bias: low risk of bias
					Other bias
					Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding The authors have indicated no significant interest with commercial supporters.	• with a history of systemic retinoid therapy within the last 6 months, immunosuppressive drugs, • hypertrophic scars or keloid formation, • pregnancy, or lactation	to receive intradermal injection of autologous PRP (area A) on one side and intradermal injection of normal saline (area B) on the other.		-63.4 (10.44) CO2 + PRP topical: -62.5 (10.44) *The depth of acne scars was assessed using a noninvasive imaging technique (optical coherence tomography (OCT); RTVue-100, SD Optovue Inc., Fremont, CA). ** calculate by the NGA technical team **Secondary outcomes** <u>Side effects</u> <u>Acneform eruption: Group I (n=15)</u> CO2 + PRP injection: 0 CO2 + saline injection: 0 <u>Group II (n=15)</u> CO2 + PRP injection: 0 CO2 + PRP topical: 0 <u>Post-inflammatory hyperpigmentation: Group I (n=15)</u> CO2 + PRP injection: 0 CO2 + saline injection: 2 <u>Group II (n=15)</u> CO2 + PRP injection: 0 CO2 + PRP topical: 0 <u>Treatment-associated</u>	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				pain* (mean (SD)): Group I (n=15) CO2 + PRP injection: 7.1 (1.2) CO2 + saline injection: 3 (0.7) Group II (n=15) CO2 + PRP injection: 7.1 (1.2) CO2 + PRP topical: 2.8 (0.6) *Pain was assessed on a scale of 0 (none) to 9 (maximum) at the end of each session, and a mean value for the three sessions of each treated area was calculated.	
Full citation Hassan, A. S., El-Hawary, M. S., Abdel Raheem, H. M., Abdallah, S. H., El-Komy, M. M., Treatment of atrophic acne scars using autologous platelet-rich plasma vs combined subcision and autologous platelet-rich plasma: A split-face comparative study, Journal of Cosmetic Dermatology., 2019 **Ref Id** 1082963 **Country/ies where the**	**Sample size** N=30 but analysed n=25 **Characteristics** Mean age (years) - mean (SD) 26.1 (5.99); male=5, female=25; skin phototype III = 21 (70%), type IV = 9 (30%) grade 3 acne scarring = 22 (73.3%), grade 4 acne scarring = 8 (27.7%) (moderate to severe) **Inclusion criteria** Participants with acne scarring.	**Interventions** Intervention (subcision + PRP intadermal): one side of the face received a combination treatment: subcision followed by autologous platelet-rich plasma (PRP) injection. Each patient received three sessions with 1-month interval. Comparator (PRP intradermal): the other side of the face received PRP alone. Each patient received three sessions with 1-month interval. *The area to be treated was sterilised, marked by a surgical marker, and locally anesthetized. An 18-gauge, 1½-inch NoKor Admix needle (Becton Dickinson and Co) capped on a 3cc syringe was inserted at a shallow angle,	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Wilcoxon-matched pairs signed rank-sum test was used for comparing paired non-parametric data, Mann-Whitney test was used for comparing 2 independent non-parametric groups, Kruskal-Wallis test was used when comparing between more than 2 non-parametric groups. Chi-squared was used for comparing different groups.	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** Scarring improvement* 6 months after the last treatment session: Mild improvement (n/N)**: Subcision + PRP group: 5/20 PRP group: 0/20 Moderate improvement (n/N): Subcision + PRP group: 5/20	**Limitations** **Cochrance RoB Tool v2.0 add** Selection bias: some concerns (no information provided about randomisation and allocation concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
study was carried out Egypt **Study type** split-face RCT **Aim of the study** To evaluate the efficacy of PRP as a monotherapy for treating atrophic acne scars and compared it with the combined use of PRP and subcision in a prospective, split-face, clinical study. **Study dates** Not reported **Source of funding** Not reported	**Exclusion criteria** Participants: • pregnant, • with history of keloids, • diabetes, • neuromuscular disease, • collagen disease, • bleeding tendency, anticoagulant medications, • who performed laser for acne scars in the preceding year, • used topical and systemic retinoids in the preceding 6 months.	with the blade facing upwards, at the periphery of the scarred area. When the needle was intradermal or into the superficial subcutaneous layer, it was turned so that the tip was in a horizontal orientation and moved backwards and forwards, until no resistance was felt. Pressure was applied for at least 5 min to achieve haemostasis. Than PRP was injected and participants were instructed to compress their faces with gauze for 15-20 min. The same volume of PRP was injected in the comparator side of the face.	**Intention-to-treat analysis** Not mentioned.	PRP group: 8/20 Marked improvement (n/N): Subcision + PRP group: 5/20 PRP group: 6/20 Excellent improvement (n/N): Subcision + PRP group: 5/20 PRP group: 6/20 *assessed using a quartile grading scale: grade 1 = mild improvement (1%-25%), grade 2 = moderate improvement (26%-50%), grade 3 = marked improvement (51%-75%), and grade 4 = excellent improvement (76%-100%). **improvement in scarring was reported as a % in the paper, recalculated by the NGA technical team.	risk of bias (n=25 participants received the entire regimen but n=5 dropped out during the study: n=2 got pregnant and n=3 refused to continue for personal reasons) Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns
Full citation Hedelund, L., Haak, C. S., Togsverd-Bo, K., Bogh, M. K., Bjerring, P., Haedersdal, M., Fractional CO2 laser resurfacing for atrophic acne scars: a randomized controlled trial with blinded response evaluation, Lasers	**Sample size** N=13 but n=12 analysed at 6 months post-treatment **Characteristics** Mean age (years)- mean (range): 33 (22-54); n=6 men; n=7 women;	**Interventions** Intervention (CO2 laser): an facial area ((9 - 30 cm²) received 3 laser treatments at 4- to 5-week intervals. The laser system was a CO2 laser (MedArt 610) equipped with a scanner (MedArt 458) developed specifically for fractional treatments (MedArt, Hvidovre, Denmark). The laser	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Non-parametric and parametric statistical methods were used. The Wilcoxon matched pair test was used for two paired comparisons and	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** **Scar skin texture improvement** Assessment (mean (SD)) of scars* at	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: low risk of bias Performance bias: low risk of bias (blinding of participants and

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
in Surgery & MedicineLasers Surg Med, 44, 447-52, 2012 **Ref Id** 868766 **Country/ies where the study was carried out** Denmark **Study type** split-face RCT **Aim of the study** To examine efficacy and adverse effects of fractional CO_2 laser resurfacing for atrophic acne scars compared to no treatment. **Study dates** December 2009 to November 2010 **Source of funding** MedArt A/S, Hvidovre, Denmark	skin type: I=6; II=6; III=1; Scar type: ice-pick=3; boxed=1; boxed+rolling=1; boxed+ice-pick=1; rolling=6; rolling+ice-pick=1; participants with moderate to severe scars **Inclusion criteria** Participants: • age of 18 - 60 years, • white, • with skin types I - III, • duration of atrophic acne scars 1 year or more, • willingness and ability to comply with the requirements of the protocol **Exclusion criteria** Participants with: • a tendency to produce hypertrophic scars or keloids, • previous treatment with ablative lasers of study areas, • photosensitivity,	procedure was performed in a single pass with spot diameter of 0.5 mm, pulse duration of 4 milliseconds, laser power of 12–14 W, microbeam energy of 48–56 mJ per pulse, 100 MTZ/cm2 and density of 13%. Comparator (no treatment): a similar facial area received no treatment. *Licocaine/prilocaine 2.5% cream was used as topical anaesthetic and applied to the treated areas under occlusion 1 hour before treatment.	Friedman's test for more than two paired comparisons. **Intention-to-treat analysis** Not mentioned.	baseline: CO2 laser group: 6.15 (1.23) No treatment group: 6.15 (1.23) Assessment (mean (SD)) of scars* 6 months after treatment: CO2 laser group: 3.89 (1.74) No treatment group: 5.22 (2.06) Mean change (SD) in the assessment of scars* 6 months after treatment: CO2 laser group: -2.26 (1.15) No treatment group: -0.93 (1.398) **Scar skin atrophy improvement** Assessment (mean (SD)) of scars* at baseline: CO2 laser group: 5.72 (1.45) No treatment group: 5.72 (1.45) Assessment (mean (SD)) of scars* 6 months after treatment: CO2 laser group: 3.56 (1.76) No treatment group: 4.89 (1.94) Mean change (SD) in the assessment of scars* 6 months after	personnel was not feasible for this study) Attrition bias: low risk of bias (n=1 participant withdrew before the final evaluation and was not included in the analysis 6 months post-operatively). Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	pregnancy or lactation, • current anticoagulative medication, • oral retinoid drugs within the past 6 months, • pigmentation after recent exposure to sun or solarium, • people not considered to be able to follow the treatment protocol.			treatment: CO2 laser group: -2.16 (1.17) No treatment group: -0.83 (1.28) *Acne scars were assessed as follows: improvement of scar texture (the smoothness of the scar) and atrophy (the depth of scars), on numerical scales ranging from 0 [0, even skin texture without scarring/atrophy] to 10 [worst possible scarring/atrophy]	

Full citation
 	
Khamthara, J., Kumtornrut, C., Pongpairoj, K., Asawanonda, P., Silicone gel enhances the efficacy of Er:YAG laser treatment for atrophic acne scars: A randomized, split-face, evaluator-blinded, placebo-controlled, comparative trial, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 20, 96-101, 2018
 	
Ref Id
 	
868974
 	
Country/ies where the study was carried out
	Sample size
	N=20 but n=19 analysed
	
	Characteristics
	Median age (years) - median (IQR): 25 (23-28);
	male=14, female=5;
	Fitzpatrick skin types:
	II=7
	II=8
	IV=4;
	Scar grade:
	moderate=10
	severe=9;
	Previous scar treatment:
	yes=10
	no=9
		Interventions
		Intervention (ablative Er:YAG laser + silicone gel): 1 side of the face received silicone gel twice daily starting from day 5 post ablative Er:YAG laser treatment. Participants were treated with three sessions of ablative Er:YAG laser with 1-month intervals.
		Comparator (ablative Er:YAG laser + hydrophilic cream): the other side of the face received hydrophilic cream base twice daily starting from day 5 post laser treatment. Participants were treated with three sessions of ablative Er:YAG laser with 1-month intervals.
		*All participants received three sessions of Er:YAG (SP Dynamis, Fotona®, Ljubljana, Slovenia) 2,940 nm spot size 7 mm short pulse (300 μs) 3 passes on
			Details
			Power Analysis
			Sample size of 20 subjects was based on clinical study of fractional carbon dioxide laser treatment for scars.
			Statistical Analyses
			Wilcoxon signed rank and Mc-Nemar tests were used for comparisons of objective measurements from week 0 to week 12.
			Intention-to-treat analysis
			Not mentioned.
				Results
				Primary outcomes
				Improvement* in scarring - participant assessed
				Scarring improvement 4 weeks after last treatment
				Excellent improvement (n/N):
				Ablative Er:YAG laser + silicone gel:3/19
				Ablative Er:YAG laser + hydrophilic cream: 2/19
				Good improvement (n/N):
				Ablative Er:YAG laser + silicone gel: 7/19
					Limitations
					Cochrance RoB Tool v2.0
					Selection bias: some concerns (no information provided about allocation concealment)
					Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study)
					Attrition bias: low risk of bias (although n=20

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Thailand **Study type** split-face RCT **Aim of the study** To investigate the additional efficacy of topical silicone gel when combined with ablative Er:YAG laser in atrophic acne scars compared to laser being performed alone. **Study dates** Not reported **Source of funding** Not reported	**Inclusion criteria** Participants: • healthy male and female subjects, • aged 18 years or older, • with atrophic acne scars on both cheeks of grades 3–4 according to Goodman and Baron's qualitative grading system were eligible. **Exclusion criteria** Participants: • pregnant, • using immunosuppressive dr ugs, • with prior laser treatment for acne scars within 3 months, • use of systemic retinoids within 6 months, • allergy to silicone gel, • history of keloid at any site or hypertrophic scars following laser treatment	weeks 0, 4 and 8. The fluences were increased at each treatment from 1.82 J/cm2 at first session to, 2.08 J/cm2, and finally 2.34 J/cm2. On days 0–4 all participants applied white petrolatum jelly (Vaseline) on all laser-treated areas. From day 5 through to the next laser session, they applied silicone gel or hydrophilic cream twice daily to their assigned half-face.		Ablative Er:YAG laser + hydrophilic cream: 6/19 *Grading scales were as follows: grade 1 = 1–25% improvement (fair improvement), grade 2 = >25–50% improvement (good improvement), grade 3 = >50–75% improvement, grade 4 = >75–100% improvement. Grades 3 and 4 were collectively reported as excellent improvement. <u>Side effects:</u> <u>Post laser hyperpigmentation:</u> Ablative Er:YAG laser + silicone gel:0/19 Ablative Er:YAG laser + hydrophilic cream: 0/19	were randomised but n=19 analysed as 1 participant dropped out for personal reasons) Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Lee, D. H., Choi, Y. S., Min, S. U., Yoon, M. Y., Suh, D. H., Comparison of a 585-nm pulsed dye laser and a 1064-nm Nd:YAG laser for the treatment of acne scars: A randomized split-face clinical study, Journal of the American Academy of DermatologyJ Am Acad Dermatol, 60, 801-7, 2009 **Ref Id** 869118 **Country/ies where the study was carried out** Korea **Study type** split-face RCT **Aim of the study** To compare the efficacies and safeties of a 585-nm PDL and a 1064-nm long-pulsed Nd:YAG laser for the treatment of atrophic facial acne scarring. **Study dates** Not reported	**Sample size** N=18 **Characteristics** Mean age (years) - mean (range): 23 (21-30); n=10 men, n=8 women; Fitzpatrick skin types: IV or V (no details given) **Inclusion criteria** Participants: • age of at least 18 years • diagnosis of mild to moderate atrophic acne scarring **Exclusion criteria** Participants: • with known photosensitivity, • pregnant, • lactating, • with a history of hypertrophic or keloidal scarring, • the use of isotretinoin,	**Interventions** Intervention (585-nm pulsed dye laser (PDL)): 1 side of the face was treated with non-overlapping pulses of 585-nm PDL (Cynergy, Cynosure Inc,Westford,MA) at a sub-purpuric fluence of 10 to 11 J/cm2 and a 40-ms pulse duration using a 7-mm hand piece. All participants received 4 treatment sessions at 2-week intervals. Comparator (1064-nm longpulsed neodymium:yttrium-aluminum-garnet laser (Nd:YAG)): at the same session, the contralateral side was treated with a 1064-nm long-pulsed Nd:YAG laser (Cynergy) at a fluence of 50 to 70 J/cm² and a 50- to 100-ms pulse duration using a 7-mm spot size. All participants received 4 treatment sessions at 2-week intervals. *No topical or intralesional anesthetic was administered prior to the treatment. Participant follow-up was scheduled at 2-week intervals during the 6-week treatment period and at 4-week intervals for 8 weeks after the final session (total study duration, 14 weeks from treatment commencement).	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Mann-Whitney test was used for comparison between two lasers and Wilcoxon signed rank test was used for comparison of before and after laser treatments **Intention-to-treat analysis** Not mentioned.	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** Mean (SD) ECCA* scores before treatment: PDL laser group = 56.4 (9.4) Nd:YAG laser group = 68.6 (8.3) Mean (SD) ECCA* scores 8 weeks after final treatment: PDL laser group = 46.1 (7.2) Nd:YAG laser group = 55.8 (8.2) Mean change (SD) in ECCA scar scores* at 8 weeks after final treatment**: PDL laser group = -10.3 (6.22) Nd:YAG laser group = -12.8 (5.83) *Quantified by assessing the degrees of improvement accordi ng to scar types, and the echelle d'e´valuation clinique des cicatrices d'acne´ [clinical evaluation scale for acne scarring] (ECCA) scores.	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: some concerns (no information provided about randomisation and allocation concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Not reported	• history of facial laser treatment or surgical procedure within 6 months of study enrolment, • medical condition that might have influenced the wound healing process			ECCA grading scales are based on semiquantitative, weighted assessments of 6 types of acne scars, that is V-shaped atrophic scars, U-shaped atrophic scars, M-shaped atrophic scars, hypertrophic inflammatory scars, keloid scars, and superficial elastolysis. **calculated by the NGA technical team	
Full citation Manuskiatti, W., Iamphonrat, T., Wanitphakdeedecha, R., Eimpunth, S., Comparison of Fractional Erbium-Doped Yttrium Aluminum Garnet and Carbon Dioxide Lasers in Resurfacing of Atrophic Acne Scars in Asians, Dermatologic Surgery., 2012 **Ref Id** 1048298 **Country/ies where the study was carried out** Thailand **Study type**	**Sample size** N=24 but analysed n=20 **Characteristics** Mean age (years)- mean (range): 33.7 (20-65); n=8 men; n=12 women; All participants had shallow or deep boxcar scars or both on their faces for least 6 months before entering the study. **Inclusion criteria** Participants aged 22–51 years with skin phototype IV.	**Interventions** Intervention (2,940-nm Er:YAG laser): one side of the face was treated with 1 pass of an ablative fractional Er:YAG laser. The Er:YAG side was set for a pulse duration of 350 ls and an energy of 14 mJ; all participants received 2 treatment sessions. Comparator (CO2 laser): the other side of the face was treated with 1 pass of an ablative fractional CO2 laser. The CO2 laser was adjusted to deliver at a pulse duration of 950 ls and a mean energy of 13.75 (12.5–15) mJ; all participants received 2 treatment sessions. *Both lasers were set to treat an average of 5% skin surface coverage. The treatment areas were cleansed of debris (dirt, makeup, and powder) using	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** The Wilcoxon signed rank test was used to determine if there was any significant difference in clinical improvement scores between the follow-up visits. Analyses of repeated measures, including repeated-measures analysis of variance and multivariate analysis were performed to test the differences in the means of skin surface smoothness and	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** >50% improvement in acne scars 6 months after the final treatment Er:YAG group: 11/20 CO2 laser group: 13/20 *Clinical improvement was assessed using a quartile grading scale (0 = <25%, 1 = 25–50%, 2 = 51–75%, 3 = >75% improvement)	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: some concerns (no sufficient information provided about the randomisation and allocation concelament) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias (although

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
split-face RCT **Aim of the study** To compare the efficacy and safety of these techniques [Er:YAG and CO2 lasers] for the treatment of atrophic acne scars using histologic, subjective and objective clinical evaluation. **Study dates** Not mentioned. **Source of funding** The authors have indicated no significant interest with commercial supporters.	**Exclusion criteria** Participants: • pregnant or lactating, • had concomitant treatment to involved skin areas, • had a propensity for keloid scarring, • had received isotretinoin, • or had undergone filler injections • or ablative • or nonablative laser skin resurfacing procedures within the preceding 12 months	a mild cleanser and 70% isopropyl alcohol. Lidocaine 2.5% and prilocaine 2.5% cream (a eutectic mixture of local anesthetic, AstraZeneca LP, Wilmington, DE) was applied under occlusion to the treatment area. After 1 hour of application, the anaesthetic cream was gently removed, and then alcohol was used to degrease the skin to obtain a completely dry skin surface.	scar volume over time. **Intention-to-treat analysis** Not mentioned.	**Secondary outcomes** Side effects (investigator-reported): Contact dermatitis: Er:YAG group: 0/20 CO2 laser group: 0/20 Difference in skin colour: Er:YAG group: 0/20 CO2 laser group: 0/20 Mild post-inflammatory hyperpigmentation: Er:YAG group: 7/20 CO2 laser group: 10/20 Scarring: Er:YAG group: 0/20 CO2 laser group: 0/20 Wound infection: Er:YAG group: 0/20 CO2 laser group: 0/20 Treatment-associated pain* (mean (SD)): Er:YAG group: 3.2 (1.4) CO2 laser group: 5.8 (2.0) *Pain was rated using a 10-point pain scale (0 = no pain to 10 = severe pain).	n=4 participants withdrawn from the study because 3 of them had scheduling conflicts and the other one was unable to be contacted during follow-up) Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Nilforoushzadeh, M. A., Faghihi, G., Jaffary, F., Haftbaradaran, E., Hoseini, S. M., Mazaheri, N., Fractional Carbon Dioxide Laser and its Combination with Subcision in Improving Atrophic Acne Scars, Advanced Biomedical ResearchAdv, 6, 20, 2017 **Ref Id** 1048388 **Country/ies where the study was carried out** Iran **Study type** split-face RCT **Aim of the study** To compare the effectiveness of two treatment methods of subcision and fractional CO2 laser and fraxel laser in recovering the atrophic acne scars. **Study dates** During 2011-2012	N=30 **Characteristics** Age not reported male=8, female=22; rolling type scars = 80% ice pick type scars = 10% other scar types = 10% **Inclusion criteria** Participants with: • ice pick type • and rolling-type atrophic acne scars **Exclusion criteria** Participants: • pregnant, • lactating, • use of any oral or topical drugs in the recent 6 months, • affected by any disease or active skin infection such as impetigo, herpes simplex, flat wart, or serious skin disease history, • tendency of keloid, • acne rosacea,	Intervention (fraxel laser + subcision): one side of the face received 1 combination session of subcision and fraxel laser (energy 30 pulse, 1 pixel pitch, and Dot cycle 6 with DOSIS M and M, Q ray FRX machine made in Korea) , then after 3 weeks, 4 sessions of fractioanal CO2 laser sessions only with 3-week interval. 1550 nm erbium laser fibers are used. Comparator (fractional CO2 laser): another side of the face received 5 fractional CO2 laser sessions with 3-week interval. *One hour before subcision, the participants were anaesthetized topically by lidocaine P cream under the plastic covers. Then, an insulin needle was entered near the scar and parallel to the skin level, under the scar, and deep in derm, with a fan-like movement to make the fibrose band in derm or subcutaneous surface deep derm, it moved forward and backward. By using the needle, the surgery place passed in order to evacuate extra blood. 1550-nm erbium laser fibres were used.	**Power Analysis** The sample size was calculated using sample size formula with d = 0.3 **Statistical Analyses** Not mentioned. **Intention-to-treat analysis** Not mentioned.	**Secondary outcomes** **Participant satisfaction with treatment** Average (SD) satisfaction* 6 months after the last treatment session: CO2 laser + subcision: 6.6 (1.2) CO2 laser: 5.2 (1.8) *Participant's satisfaction was assessed using visual analog scale score (no details given).	**Cochrance RoB Tool v2.0** Selection bias: some concerns (no information provided about randomisation and allocation concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias: Overall risk of bias: some concerns **Other information** Extremely poor reporting.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Nil	• psychological disorders, • those who did not agree to continue the research.				
Full citation Osman, M. A. R., Shokeir, H. A., Fawzy, M. M., Fractional erbium-doped yttrium aluminum garnet laser versus microneedling in treatment of atrophic acne scars: A randomized split-face clinical study, Dermatologic Surgery, 43, S47-S56, 2017 **Ref Id** 1048419 **Country/ies where the study was carried out** Egypt **Study type** split-face RCT **Aim of the study** To evaluate and compare the efficacy and safety of fractional ablative 2,940-nm Er:YAG laser and microneedling for the treatment of atrophic	**Sample size** N=30 **Characteristics** Mean age (years) - mean (SD) 27 (3.75); male=10, female=20; Fitzpatrcik skin types: III=14/30 IV=15/30 V=1/30; Acne severity: mild= 7/30 moderate = 17/30 severe = 6/30 **Inclusion criteria** Participants with: • Fitzpatrick skin phototypes III to V • atrophic acne scars. **Exclusion criteria** Participants with:	**Interventions** Intervention (fractional Er:YAG laser): one side of the face received fractional ablative 2,940-nm Er:YAG laser (Fotona Xs Dynamics, Slovenia) laser. All participants received 5 treatment sessions at 1-month intervals. Comparator (microneedling): other side of the face received automated microneedling device (Derma stamp electric pen, Auto-Stamp Motorized Meso Machine,Model My-M). All participants received 5 treatment sessions at 1-month intervals. *Before the procedure, the face was cleansed with a mild cleanser. To relieve patient discomfort, 5% lidocaine cream (EMLA; AstraZeneca, UK) was applied to the treatment area and removed 1 hour later. The Er:YAG laser settings: fluence 250 to 300 mJ, 30 to 40 mm ablation depth, spot size 7 mm in diameter, MTZ density level of 2 to 3, and frequency 5 to 7 Hz. A protocol of 2-step pulse duration was used, short pulse duration (SP) and very long pulse duration, which produces balanced vaporization, coagulation, and thermal effects on the tissues. Three passes in vertical, horizontal, and oblique directions were	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Wilcoxon signed rank test was used to assess both improvements in scars and duration of complications, and paired T-test was used to assess collagen areas. **Intention-to-treat analysis** Not mentioned.	**Results** **Secondary outcomes** **Participant satisfaction with treatment** Satisfaction* with the treatment 3 months after the final treatment session (n/N): Excellent: Er:YAG laser group: 10/30 Microneedling group: 5/30 Good: Er:YAG laser group: 12/30 Microneedling group: 7/30 Fair: Er:YAG laser group: 6/30 Microneedling group: 12/30 Poor: Er:YAG laser group: 2/30 Microneedling group: 6/30 *Participant satisfaction was	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: some concerns (no information provided about randomisation and allocation concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
acne scars. **Study dates** Not reported **Source of funding** The authors have indicated no significant interest with commercial supporters.	• history of active herpes, • photosensitivity, • pregnant, • lactating, • with a previous history of hypertrophic or keloidal scarring, • the use of isotretinoin, • previous history of facial laser treatment, • surgical procedure within 6 months of study enrolment.	done over scar areas. The needle cartridge (containing 12 stainless steel needles) of the dermapen device was adjusted at 2 mm depth and speed level 2 and was applied over the skin with one hand while stretching the skin with the other hand so that the base of the scars could be reached. The device was moved back and forth in 4 directions (horizontally, vertically, and diagonally right and left) until uniform pinpoint bleeding was seen.		graded on a 4-point scale and recorded 3 months after the final session. Side effects (not clear if investigator or participant reported): Post-inflammatory hyperpigmentation (n/N): Er:YAG laser group: 1/30 Microneedling group: 0/30 Treatment-associated pain* (mean (SD)): Er:YAG laser group: 4.27 (1.61) Microneedling group: 6.6 (1.67) *Pain was assessed using a 10-point pain scale (0 = no pain to 10 = severe pain), and a mean value for the 5 sessions of each treated side was calculated.	

Full citation
 	
Reinholz, M., Schwaiger, H., Heppt, M. V., Poetschke, J., Tietze, J., Epple, A., Ruzicka, T., Kaudewitz, P., Gauglitz, G. G., Comparison of Two Kinds of Lasers in the Treatment of Acne Scars, Facial plastic surgery: FPS,
	Sample size
	N=14
	
	Characteristics
	Mean age (years)- mean (SD): 28.6 (9.2);
	n=9 men; n=5 women;
	skin type: II=4; III=6; IV=4;
	ethnicity: Caucasian=13,
		Interventions
		Intervention (2,940-nm Er:YAG laser):
		one side of the face received a Er:YAG laser treatment (MCL 30 Dermablate Er:YAG laser by Asclepion Laser Technologies GmbH (Jena, Germany)) classed as a class 4 laser with a pulse energy of up to 1.5 J. For the treatment a fluence of 108 J/cm2 was used; only one pass was delivered.
			Details
			Power Analysis
			Not mentioned.
			Statistical Analyses
			Statistical significance of the results was calculated with the student's t-test. Data with a Gaussian distribution were analysed using an
				Results
				Primary outcomes
				Improvement in scarring - investigator assessed
				Mean (SD) scar depth* (mm) at baseline:
				Er:YAG laser group =
					Limitations
					Cochrance RoB Tool v2.0
					Selection bias: some concerns (no sufficient information provided about randomisation and allocation

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
31, 523-531, 2015 **Ref Id** 1048508 **Country/ies where the study was carried out** Germany **Study type** split-face RCT **Aim of the study** To evaluate subjective and objective therapeutic results of acne scar treatment with a fractional Er:YAG (2,940 nm) and a fractional CO2 laser (10,600 nm) in a split-face approach at maximum energy. **Study dates** Not reported **Source of funding** The lasers were provided by Asclepion Laser Technologies GmbH (Jena, Germany).	Asian=1; all had severe scars **Inclusion criteria** Participants: • suffering from severe atrophic acne scars (rolling scars, ice pick scars, boxcar scars) • atrophic acne scars in comparable severity on both cheeks • over 18 years old • atrophic acne scars medium to severe • nonactive acne visible, no oral isotretinoin for at least 6 months • no active skin infections in the respective area • no history of keloids or hypertrophic scarring • female participants: no pregnancy • no participation in any other studies **Exclusion criteria** Not reported	Treatment was given 4 times every 4 weeks. Fractional ablative laser. Comparator (10,600-nm CO2 laser): another side of the face received a CO2 laser treatment, the MultiPulse by Asclepion Laser Technologies GmbH (Jena, Germany) classed as a class 4 laser with a wavelength of 10,600 nm. The default settings were: strong fractional mode; energy: 25 W (maximum energy); pitch: 500 µm; and dwell: 1,500 µs. The area (approximately 12 cm2) was treated in its entirety with only one passage. Treatment was given 4 times every 4 weeks. Fractional ablative laser.	unpaired t-test and non-parametric data with the Wilcoxon test for matched pairs. Correlation analysis was performed with linear regression with the R2 test. **Intention-to-treat analysis** Not mentioned.	1.87 (0.73) CO2 group = 2.02 (0.83) Mean (SD) scar depth* (mm) 4 weeks after the last treatment: Er:YAG laser group = 1.59 (0.73) CO2 group = 1.48 (0.74) Mean (SD) scar depth* (mm) change** 4 weeks after the last treatment: Er:YAG laser group = -0.28 (0.52) CO2 group = -0.54 (0.56) *Scar depth was evaluated using PRIMOS (Canfield; Fairfield, New Jersey, United States) 3D Imaging and digital photography. **calculated by the NGA technical team. **Secondary outcomes** **Satisfaction with treatment - participant and observer assessed** Mean (SD) POSAS score*** at baseline:	sequence) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Er:YAG laser group = 5.9 (0.3) CO2 group = 5.8 (0.3) Mean (SD) POSAS score*** at 4 weeks after the last treatment: Er:YAG laser group = 4.8 (0.3) CO2 group = 3.9 (0.3) Mean (SD) change** in POSAS score*** at 4 weeks after the last treatment: Er:YAG laser group = -1.1 (0.21) CO2 group = -1.9 (0.21) ***Assessed using the "Patient and Observer Scar Assessment Scale" (POSAS), which is as validated scar assessment scale, divided into the 2 sections of patient and observer, and provides a comprehensive estimation of the aesthetic outcome. Both scales contain 6 items rated on a 10-point scale from 0 (patient is not affected) to 10, as well as an extra category "overall opinion" that is rated	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				likewise. It covers features such as vascularity, pigmentation disorders, thickness, relief/texture, pliability, and surface area of the scars as well as scar related symptoms like pain and pruritus. **calculated by the NGA technical team. <u>Side effects (participant reported):</u> <u>Erythema (3 days after treatment):</u> Er:YAG laser group = 14/14 CO2 group = 14/14 <u>Incrustation/scab formation:</u> Er:YAG laser group = 2/14 CO2 group = 5/14 <u>Treatment-associated pain* (participant reported; mean (SD)):</u> Er:YAG laser group = 3.9 (2.3) CO2 group = 5.0 (2.2) *Pain during the treatment was evaluated with a visual analog scale (VAS) for pain, a 10-point rating scale from 0 to 10.	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Rongsaard, N., Rummaneethorn, P., Comparison of a fractional bipolar radiofrequency device and a fractional erbium-doped glass 1,550-nm device for the treatment of atrophic acne scars: a randomized split-face clinical study, Dermatologic SurgeryDermatol Surg, 40, 14-21, 2014 **Ref Id** 870091 **Country/ies where the study was carried out** Thailand **Study type** split-face RCT **Aim of the study** To compare the clinical effectiveness and side effects of the fractional bipolar RF device with those of the fractional erbium-doped glass 1,550-nm device for the treatment of atrophic acne scars.	**Sample size** N=20 but n=19 analysed in radiofrequency group **Characteristics** Age 18-55 years; n=12 men; n=8 women; Fitzpatrick skin types: type III = 14, type IV = 2, type V = 3 **Inclusion criteria** Participants with: • Fitzpatrick skin types III -V, • atrophic acne scars on both cheeks **Exclusion criteria** Participants: • pregnant, • lactating, • photosensitivity, • electrical implantation, • immunocompromise, history of deep chemical peeling or laser resurfacing, • botulinum toxin or filler injection in the previous 6 months,	**Interventions** Intervention (radiofrequency): 1 side of the face received the fractional bipolar radiofrequency (RF) device (eMatrix, Syneron, Haifa, Israel) with 64-electrode-pin disposable tips was Program C (53 - 59 mJ/pin for 2 passes). 3 treatment sessions were done at 4-week intervals. Comparator (erbium-doped glass laser): the other side of the face received the fractional erbium-doped glass 1550-nm device (Fraxel re:store DUAL1550/1927, Solta Medical, Hayward, CA) with energy settings ranged from 30 - 50 mJ/MTZ, with treatment levels 4 - 5 for 8 passes. 3 treatment sessions were done at 4-week intervals.	**Details** **Power Analysis** The sample size of 20 participants would have had 80%power to detect an effect size between 2 time points of 0.89. **Statistical Analyses** Paired samples t-test was used to compare the effectiveness and side effects of the two treatment devices. **Intention-to-treat analysis** Not mentioned.	**Results** **Secondary outcomes** **Patient satisfaction with treatment** Satisfaction* with treatment 1 month after the last treatment section: Moderateley satisfied: Radiofrequency group: 6/19 Erbium-doped glass laser: 5/20 Very satisfied: Radiofrequency group: 10/19 Erbium-doped glass laser: 13/20 Most satisfied: Radiofrequency group: 3/19 Erbium-doped glass laser: 1/20 *Satisfaction with the treatment was evaluated using a grading scale: 0=dissatisfied, 1=less satisfied, 2=moderately satisfied, 3=very satisfied, 4=most satisfied Side effects Erythema: Radiofrequency group: 0/19 Erbium-doped glass	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: low risk of bias Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias (1 participant withdrew from the study because he developed side effects in the form of prolonged dyspigmentation, which became evident after the 2nd treatment session and negatively affected his professional life) Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: low risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates Not reported **Source of funding** The authors have indicated no significant interest with commercial supporters.	• history of hypertrophic scars and keloids, • use of isotretinoin within 6 months, • allergy to anaesthesia, • active inflammatory skin disease or pre-malignant and malignant lesions in the treatment area, • history of herpes simplex or herpes zoster on the face			laser: 1/20 Treatment-associated pain* (mean (SD)): Radiofrequency group: 5.9 (1.21) Erbium-doped glass laser: 7.75 (1.37) *Pain was assessed using a scale (0, no pain to 10, the most pain).	
Full citation Sage, R. J., Lopiccolo, M. C., Liu, A., Mahmoud, B. H., Tierney, E. P., Kouba, D. J., Subcuticular incision versus naturally sourced porcine collagen filler for acne scars: a randomized split-face comparison, Dermatologic SurgeryDermatol Surg, 37, 426-31, 2011 **Ref Id** 870127 **Country/ies where the study was carried out** USA **Study type** split-face RCT	**Sample size** N=10 but analysed n=9 at 3-month follow-up visit and n=10 at the 6-month follow-up visit **Characteristics** Mean age (years)- mean (range): 50 (33-65); skin types II–V; n=6 Caucasians, n=1 Middle-Eastern, n=1 Hispanic, n=1 Asian, n=1 African-American **Inclusion criteria** Participants: • aged 18+ • with approximately symmetric depressed and rolling types of	**Interventions** Intervention (subcision): one half of the face received subcision using an 18-gauge Nokor subcision needle (Becton Dickinson & Co, Franklin Lakes, NJ) for a single session. Comparator (collagen filler): the other half was received an injection with the naturally sourced porcine collagen (NSPC) filler using the supplied 0.5 mL 27-gauge prepackaged syringe to the base of the depressed scars for a single session. *After participants washed their faces, treatment areas were marked with a sterile marking pen. A thick layer of topical lidocaine 30% gel was applied to all treatment areas, occluded with plastic wrap, and left to sit for 1 hour, then the treatment sites were cleansed with chlorhexidine 4% solution.	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Wilcoxon matched-pairs signed-ranks test was used to compare treatment groups and the paired t-test to compare the composite scores of the treatment groups. **Intention-to-treat analysis** Not mentioned.	**Results** **Secondary outcomes** Side effects (investigator reported): Post-inflammatory dyspigmentation (1 week after treatment): Subcision group = 0/9 Collagen filler group = 0/9	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: low risk of bias (although randomisation was done by flipping a coin) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias (all 10 participants completed the 1-week post-procedure follow-up visit, however 9/10

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To determine whether the newly approved NSPC filler could provide better efficacy and patient satisfaction and fewer adverse effects than subcision in the treatment of depressed and rolling types of acne scars. **Study dates** Not reported **Source of funding** The authors have indicated no significant interest with commercial supporters.	acne scars. **Exclusion criteria** Participants with: • active or unstable acne, • ice-pick or boxcar type scarring, • history of isotretinoin therapy within the last 6 months, • history of prior resurfacing or cosmetic procedure within the last 6 months				completed the 3-month follow-up visit and all 10 completed the 6-month follow-up visit) Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: low risk of bias
Full citation Tanzi, E. L., Alster, T. S., Comparison of a 1450-nm diode laser and a 1320-nm Nd:YAG laser in the treatment of atrophic facial scars: a prospective clinical and histologic study, Dermatologic SurgeryDermatol Surg, 30, 152-7, 2004 **Ref Id**	**Sample size** N=20 **Characteristics** Mean age (years) - 36.7; no other details provided **Inclusion criteria** Participants with: • mild to moderate	**Interventions** Intervention (1320-nm Nd:YAG laser): 1 facial half received treatment with a 1320-nm Nd:YAG laser (CoolTouch; CoolTouch Corp., Auburn, CA). The 1320-nm Nd:YAG laser applied fluences ranging 12 to 17 J/cm² (average of 14.8 J/cm²) through a 10-mm spot size for 2 passes over the treatment area. Each participant received 3 laser treatments by a single operator (ELT) using an identical laser technique at 4-week intervals. Comparator (1450-nm diode laser): the other half received treatment with a	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Student's t-test was used to compare the difference in roughness average values at baseline with follow-up visits in both 1320-nm Nd:YAG and 1450-nm diode laser-treated areas. **Intention-to-treat analysis** Not mentioned.	**Results** **Secondary outcomes** Side effects: Post-treatment erythema (6 hrs after treatment with 1320-nm Nd:YAG laser and 24 hrs after treatment with 1450-nm diode laser): 1320-nm Nd:YAG laser group = 20/20 1450-nm diode laser group = 20/20	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: some concerns (no sufficient information provided about the randomisation and allocation concealment) Performance bias: low risk of bias (blinding of participants and

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
870381 **Country/ies where the study was carried out** USA **Study type** split-face RCT **Aim of the study** To report the long-term clinical and histologic results of two different nonablative, midinfrared laser systems on atrophic facial acne scars. **Study dates** Not reported **Source of funding** Supported by the ASDS Cutting Edge research grant programme.	atrophic facial scars; • skin phototype V **Exclusion criteria** Participants with: • history of isotretinoin use, • dermabrasion, • phenol peel, • temporary filler (for example collagen, fat) injections within 3 years, • any prior history of injectable silicone or other permanent fillers in the facial areas	1450-nm midinfrared diode laser (SmoothBeam; Candela Corp., Wayland, MA). The 1450-nm diode laser was used at fluences ranging 9 to 14 J/cm² through a 6-mm spot size in a single non-overlapping pass. Each participant received 3 laser treatments by a single operator (ELT) using an identical laser technique at 4-week intervals. *Topical anesthetic cream (ELA-Max 5 Ferndale Laboratories, Inc., Ferndale, MI) was applied to the treatment areas for 20 to 30 minutes and then completely removed from the skin with water-soaked gauze before each laser procedure.		Post-inflammatory hyperpigmentation after treatment: 1320-nm Nd:YAG laser group = 2/20 1450-nm diode laser group = 4/20 Hypopigmentation: 1320-nm Nd:YAG laser group = 0 1450-nm diode laser group = 0 Hypertropic scarring 1320-nm Nd:YAG laser group = 0 1450-nm diode laser group = 0	personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns
Full citation Zhang, Z., Fei, Y., Chen, X., Lu, W., Chen, J., Comparison of a fractional microplasma radio frequency technology and carbon dioxide fractional laser for the treatment of atrophic acne scars: a randomized split-	**Sample size** N=33 **Characteristics** Mean age (years)- mean (SD): 26.4 (3.7) n=19 men, n=14 women; Fitzpatrick skin types III and IV	**Interventions** Intervention (fractional micro-plasma radiofrequency): one half of the face received treatment with a fractional micro-plasma radiofrequency (RF) device (Accent; Alma Lasers, Caesarea, Israel). 4 passes of the roller tip at 50 ro 60 W. All participants received 3 treatment sessions at intervals of 6 to 12 (average 8) weeks.	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Mann-Whitney test was used for comparison between two lasers and Wilcoxon signed rank test for comparison of before and after laser	**Results** **Primary outcomes** **Improvement in scarring - investigator assessed** Mean (SD) ECCA scores*at baseline: Fractional micro-plasma RF group:	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: some concerns (no sufficient information provided about the randomisation and allocation

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
face clinical study, Dermatologic SurgeryDermatol Surg, 39, 559-66, 2013 **Ref Id** 870709 **Country/ies where the study was carried out** China **Study type** split-face RCT **Aim of the study** To determine whether fractional microplasma RF could provide better efficacy and patient satisfaction and fewer adverse effects than CO2 FS in the treatment of atrophic facial acne scars in Asians. **Study dates** Not reported **Source of funding** The authors have indicated no significant interest with commercial supporters.	**Inclusion criteria** Participants with mild to severe atrophic acne scars on both sides of the face. **Exclusion criteria** Participants: • pregnant; • breastfeeding; • history of keloid tendency; • immunosuppression; photosensitivity or current use of photosensitive medication; • oral isotretinoin use in the preceding 6 months; • use of topical retinoids in the preceding 2 weeks; • active dermatitis; infection or malignancy over the treatment area; • having received light source, radiofrequency , or laser skin resurfacing treatments in the 6 months before the study.	Comparator (CO2 laser): the other half of the face received treatment with a CO2 fractional laser system (FS) (10600-nm Ultrapulse Encore; Lumenis Inc., SantaClara,CA)with 20 to 25mJ, density, 2 to 4 (10% - 20% coverage/cm² per pass), 300 Hz, using the Deep FX mode and 1 pass without overlapping. All participants received 3 treatment sessions at intervals of 6 to 12 (average 8) weeks. *For local anaesthesia, after the face was cleansed with a mild soap and 70% alcohol, a topical eutectic mixture of 2.5% lidocaine hydrochloric acid and 2.5% prilocaine (Beijing Ziguang MedicationManufacture Corporation Ltd, Beijing, China) was applied to the entire face under occlusion 1 hour before the therapy.	treatments. **Intention-to-treat analysis** Not mentioned.	51.1 (14.2) CO2 laser group: 48.8 (15.1) Mean (SD) ECCA scores* 6 months after the final treatment: Fractional micro-plasma RF group: 22.3 (8.6) CO2 laser group: 19.9 (7.9) Mean (SD) change in ECCA scores* 6 months after the final treatment: Fractional micro-plasma RF group: -28.8 (9.61) CO2 laser group: -28.9 (10.56) *ECCA (Clinical Evaluation Scale for Acne Scarrings) cores were calculated to compare treatment-associated changes. **Secondary outcomes** Patient satisfaction with the treatment Very satisfied/satisfied (n/N): Fractional micro-plasma RF group: 22/33 CO2 laser group:	concealment) Performance bias: low risk of bias (blinding of participants and personnel was not feasible for this study) Attrition bias: low risk of bias Detection bias: low risk of bias Reporting bias: low risk of bias Other bias Overall risk of bias: some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				20/33 Slightly satisfied (n/N): Fractional micro-plasma RF group: 9/33 CO2 laser group: 10/33 Unsatisfied (n/N): Fractional micro-plasma RF group: 2/33 CO2 laser group: 3/33 *the overall level of satisfaction was measured as follows: very satisfied, satisfied, slightly satisfied, or unsatisfied, with separate evaluations of each side of the face. Side effects (participant reported) Post-inflammatory pigmentation: Fractional micro-plasma RF group: 0/33 CO2 laser group: 12/33	

Table 8: Evidence table for parallel-group studies

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Ahmed, R., Mohammed, G., Ismail, N., Elakhras, A., Randomized clinical trial of CO2 LASER pinpoint irradiation technique versus chemical reconstruction of skin scars (CROSS) in treating ice pick acne scars, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 16, 8-13, 2014 **Ref Id** 867855 **Country/ies where the study was carried out** Egypt **Study type** Randomised controlled trial **Aim of the study** To compare the use of a pinpoint irradiation technique versus TCA CROSS in treating ice pick acne scars. **Study dates**	**Sample size** N=28 (20 females and 8 males) TCA CROSS: n=14 CO_2 laser: n=14 **Characteristics** <u>Mean age (years)- mean (±SD)</u> TCA CROSS: 23.7 (3.94) CO_2 laser: 27.4 (4.1) Mean overall age: 22.7 (8.4) <u>Fitzpatrick skin photo types-Type II- number (%)</u> TCA CROSS: 1/14 (7.3) CO_2 laser: 2/14 (14.2) <u>Fitzpatrick skin photo types-Type III- number (%)</u> TCA CROSS: 7/14 (50) CO_2 laser: 6/14 (42.8) <u>Fitzpatrick skin photo types-Type IV- number (%)</u> TCA CROSS: 4/14 (28.5) CO_2 laser: 5/14 (35.7)	**Interventions** TCA CROSS: ice pick acne scars were prepped and treated with 100% TCA focally applied by pressing hard on the entire depressed area of atrophic acne scars using a toothpick, targeting the pit of each scar by stretching the skin. The skin was kept stretched and monitored carefully until a refrigerator ' frosted ' appearance after a single application wass seen. CO_2 laser: ice pick acne scars were prepped (cleaned with soap, water, and degreasing acetone) and irradiated using a single spot hand piece, targeting the pit of each scar by stretching the skin. Investigators started on the forehead and proceeded down the rest of the face. *Participants were initially primed for 2 weeks with 0.5-1g Retin-A cream at night and a sunscreen containing avobenzone, octinoxate, and 2-4% Eldoquin Forte in the morning before starting either interventions. *In both treatments there were four sessions at 3-week intervals, and 6 months of follow-up.	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Chi square was used to compare categorical variables and paired t-test was used to compare numerical variables. The results are statistically significant if p<0.05. **Intention-to-treat analysis** Not mentioned.	**Results** **<u>Primary outcomes</u>** **Improvement in scarring-Investigator assessed** <u>Percent of scar reduction- Excellent (>70% improvement)-Investigator-assessed improvement (%)</u> TCA CROSS: 0 CO_2 laser: 0 <u>Percent of scar reduction- Good (51-70% improvement)-Investigator-assessed improvement (%)</u> TCA CROSS: [3/14] 21% CO_2 laser: [5/14] 36% <u>Percent of scar reduction- Fair (30-50% improvement)-Investigator-assessed improvement (%)</u> TCA CROSS: [7/14] 50% CO_2 laser: [6/14]	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: Some concerns (computer based randomisation) Performance bias: Some concerns (blinding of participants and personnel was not feasible for this study) Attrition bias: Low risk of bias (high retention and no reported loss to follow up) Detection bias: Low risk of bias (evaluation and assessment of results by photography) Reporting bias: Some concerns (assessment from published study report- no trial protocol reported) Other bias: No

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Not mentioned. **Source of funding** Not mentioned.	Fitzpatrick skin photo types-Type V- number (%) TCA CROSS: 2/14 (14.2) CO_2 laser: 1/14 (7.3) Acne scar severity index at baseline- Mild (1-25)- % TCA CROSS: 0 CO_2 laser: 0 Acne scar severity index at baseline- Moderate (26-50)- % TCA CROSS: 21.4% CO_2 laser: 0 Acne scar severity index at baseline- Severe (>50)- % TCA CROSS: 78.6% CO_2 laser: 100% **Inclusion criteria** • People with predominately ice pick acne scarring. **Exclusion criteria** Participants with: • Active inflammatory lesions; • Keloidal tendancy;			42.3% Percent of scar reduction- Poor (<30% improvement)-Investigator-assessed improvement (%) TCA CROSS: [4/14] 29% CO_2 laser: [3/14] 22% **Secondary outcomes** **Participant satisfaction with treatment** Participant satisfaction at the end of the treatments- Well (%) TCA CROSS: [9/14] 64.2% CO_2 laser: [12/14] 86% Participant satisfaction at the end of the treatments- Fair (%) TCA CROSS: [4/14] 28.5% CO_2 laser: [2/14] 14.3% Participant satisfaction at the end of the treatments- Poor (%)	other bias detected Overall bias: Some concerns Results reported at follow-up, 6 months after last treatment.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Immunosuppression; • Filler injections within the preceding 6-12 months; • Infections such as herpes labialis, • Those on systemic isotretinoin.			TCA CROSS: [1/14] 7.3% CO_2 laser: [0/14] 0% **Side effects** No complications- number (%) TCA CROSS: 0 CO_2 laser: 5/14 (35.7) Persistent swelling- number (%) TCA CROSS: 0 CO_2 laser: 0 Temporary post procedure hypo-pigmentation- number (%) TCA CROSS: 0 CO_2 laser: 0 Temporary post procedure hyper-pigmentation- number (%) TCA CROSS: 9/14 (64.2) CO_2 laser: 2/14 (14.2) Infection- number (%)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				TCA CROSS: 6/14 (42.8) CO_2 laser: 2/14 (14.2) Itching (picking at scabs)- number (%) TCA CROSS: 1/14 (7.1) CO_2 laser: 0 Contact dermatitis- number (%) TCA CROSS: 0 CO_2 laser: 0	
Full citation Anupama, Y. G., Wahab, A. J., Effectiveness of CO₂ laser with subcision in patients with acne scars, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 18, 367-371, 2016 **Ref Id** 867935 **Country/ies where the study was carried out** India	**Sample size** N=50 (n=44 analysed) Subcision followed by CO_2 laser: n=25 (n=23 analysed) CO_2 laser only: n=25 (n=21 analysed) **Characteristics** Age (years)- Mean (range): Overall: 21 (20-25) Type of acne scars- Ice pick-number	**Interventions** Subcision + CO_2 laser: • Subcision done using a 24-gauge needle one day before laser therapy. • CO_2 laser (Ultra CO_2, HM-30) was cleansed and degreased with acetone. • A thick film of topical anaesthesia (eutectic mixture of lignocaine 2% and prilocaine 2% cream) was pplied and left for 30-45 minutes. • Treatment started from 3W in	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Not mentioned. **Intention-to-treat Analysis** Not mentioned.	**Results** **Primary outcomes** **Improvement in scarring- investigator assessed** Assessment of scarring at end of treatment- Grade 4- Number (%) Subcision + CO_2 laser: 4/23 (17.3) CO_2 laser: 2/21 (9.5) Assessment of	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: Some concerns (there are no details provided) Performance bias: Some concerns (there are no details provided) Attrition bias: Low risk of bias (high retention and low loss to follow-up

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study type Randomised controlled trial. **Aim of the study** To study the effectiveness and side effects of CO_2 laser with subcision in patients with atrophic acne scars. **Study dates** Not mentioned. **Source of funding** Not mentioned.	Subcision + CO_2 laser: 5/25 CO_2 laser: 4/25 Type of acne scars- Boxcar-number Subcision + CO_2 laser: 4/25 CO_2 laser: 9/25 Type of acne scars- Rolled-number Subcision + CO_2 laser: 4/25 CO_2 laser: 3/25 Type of acne scars- Mixed-number Subcision + CO_2 laser: 12/25 CO_2 laser: 9/25 Assessment of scarring at baseline- Grade 4 Subcision + CO_2 laser: 4/25 CO_2 laser: 2/25 Assessment of scarring at baseline- Grade 3 Subcision + CO_2 laser: 16/25 CO_2 laser: 20/25 Assessment of scarring at baseline- Grade 2	the ultra-pulsed mode along the edge of the scar and at the centre. If required, one more pass was made along the edge of the scar. CO_2 laser only: • CO_2 laser (Ultra CO_2, HM-30) was cleansed and degreased with acetone. • A thick film of topical anaesthesia (eutectic mixture of lignocaine 2% and prilocaine 2% cream) was pplied and left for 30-45 minutes. • Treatment started from 3W in the ultra-pulsed mode along the edge of the scar and at the centre. If required, one more pass was made along the edge of the scar. *Each participant received four sessions at 4 week intervals.		scarring at end of treatment- Grade 3-Number (%) Subcision + CO_2 laser: 14/23 (60.9) CO_2 laser: 16/21 (76.2) Assessment of scarring at end of treatment- Grade 2-Number (%) Subcision + CO_2 laser: 5/23 (21.7) CO_2 laser: 3/21 (14.3) **Secondary outcomes** **Participant Satisfaction with treatment** Participant satisfaction level-Excellent- Number (%) Subcision + CO_2 laser: 16/23 CO_2 laser: 8/21 Participant satisfaction level- Good-Number (%)	(12%)) Detection bias: Low risk of bias (assessment of outcomes by digital photographs and graded using Goodman and Baron grading system) Reporting bias: Some concerns (there are no details provided) Other bias: No other bias detected Overall bias: Some concerns Acne was graded by the Goodman and Baron scale. Participant satisfaction: improvement in scars was measured on a 10-point scale. Questions were asked on occurrence of new acne lesions, side effects, improvement in

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Subcision + CO_2 laser: 5/25 CO_2 laser: 3/25 **Inclusion criteria** • Atrophic facial acne scars; • Grade -2 to -4 atrophic scarring as assessed clinically by the Goodman and Baron grading system (mild to severe atrophic acne scars). **Exclusion criteria** • Intake of isotretinoin in the past six months; • Intake of acne-inducing drug; • Active acne; • Keloidal tendency; • Herpes labialis; • Pregnancy; • Lactation; • Unrealistic expectations;			Subcision + CO_2 laser: 4/23 CO_2 laser: 8/21 <u>Participant satisfaction level- Poor- Number (%)</u> Subcision + CO_2 laser: 3/23 CO_2 laser: 5/21	depth of scars, skin texture and complexion and each given 2 points. Rating above 6 was graded as "excellent response," rating between 4 and 6 as "good response," and rating below 4 as "poor response." Results reported 4 weeks after last treatment

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• History of facial surgery or procedure for scars.				
Full citation Asilian, A., Salimi, E., Faghihi, G., Dehghani, F., Tajmirriahi, N., Hosseini, S. M., Comparison of Q-Switched 1064-nm Nd: YAG laser and fractional CO2 laser efficacies on improvement of atrophic facial acne scar, Journal of research in medical sciences, 16, 1189-95, 2011 **Ref Id** 867956 **Country/ies where the study was carried out** Iran **Study type** Randomised controlled trial. **Aim of the study** To compare the efficacy of Q-switched 1064-nm Nd: YAG laser and that of fractional CO_2 laser in the treatment of patients with moderate to severe acne scarring.	**Sample size** N=64 Nd:YAG laser: n=32 CO_2 laser: n=32 **Characteristics** Mean age (years)- Mean (±SD) Nd:YAG laser: 26.3 (5.5) CO_2 laser: 26.9 (5.8) Gender- Male- Number (%) Nd:YAG laser: 10/32 (31%) CO_2 laser: 10/32 (31%) Gender- Female- Number (%) Nd:YAG laser: 22/32 (69%) CO_2 laser: 22/32 (69%) **Inclusion criteria** • Any type of moderate to severe facial atrophic acne scar (rolling, boxcar, ice	**Interventions** Nd:YAG laser: A 1064-nm Q-switched Nd: YAG laser (Venus 3, Input Voltage 22v/50Hz, April 2003, Korea) was used with an average fluence of 2.5 J/cm^2, spot size: 7 mm. A total of 4 treatments at 4-week intervals were administered (3 pass in every session). CO_2 laser: A fractional CO_2 laser (Pixel Alma 10600nm) was used. A 3-pass treatment was then performed using pulse width of 110 msec (on-time), 600 msec (off-time) and pulse duration of 350 µs. The diameter of each individual MTZ was 350 µm. A total of 4 treatments at 4-week intervals were administered (3 pass in every session). *Treatment for both interventions was given by a single operator. Participants were followed for 6 months after the last session. A total of 4 treatments at 4-week intervals were administered (3 pass in every session).	**Details** **Power analysis** No details provided. **Statistical analyses** The statistical analysis was done by SPSS for Windows software (SPSS Inc., Chicago, IL, USA, version 18.0) by using Chi-square, t-test, Man-Whitney and Kruskal-Wallis analyses. The significance level was set at P value of less than 0.05. **Intention-to-treat analysis** No details provided.	**Results** **Primary outcomes** **Improvement in scarring- investigator assessed** Clinical improvement at 6 months after the last treatment- Blinded investigators assessment- Mild- Number (%) Nd:YAG laser: 8/32 (25) CO_2 laser: 6/32 (18.8) p=0.06 Clinical improvement at 6 months after the last treatment- Blinded investigators assessment- Moderate- Number (%) Nd:YAG laser: 20/32 (62.5) CO_2 laser: 14/32 (43.8)	**Limitations** **Cochrane RoB v.2** Selection bias: Some concerns (the participants were divided into two different treatment groups, using a table of random numbers. There is no information about allocation concealment) Performance bias: Some concerns (there are no details provided) Attrition bias: Low risk of bias (high retention and no reported loss to follow up) Detection bias: Low risk of bias (assessments of the treatment areas using comparative photographs were performed by two

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates March 2009 to October 2010. **Source of funding** Not mentioned.	pick). **Exclusion criteria** • People with pregnancy; • Lactation; • History of keloid formation; • Immunosuppressant or isotretinoin use; • Filler substance injections; • Skin resurfacing by dermabrasion; • Lasers within the preceding 6 months.			p=0.06 <u>Clinical improvement at 6 months after the last treatment- Blinded investigators assessment- Good- Number (%)</u> Nd:YAG laser: 4/32 (12.5) CO_2 laser: 11/32 (34.4) p=0.06 <u>Clinical improvement at 6 months after the last treatment- Blinded investigators assessment- Excellent- Number (%)</u> Nd:YAG laser: 0 CO_2 laser: 1/32 (3.1) p=0.06 **Improvement in scarring- participant assessed** <u>Clinical improvement at 6 months after the last treatment- Participant assessment- Mild- Number (%)</u>	blinded dermatologists) Reporting bias: Some concerns (there are no details provided) Other bias: No other bias detected Overall bias: Some concerns The improvement of acne scars at 6 months was graded by a quartile grading scale: less than 25%: mild, 25% to 50%: moderate, 51% to 75%: good, and 76% to 100%: excellent response. Participant satisfaction (6 months), using satisfaction survey: mild = < 25%; moderate = 25% - 50%; good = 51% - 75%; excellent = 76% to 100%.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Nd:YAG laser: 8/32 (25) CO_2 laser: 4/32 (12.5) p=0.01 Clinical improvement at 6 months after the last treatment- Participant assessment- Moderate- Number (%) Nd:YAG laser: 21/32 (65.6) CO_2 laser: 16/32 (50) p=0.01 Clinical improvement at 6 months after the last treatment- Participant assessment- Good- Number (%) Nd:YAG laser: 3/32 (9.4) CO_2 laser: 11/32 (34.4) p=0.01 Clinical improvement at 6 months after the last treatment- Participant	Qualitative scarring grading system used.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				assessment- Excellent- Number (%) Nd:YAG laser: 0 CO_2 laser: 1/32 (3.1) p=0.01 **Secondary outcomes** **Side effects** Mild post-inflammatory hyperpigmentation- Number (%) Nd:YAG laser: 6/32 (19.6) CO_2 laser: 10/32 (31.2) *Participant satisfaction surveys reported at the end of the study	
Full citation Bhargava, S., Kroumpouzos, G., Varma, K., Kumar, U., Combination therapy using subcision, needling, and platelet-rich plasma in the management of grade 4 atrophic acne scars: A pilot study, Journal of Cosmetic Dermatology., 2019	**Sample size** N=30 Subcision + needling + PRP: n=15 Subcision + needling: n=15 **Characteristics**	**Interventions** Subcision + needling + PRP: • Subcision was performed using an 18-gauge needle. A modified technique was used, in which the needle is bent at 90° twice before the syringe is attached to it for better stability and ease to perform the procedure.	**Details** **Power Analysis** Not mentioned. **Statistical Analyses** Fisher's exact test used for statistical analysis of scar improvement and	**Results** **Primary outcomes** **Improvement in scarring- investigator assessed** Scar grading- Investigator	**Limitations** **Cochrane RoB v.2** Selection bias: Some concerns (no details provided. Quote "The patients were divided randomly

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 1047588 **Country/ies where the study was carried out** USA **Study type** Randomised controlled trial **Aim of the study** To evaluate the efficacy of PRP when combined with needling and subcision in severe (grade 4) atrophic acne scars. **Study dates** February 2017 and February 2018 **Source of funding** Not mentioned.	Mean age (years)- Mean [range] Subcision + needling + PRP: 28.2 [21-35] Subcision + needling: 27.1 [22-37] Gender- Female- Number Subcision + needling + PRP: 10/15 Subcision + needling: 9/15 Gender- Male- Number Subcision + needling + PRP: 5/15 Subcision + needling: 6/15 Fitzpatrick skin type- III- Number Subcision + needling + PRP: 2/15 Subcision + needling: 2/15 Fitzpatrick skin type- IV- Number Subcision + needling + PRP: 12/15 Subcision + needling: 11/15 Fitzpatrick skin type- V- Number	• Needling was performed using a dermaroller (1.5-mm needle size, 192 needles) that was rolled on the affected skin in vertical, horizontal, and diagonal directions until the appearance of uniform, fine pinpoint bleeding points. • Platelet-rich plasma was prepared under aseptic precautions using double-spin method in a laboratory centrifuge. Then, 2 mL of PRP was applied topically over the treated area. Subcision + needling: • Subcision was performed using an 18-gauge needle. A modified technique was used, in which the needle is bent at 90° twice before the syringe is attached to it for better stability and ease to perform the procedure. • Needling was performed using a dermaroller (1.5-mm needle size, 192 needles) that was rolled on the affected skin in vertical, horizontal, and diagonal directions until the appearance of uniform, fine pinpoint bleeding points. *Participants received three treatments at 3-week intervals. *For all participants, eutectic mixture of	chi-square test used for statistical analysis of scar grading. **Intention-to-treat Analysis** Not mentioned.	assessed- Level 4 (Goodman and Baron scale)- Number Subcision + needling + PRP: 0/15 Subcision + needling: 1/15 Scar grading- Investigator assessed- Level 3 (Goodman and Baron scale)- Number Subcision + needling + PRP: 10/15 Subcision + needling: 12/15 Scar grading- Investigator assessed- Level 2 (Goodman and Baron scale)- Number Subcision + needling + PRP: 5/15 Subcision + needling: 2/15 Improvement by two grades on Goodman and Baron scale- Number (%) Subcision + needling + PRP: 5/15	into two groups") Performance bias: Some concerns (no details provided) Attrition bias: Low risk of bias (high retention and no reported loss to follow up) Detection bias: Low risk of bias (scarring severity grading was evaluated by blinded dermatologists) Reporting bias: Some concerns (no details provided) Other bias: No other bias detected Overall bias: Some concerns All results were recorded 3 months after last treatment, at follow-up.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Subcision + needling + PRP: 1/15 Subcision + needling: 2/15 <u>Scar grading- Level 4 (Goodman and Baron scale)- Number</u> Subcision + needling + PRP: 15/15 Subcision + needling: 15/15 **Inclusion criteria** • Grade 4 atrophic scars as graded by Goodman and Baron (severe atrophic acne scars); • Aged 18 years and over. **Exclusion criteria** • Active herpes labialis; • Active acne; • History of keloid scars; • Bleeding disorder; • Pregnancy or lactation;	lignocaine 2% and prilocaine 2% cream was applied under occlusion over the affected areas for 1 hour before the procedure. *For all participants, cold compresses were applied for comfort and pain relief immediately after the procedure. They were also advised to apple a broad-spectrum, sunscreen daily for several weeks after the procedure.		Subcision + needling: 2/15 <u>Improvement by one grade on Goodman and Baron scale- Number (%)</u> Subcision + needling + PRP: 10/15 Subcision + needling: 12/15 <u>Improvement by no grades on Goodman and Baron scale- Number (%)</u> Subcision + needling + PRP: 0/15 Subcision + needling: 1/15 **<u>Secondary outcomes</u>** **Participant satisfaction with treatment** <u>Participant-rated scar grading- Poor (0-24% improvement)- Number</u> Subcision + needling + PRP: 0/15 Subcision + needling:	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• History of any facial surgery or procedure for scars; • People with HIV or hepatitis B; • Those with unrealistic expectations; • Those who had received treatment for acne or acne scars within 6 months before entry to study.			1/15 Participant-rated scar grading- Good (25-49% improvement)-Number Subcision + needling + PRP: 3/15 Subcision + needling: 9/15 Participant-rated scar grading- Very good (50-74% improvement)-Number Subcision + needling + PRP: 10/15 Subcision + needling: 4/15 Participant-rated scar grading- Excellent (75-100% improvement)-Number Subcision + needling + PRP: 2/15 Subcision + needling: 1/15	
Full citation Cachafeiro, T., Escobar, G., Maldonado, G., Cestari, T., Corleta, O., Comparison of	**Sample size** N=46 (42 analysed) Laser: n=22 (11 females, 11	**Interventions** Laser: nonablative fractional erbium laser ProDeep 1,340nm (Etheria/Industra platform) was performed with a 100	**Details** **Power Analysis** To detect a difference of	**Results** **Primary outcomes** **Improvement in**	**Limitations** **Cochrane RoB v.2**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Nonablative Fractional Erbium Laser 1,340 nm and Microneedling for the Treatment of Atrophic Acne Scars: A Randomized Clinical Trial, Dermatologic SurgeryDermatol Surg, 42, 232-41, 2016 **Ref Id** 868131 **Country/ies where the study was carried out** Brazil **Study type** Randomised controlled trial **Aim of the study** To compare the effectiveness and safety of nonablative fractional erbium laser 1,340 nm and microneedling for the treatment of facial atrophic acne scars. **Study dates** Not mentioned. **Source of funding**	males) Microneedling: n=20 (10 females, 10 males) **Characteristics** Mean age (years)- Mean (SE) Laser: 25.41 (8.77) Microneedling: 27.35 (10.72) Phototype- II- Number (%) Laser: 0 Microneedling: 1/20 (5) Phototype- III- Number (%) Laser: 15/22 (68.2) Microneedling: 14/20 (70) Phototype- IV- Number (%) Laser: 5/22 (27) Microneedling: 5/20 (25) Phototype- V- Number (%) Laser: 2/22 (9.1) Microneedling: 0 Average score on QGGSPS at baseline- Mean (SE) Laser: 15.82 (0.86) Microneedling: 14.9 (0.97)	microbeams per cm^2 in the whole face, followed by a second pass in the areas with the highest concentration of scars. The instrument was calibrated to use energy of 120 mJ per microbeam and 5-millisecond pulse duration. The parameters used were calculated so that it would be possible to reach a treatment coverage of 20% to 35%. Microneedling: Performed using a device containing 192 fine microneedles of 2mm(Dr. Roller/MTO Importer and Distributor). Approximately 20 passes in 4 different directions were applied to the face. After the procedure, the skin was cleaned with saline-soaked gauze. The microneedling device was thrown away after each session. *Before each session, topical anaesthetic (lidocaine cream 4%) was applied on the face 30 minutes before each treatment session. This was removed prior to treatment and skin was cleaned using an aqueous 2% chlorhexidine solution. *After each session, participants were instructed to avoid sun exposure and use sunscreen of at least SPF 30. *Participants of both groups were assigned to 3 sessions of laser treatment or 3 sessions of treatment with microneedling, performed monthly by the same dermatologist.	1 SD in the score between groups, assuming a power of 90% and an α error ≤0.05, a sample of 23 participants for each treatment group was necessary. **Statistical Analyses** Student t-test used for paired samples and the intraclass correlation coefficient. The generalized estimating equation (GEE) used to assess the difference in the degree of scarring (with the score established by the scale) before and after treatment and to compare the degree of pain. Post-treatment erythema was compared by the Mann–Whitney test. The χ2 test was used for the evaluation of other symptoms. The degree of improvement perceived by the participants was compared between both groups using the Student t-test. Data were processed	**scarring- investigator assessed** Change in score on QGGSPS from baseline, 6 months after treatment- Investigator assessed improvement- Mean (SD)* Laser: 3.41 (0.53) Microneedling: 4.05 (0.69) *For both interventions there was a difference of 3-5 points on the scale, which represents a clinically significant difference, according to information provided by the author of the scale. **Secondary outcomes** **Participant satisfaction with treatment** Number of participants who noted an improvement after the first treatment session- Number (%)	Selection bias: Some concerns (participants were allocated by simple drawing to one of the study groups through computer software) Performance bias: Some concerns (neither participants nor personnel were blinded since it was not feasible with study design) Attrition bias: Low risk of bias (high retention and no reported loss to follow up) Detection bias: Low risk of bias (two independent and blinded dermatologists applied the QGGSPS scale) Reporting bias: Some concerns (no details available) Other bias: No other bias detected Overall bias: Some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Funded by HCPA Research Fund (FIPE) and Capes. Materials (dermaroller) and equipment (Etherea laser) were donated byMTOImportadora e Distribuidora Industrie and Industra Industrie, respectively, for unrestricted use.	**Inclusion criteria** • Moderate to severe atrophic acne scars. **Exclusion criteria** • Personal history of photosensitivity or photosensitive diseases such as systemic lupus erythematosus and xeroderma pigmentosum; • History or presence of PIH; • Use of drugs that induce hyperpigmentation (such as amiodarone, clofazimine, minocycline, and chloroquine); • Presence of only ice pick acne scars; • Pregnancy or breast feeding; • Oral isotretinoin use in the last 6 months; • Facial surgical or laser treatment in the		using IBM SPSS 18.0 version software for statistical analysis and a 5% significance level was considered. **Intention-to-treat Analysis** Not mentioned.	Laser: 19/22 (86.4) Microneedling: 13/20 (65) Degree of improvement perceived by participants 6 months after treatment*- Mean (±SD) [SE] Laser: 7.95 (1.17) [0.25] Microneedling: 7.65 (1.92) [0.43] p=0.536 *Rated on a scale of 0 to 10. **Side effects** Degree of pain during treatment- Mean (SE) Laser: 6.18 (0.4) Microneedling: 5.72 (0.4)	Brazilian Portuguese Quantitative Global Grading System for Postacne Scarring Instrument (QGGSPS) applied to evaluate the degree of scars. This quantitative scale evaluates the type, number, and severity of scars attributing a value that ranges from 0 to 84. Participant satisfaction of treatment rated on scale from 0 to 10, where 0= max dissatisfaction, 10= max satisfaction

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	last 3 months; • Herpes infection, warts, or any other active skin infection in the treatment area; • Presence of skin cancer or actinic keratoses over the treatment area; • Coagulopathies or anticoagulant therapy; • Personal history or presence of hypertrophic scars or keloids; • People in chemotherapy, radiation therapy, or with high-dose of corticosteroids; • Diabetes mellitus; • Inability to understand the objectives and risks of treatment or people who refused to participate or to sign the consent form.				
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Chae, W. S., Seong, J. Y., Jung, H. N., Kong, S. H., Kim, M. H., Suh, H. S., Choi, Y. S., Comparative study on efficacy and safety of 1550 nm Er: Glass fractional laser and fractional radiofrequency microneedle device for facial atrophic acne scar, Journal of Cosmetic Dermatology, 14, 100-106, 2015 **Ref Id** 1047653 **Country/ies where the study was carried out** Korea **Study type** Randomised controlled trial **Aim of the study** To evaluate the clinical efficacy and safety of a Er:Glass fractional laser and fractional radiofrequency microneedle device in the treatment of facial atrophic acne scars and to assess the difference between the treatment modalities depending on facial compartment.	N=40 Laser: n=20 Microneedling: n=20 **Characteristics** Mean age (years)- Mean (±SD) Laser: 25.5 (3.76) Microneedling: 28.3 (5.39) Scar duration (years)- Mean Laser: 5.2 Microneedling: 8.9 Gender- Female- Number Laser: 7/20 Microneedling: 4/20 Gender- Male- Number Laser: 13/20 Microneedling: 16/20 Fitzpatrick skin type III- Number Laser: 3/20 Microneedling: 4/20 Fitzpatrick skin type IV- Number	Laser: 1550 nm Er:Glass fractional laser (FXL) witha Sellas apparatus (Dinona, Daejeon, Korea) at 4-week intervals. Intervention was performed on the basis of 500 MTZ/cm^2 and 15-20 mJ/MTZ energy level. Microneedling: fractional radiofrequency microneedle (FRM) utilising the Inskin device (Einsmed, Seongnam, Korea) at an intensity of 40 -60 W (maximum power 80 W, 2-mm-depth needle with 36 microneedle electrode tip)and 0.1 ms radiofrequency conduction time in the continuous wave mode. *For all participants, the face was washed with a mild cleanser and topical EMLA cream (eutectic mixture of 2.5% lidocaine HCL and 2.5% prilocaine) was applied to the entire face under occlusion 30–60 min prior to the treatment. *The face was sterilised with chlorhexidine 5% followed by alcohol before performing the treatment. *Each group of 20 participants received three treatments at 4-week interval	**Power analysis** Not mentioned. **Statistical analyses** Statistical Package for Social Sciences (SPSS version 19.0, SPSS Inc, Chicago, IL, USA) was used for all statistical analysis. Paired t-tests were used to evaluate ECCA grading scale between treatment sessions. Significance level was set at 0.05. **Intention-to-treat analysis** Not mentioned.	**Primary outcomes** **Improvement in scarring- investigator assessed** Acne scar improvement on ECCA grading scale after first treatment- Investigator assessed improvement- Mean (SD) Laser: 71.25 (24.7) Microneedling: 68.75 (27.9) Acne scar improvement on ECCA grading scale after second treatment- Investigator assessed improvement- Mean (SD) Laser: 66.75 (21.54) Microneedling: 65.75 (26.82) Acne scar improvement on ECCA grading scale after third treatment- Investigator assessed improvement- Mean (SD)	**Cochrane RoB v.2** Selection bias: Some concerns (no information provided. Quote: patients were equally randomised into two groups) Performance bias: Some concerns (blinding of participants and personnel was not feasible for this study) Attrition bias: Low risk of bias (high retention and no reported loss to follow up) Detection bias: Low risk of bias (two physicians who were not involved in treatment performed the scoring based on clinical images) Reporting bias: Some concerns (no trial protocol reported) Other bias: No other bias detected

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates September 2012 to March 2013 **Source of funding** No details provided	Laser: 14/20 Microneedling: 14/20 Fitzpatrick skin type V-Number Laser: 3/20 Microneedling: 2/20 **Inclusion criteria** • Health with no dermatologic or any other disorder, except for acne scars. **Exclusion criteria** • Participants who had received acne scar treatment during the prior 6 months; • Participants who are pregnant or lactating.			Laser: 55.50 (23.78) p<0.001 Microneedling: 56.00 (22.40) p<0.01 Evaluation of improvement using physician's global assessment 8 weeks after treatment- None (0%)- Number Laser: 1/20 Microneedling: 2/20 Evaluation of improvement using physician's global assessment 8 weeks after treatment- Slight (0-25%)- Number Laser: 3/20 Microneedling: 5/20 Evaluation of improvement using physician's global assessment 8 weeks after treatment- Average (26-50%)- Number Laser: 5/20 Microneedling: 5/20 Evaluation of	Overall bias: Some concerns 1. The échelle d'évaluation clinique des cicatrices d'acné (ECCA) grading scale system was used to score the severity of atrophic acne scars. 2. Improvement of acne scars (8 weeks), using a 5-point scale (1 = none, 0%; 2 = slight, 0% - 25%; 3 = average, 26% - 50%; 4 = good, 51% - 75%; 5 = very good, 76%

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				improvement using physician's global assessment 8 weeks after treatment- Good (51-75%)- Number Laser: 8/20 Microneedling: 7/20 Evaluation of improvement using physician's global assessment 8 weeks after treatment- Very good (76-100%)- Number Laser: 3/20 Microneedling: 1/20 **Secondary outcomes** **Participant satisfaction with treatment** Evaluation of improvement using patient's self-assessments of percentage of improvement 8 weeks after treatment- None (0%)- Number Laser: 1/20 Microneedling: 1/20	-100%) 3. Participant satisfaction (8 weeks), using 5-point scale of self-assessed participant satisfaction (1 = none, 0%; 2 = slight, 0% - 25%; 3 = average, 26% - 50%; 4 = good, 51% - 75%; 5 = very good, 76% - 100%)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Evaluation of improvement using patient's self-assessments of percentage of improvement 8 weeks after treatment- Slight (0-25%)- Number Laser: 4/20 Microneedling: 8/20 Evaluation of improvement using patient's self-assessments of percentage of improvement 8 weeks after treatment- Average (26-50%)- Number Laser: 8/20 Microneedling: 6/20 Evaluation of improvement using patient's self-assessments of percentage of improvement 8 weeks after treatment- Good (51-75%)- Number Laser: 5/20 Microneedling: 4/20	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Evaluation of improvement using patient's self-assessments of percentage of improvement 8 weeks after treatment- Very good (76-100%)- Number Laser: 2/20 Microneedling: 1/20 **Side effects**** Participant report of pain during treatment- VAS scale (0-10, where 10=worst pain)- Mean (SD) Laser: 5.55 (1.10) Microneedling: 4.70 (1.08) p<0.05 Participant report of temporary erythema (>5 days)- Number (%) Laser: 5/20 (25) Microneedling: 3/20 (15) Participant report of	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				temporary edema (>5 days)- Number (%) Laser: 3/20 Microneedling: 1/20 Participant report of temporary dryness (>5 days)- Number (%) Laser: 2/20 (10) Microneedling: 2/20 (10) Induction of acne vulgaris- Number (%) Laser: 2/20 Microneedling: 0/20 Temporary post-inflammatory hyperpigmentation- Number (%) Laser: 2/20 (10) Microneedling: 0/20 (0) **No reports of second infection or hypertrophic scars in either intervention group.** **All side effects measured 8 weeks	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				after the intervention.	
Full citation Erbagci, Z., Akcali, C., Biweekly serial glycolic acid peels vs. long-term daily use of topical low-strength glycolic acid in the treatment of atrophic acne scars, International Journal of DermatologyInt J Dermatol, 39, 789-94, 2000 **Ref Id** 868486 **Country/ies where the study was carried out** Turkey **Study type** Randomised controlled trial **Aim of the study** To determine the efficacy and tolerability of glycolic acid and to compare two different application regimens in the treatment of atrophic acne scars. **Study dates**	**Sample size** N= 58 women (n=48 analysed) Glycolic acid peel: n=23 (n=16 analysed) Glycolic acid cream: n=20 (n=18 analysed) Placebo: n=15 (n=14 analysed) **Characteristics** <u>Age (years)- Range</u> 18-41 years <u>Mean overall acne scar severity scores at baseline- reported on 10 point scale- Mean (range)</u> Glycolic acid peel: 5.312 (2 to 10) Glycolic acid cream: 4.88 (2 to 8) Placebo: 4.857 (2 to 8) p>0.05	**Interventions** Glycolic acid peel: performed biweekly in a gradual increase in time and concentration. Skin was cleaned twice using alcohol and acetone. Solutions of 20%, 35%, 50%, and 70% were applied for 2 minutes to the face. Exposure times were gradually increased by 2-3 minutes according to tolerance. At 4-5 minutes of tolerance, subsequent peels were performed at the higher concentration. Glycolic acid cream: 15% glycolic acid home-care product applied twice daily for 24 weeks. Placebo: base cream including the same vehicle as the glycolic acid cream, applied twice daily for 24 weeks. *Two weeks prior to enrolment and during the study period, participants were advised to avoid sun exposure and apply a sunscreen with a SPF of at least 45 when sun exposure was unavoidable. *The use of facial cosmetics, including perfumes, and the ingestion of potentially photosensitising agents were not allowed during the study period.	**Details** **Power analysis** No details provided. **Statistical analyses** Data were analysed using the nonparametric Wilcoxon signed rank sum test, Kruskal-Wallis analysis of variance, Mann-Whitney *U*-test, and χ^2 test. **Intention to treat analysis** No details provided.	**Results** **<u>Primary outcomes</u>** **Improvement in scarring- investigator assessed** <u>Overall response to intervention at end of treatment- Investigator assessed improvement- Good response- Number (%)</u> Glycolic acid peel: 6/16 (37.5) Glycolic acid cream: 0/18 (0) Placebo: 0/14 (0) <u>Overall response to intervention at end of treatment- Investigator assessed improvement- Partial response- Number (%)</u> Glycolic acid peel: 9/16 (56.25) Glycolic acid cream:	**Limitations** **Cochrane RoB v.2** Selection bias: Some concerns (no details provided other than participants being randomly divided into three groups) Performance bias: Some concerns (blinding of participants and personnel was not feasible for this study) Attrition bias: High risk of bias (48/58 participants (16 in group A, 18 in group B, 14 in group C) completed the study. 7 women from group A withdrew because they were unable to tolerate concentrations > 20% or 35% and contact times > 2 mins. 3 women (2 from group B and 1 from group C) were lost to follow-up)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
No details provided. **Source of funding** No details provided.	**Inclusion criteria** • Mild, moderate, and severe trophic acne scars. **Exclusion criteria** • Hypertrophic, depressed-fibrotic, and ice-pick scars or keloids; • Severe active inflammatory acne lesions; • Pregnancy; • Lactation; • A history of isotretinoin ingestion in the preceding 6 months; • Concomitant use of an oral contraceptive or any hormone preparation; • The presence of active herpes infection; • Concomitant serious systemic or skin disease;			13/18 (72.22) Placebo: 5/14 (35.71) <u>Overall response to intervention at end of treatment- Investigator assessed improvement- Minor response- Number (%)</u> Glycolic acid peel: 1/16 (6.25) Glycolic acid cream: 5/18 (27.77) Placebo: 6/14 (42.85) <u>Overall response to intervention at end of treatment- Investigator assessed improvement- No response- Number (%)</u> Glycolic acid peel: 0/16 (0) Glycolic acid cream: 0/18 (0) Placebo: 6/14 (42.85)	Detection bias: Low risk of bias (clinical assessments were conducted by an independent blind investigator) Reporting bias: Some concerns (no trial protocol reported) Other bias: No other bias detected Overall bias: High risk of bias Improvement of acne scars was measured using a 10-point scale as follows: 0 = No scar; 1 = very mild; 2 - 3 = mild; 4 - 7 = moderate; 8 - 9 = severe; 10 = very severe.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Depression and antidepressive therapy; • A history of hypertrophic scar or keloid.				
Full citation Leheta, T., El Tawdy, A., Abdel Hay, R., Farid, S., Percutaneous collagen induction versus full-concentration trichloroacetic acid in the treatment of atrophic acne scars, Dermatologic SurgeryDermatol Surg, 37, 207-16, 2011 **Ref Id** 869137 **Country/ies where the study was carried out** Egypt **Study type** Randomised controlled trial **Aim of the study** To compare the safety and efficacy of PCI and the 100% TCA CROSS method for the	**Sample size** N= 30 (27 analysed)- 14 females and 16 males PCI: n=15 TCA CROSS: n=15 (n=12 analysed) **Characteristics** <u>Mean age (years)- Mean (±SD)</u> PCI: 29.7 (7.3) TCA CROSS: 23.8 (5.8) **Inclusion criteria** • Participants with different types of atrophic acne scars (Acne scar severity means from 74 to 79 (3 points for deep, 2 points for shallow	**Interventions** PCI: • Local anaesthetic cream was applied to the face under occlusion for approximately 45 to 60 minutes before the procedure. • The face was sterilized with povidone-iodine and alcohol. • The needling tool Dermaroller MF 8 was used. It was rolled over the affected areas five times in four directions without pressing too hard. • Those with deep scars, had their skin stretched perpendicular to the Dermaroller movement to reach the base of the scar. • The skin bled for 30 seconds to 2 minutes, which was less than normal clotting time, and wet gauze swabs were used to soak up any fluid ooze.	**Details** **Power analysis** Not mentioned. **Statistical analyses** Data were coded and entered using SPSS version 17 (SPSS, Inc., Chicago, IL). Data were summarised using mean±standard deviations for quantitative variables and percentages for qualitative variables. Comparisons between groups were made usingnonparametric tests (for example, Mann-Whitney and Wilcoxon signed-rank tests). Correlation was done to test linear relation between quantitative variables. p≤.05 was considered statistically significant.	**Results** **<u>Primary outcomes</u>** **Improvement in scarring- Investigator assessed** <u>Overall scar severity score 4 weeks after last session- Investigator assessed improvement- Mean (±SD)</u> PCI: 25.2 (23.0) TCA CROSS: 19.7 (13.7) p=0.98 <u>Global response to treatment 4 weeks after last session- Investigator assessed improvement- Significant improvement- Number (%)</u>	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: Some concerns (no details provided) Performance bias: Some concerns (blinding of participants and personnel was not feasible for this study) Attrition bias: Low risk of bias (three participants received one session only and therefore were not analysed at the end of the study) Detection bias: Low risk of bias (the assessor was blinded to the intervention used)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
treatment of atrophic scars. **Study dates** No details provided **Source of funding** No details provided	and 1 point for superficial scars)). **Exclusion criteria** • Systemic retinoids or immunosuppressive drug intake during the previous 6 months; • Coagulation defects or blood diseases; • Evidence or history of keloid scars; • Pregnancy or lactation; • Unrealistic expectations.	TCA CROSS: • Skin was cleaned and degreased with acetone. • Wooden applicators tips were sized to a dull point approximately the size of the scars and used to apply 100% TCA. • Focal pressing by the applicator was maintained until an even white frosting formed in each scar. • Topical antibiotic cream and sunscreen were applied immediately after the procedure. Each participant received four sessions of treatment at 4-week intervals. Participants were instructed to minimise sun exposure, trauma, and tension at the scar site and to apply sunscreen daily with a sun protection factor of 50 or more. Participants in the TCA CROSS group were asked to apply antibiotic cream until focal crust formation and to avoid disturbing the crusts.	**Intention-to-treat analysis** Not mentioned.	PCI: 7 (46.7) TCA CROSS: 8 (66.7) Global response to treatment 4 weeks after last session- Investigator assessed improvement- Moderate improvement- Number (%) PCI: 5 (33.3) TCA CROSS: 3 (25) Global response to treatment 4 weeks after last session- Investigator assessed improvement- Mild improvement- Number (%) PCI: 2 (13.3) TCA CROSS: 1 (8.3) Global response to treatment 4 weeks after last session- Investigator assessed improvement- Minimal improvement- Number (%) PCI: 1 (6.7)	Reporting bias: Some concerns (assessment from published study report- no trial protocol reported) Other bias: No other bias detected Overall bias: Some concerns Global response to treatment was rated using a quartile grading scale (0, slight improvement, <25%; 1, moderate improvement, 25–49%; 2, significant improvement, 50–74%; 3, marked improvement, ≥75%). Pain was graded on a scale of 0 (none) to 9 (maximum).

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				TCA CROSS: 0 (0) p=0.25 **<u>Secondary outcomes</u>** **Side effects** <u>Participant report of pain on a 9 point pain scale- Mean (±SD)</u> PCI: 5.4 (1.9) TCA CROSS: 3.8 (1.6) p=0.03 <u>Transient post-inflammatory hyperpigmentation lasting 2 to 6 months-Number (%)</u> PCI: 0 (0) TCA CROSS: 6 (50)	
Full citation Leheta, T. M., Abdel Hay, R. M., Hegazy, R. A., El Garem, Y. F., Do combined alternating sessions of 1540 nm nonablative fractional laser and percutaneous collagen induction with trichloroacetic acid 20% show better results than each	**Sample size** N= 39 (N=38 analysed) PCI + TCA 20%: n=13 (n=1 lost to follow but analysed according to ITT) Laser: n=13 Alternating treatment of both:	**Interventions** <u>PCI + TCA 20%:</u> Received six sessions (4 weeks apart) of PCI, using the Dermaroller® (model MF8) by rolling it over acne scars areas, five times in four directions, combined with TCA 20% in the same session using 4 x 4 gauze until frosting occurred. <u>Laser:</u> Received six sessions (4 weeks	**Details** **Power analysis** Not mentioned. **Statistical analyses** Comparisons between groups were done using T-test (with 95%	**Results** **<u>Primary outcomes</u>** **Improvement in scarring – investigator assessed** <u>Overall scar severity score 12 months after</u>	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: Some concerns (randomisation was done using computer-generated random

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
individual modality in the treatment of atrophic acne scars? A randomized controlled trial, Journal of Dermatological TreatmentJ Dermatolog Treat, 25, 137-41, 2014 **Ref Id** 869142 **Country/ies where the study was carried out** Egypt **Study type** Randomised controlled trial **Aim of the study** To investigate whether combining alternating sessions of 1540nm non-ablative fractional laser and percutaneous collagen induction with trichloroacetic acid 20% shows better results than each individual modality in the treatment of atrophic scars. **Study dates** Not mentioned.	n=13 **Characteristics** Mean age (years)- Mean (±SD) PCI + TCA 20%: 31.88 (7.5) Laser: 32.54 (7.6) Alternating treatment of both: 31.23 (6.56) Skin phototype- III- Number PCI + TCA 20%: 5/13 Laser: 6/13 Alternating treatment of both: 6/13 Skin phototype- IV- Number PCI + TCA 20%: 8/13 Laser: 7/13 Alternating treatment of both: 7/13 Gender- Female- Number PCI + TCA 20%: 9/13 Laser: 7/13 Alternating treatment of both: 8/13 Gender- Male- Number	apart) of 1540 nm fractional photothermolysis (StarluxTM 1540) laser system, with spot size 10 mm. The pulse energy used was 40–50 mJ, density 100 MTZ/cm2/pass for six passes in different directions with 50% overlap/session. Alternating treatment of both: Received combined alternating sessions of the previously mentioned two modalities (three sessions of each with 4 weeks in between).	confidence interval) and ANOVA for normally distributed quantitative variables, and chi square test for categorical data. $p < 0.05$ was considered statistically significant. **Intention-to-treat analysis** ITT analysis used in study.	the treatment- Mean (±SD) PCI + TCA 20%: 24.85 (16.74) 95% CI (14.73 to 34.96) Laser: 29.62 (20.11) 95% CI (17.46 to 41.77) Alternating treatment of both: 16.92 (10.73) 95% CI (10.44 to 23.41) p=0.150 Change score from baseline- Mean (±SD) PCI + TCA 20%: -42.00 (26.40) Laser: -46.07 (30.02) Alternating treatment of both: -58.70 (28.83)	sequence) Performance bias: Low risk of bias (blinding of participants and personnel was not feasible for this study. ITT analysis used.) Attrition bias: Low risk of bias (high retention, only 1 participant lost to follow up) Detection bias: Low risk of bias (clinical evaluation done by the same dermatologist who was blinded to the modality) Reporting bias: Some concerns (assessment from published study report- no trial protocol reported) Other bias: No other bias detected Overall bias: Some concerns

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Not mentioned.	PCI + TCA 20%: 4/13 Laser: 6/13 Alternating treatment of both: 5/13 <u>Baseline scar severity score-Mean (±SD)</u> PCI + TCA 20%: 66.85 (37.33) 95% CI (44.29 to 89.41) Laser: 75.69 (42.45) 95% CI (50.04 to 101. 35) Alternating treatment of both: 75.62 (40.77) 95% CI (50.98 to 100.25) **Inclusion criteria** • Participants with skin phototype III and IV; • Those seeking treatment for atrophic post acne scars (acne scar severity means from 66 to 75 (3 points for deep, 2 points for shallow and 1 point for superficial scars)). **Exclusion criteria**				Clinical evaluation done using a quartile grading scale (0. minimal improvement <25%, 1. mild improvement 25–50%, 2. moderate improvement 51–75%, 3. significant improvement >75% improvement). Scar severity score measured by weighted scale: 3 points for deep, 2 points for shallow and 1 point for superficial scars

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Pregnancy or lactation; • History of hypertrophic scarring or keloid formation; • History of active or recurrent herpes simplex; • Presence of infected skin lesions; • Diabetes; • Bleeding disorder; • Acute or chronic corticosteroid or anticoagulant treatment; • Presence of skin cancers; • Use of isotretinoin within 6 months before treatment.				
Full citation Mohammed, G., Randomized clinical trial of CO2 laser pinpoint irradiation technique with/without needling for ice pick acne scars, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 15, 177-	**Sample size** N=60 CO_2 laser + needling: n=30 CO_2 laser: n=30	**Interventions** CO_2 laser + needling: face was cleaned and degreased with acetone. Using a single-spot hand piece (CO_2 laser at 99Hz, level 2 pulse control, 0.9W power), and after stretching the skin to reach the bottom of the scar, the hand piece was directed into the pit of each ice pick scar	**Details** **Power analysis** Not mentioned. **Statistical analyses** Chi-square test was used to compare categorical	**Results** **Primary outcomes** **Improvement in scarring – investigator assessed**	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: Some concerns (no details provided)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
82, 2013 **Ref Id** 869392 **Country/ies where the study was carried out** Egypt **Study type** Randomised controlled trail **Aim of the study** To evaluate the use of a pinpoint irradiation technique without needling in the treatment of ice pick acne scars. **Study dates** Not mentioned. **Source of funding** Not mentioned	**Characteristics** Age (years)- Range CO2 laser + needling: 19-32 years CO2 laser: 19-32 years Acne scar severity index at baseline- Healed- Number (investigator reported) CO2 laser + needling: 0 CO2 laser: 0 Acne scar severity index at baseline- Mild- Number (investigator reported) CO2 laser + needling: 5 CO2 laser: 4 Acne scar severity index at baseline- Moderate- Number (investigator reported) CO2 laser + needling: 5 CO2 laser: 8 Acne scar severity index at baseline- Severe- Number (investigator reported) CO2 laser + needling: 20 CO2 laser: 17 Goodman and Baron grading	for pinpoint irradiation (without needling) in a systematic fashion beginning on the forehead and proceeding down the remainder of the face. *Topical antibiotic cream (Garamycin) was applied twice per day for 1 week and panthenol cream twice daily for 2 weeks. CO_2 laser: The same as above followed by needling on the scar area with a 26G needle, with a depth of about 1 mm. Pricking was done only with the bevel of the needle tip. About 5 to 10 needling punctures made on two 0.5- to 1 mm atrophic areas. All participants were initially primed for two weeks with 0.5 – 1 g Retin-A cream at night and a sunscreen containing avobenzone, octinoxate, and 2 – 4% Eldoquin Forte in morning before starting the CO_2 laser session. The treatments repeated for four sessions at 3-week interval.	variables, and paired t-test was used to compare numerical variables. The level of significance (p value) was 0.05. Results are statistically significant, if p value was <0.05. **Intention-to-treat analysis** Not mentioned.	Acne scar severity index- Healed- Number (investigator reported) CO2 laser + needling: 9 CO2 laser: 9 Acne scar severity index- Mild- Number (investigator reported) CO2 laser + needling: 11 CO2 laser: 14 Acne scar severity index- Moderate- Number (investigator reported) CO2 laser + needling: 10 CO2 laser: 7 Acne scar severity index- Severe- Number (investigator reported) CO2 laser + needling: 0 CO2 laser: 0 Goodman and Baron	Performance bias: Some concerns (blinding of participants and personnel was not feasible for this study) Attrition bias: Low risk of bias (high retention and no reported loss to follow up) Detection bias: Low risk of bias (independent assessors clinically examined outcomes) Reporting bias: Some concerns (assessment from published study report- no trial protocol reported) Other bias: No other bias detected Overall bias: Some concerns Acne scars severity

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	scale at baseline- Macular- Number (investigator reported) CO2 laser + needling: 0 COs laser: 0 Goodman and Baron grading scale at baseline- Mild- Number (investigator reported) CO2 laser + needling: 5 COs laser: 4 Goodman and Baron grading scale at baseline- Moderate- Number (investigator reported) CO2 laser + needling: 8 COs laser: 8 Goodman and Baron grading scale at baseline- Severe- Number (investigator reported) CO2 laser + needling: 18 COs laser: 18 **Inclusion criteria** • Participants with moderate to severe ice pick acne scarring. **Exclusion criteria** • People with active inflammatory lesions;			grading scale- Macular- Number (investigator reported) CO2 laser + needling: 9 COs laser: 10 Goodman and Baron grading scale- Mild- Number (investigator reported) CO2 laser + needling: 11 COs laser: 13 Goodman and Baron grading scale- Moderate- Number (investigator reported) CO2 laser + needling: 10 COs laser: 7 Goodman and Baron grading scale- Severe- Number (investigator reported) CO2 laser + needling: 0 COs laser: 0	index (healed if scars counts <1, mild if scars counts 1 – 25, moderate if scars counts 26 – 50, and severe if scars counts >50) and using the Goodman and Baron grading scale. Patient satisfaction evaluated according to a fourpoint scale at the end of the treatment (A, excellent improvement if >75% reduction of scars observed; B, good if 51 – 75% improvement; C, fair if 26 – 50% improvement; and D, poor if <30% improvement seen). Results reported at 3 months follow-up, after last treatment.

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Keloidal tendency; • Immunosuppression; • Filler injections within the preceding 6 – 12 months; • Infections such as herpes labials; • Those on systemic isotretinoin.			**Secondary outcomes** **Participant satisfaction with treatment** Number of participants reporting excellent improvement- Number CO2 laser + needling: 21 CO2 laser: 24 Number of participants reporting good improvement- Number CO2 laser + needling: 9 CO2 laser: 6 **Side effects** Minimal adverse effects consisting of mild transient erythema and edema immediately after treatment. Some pin-point-sized crusts and mild erythema were observed for 3–6 days after each treatment session.	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Nofal, E., Helmy, A., Nofal, A., Alakad, R., Nasr, M., Platelet-rich plasma versus CROSS technique with 100% trichloroacetic acid versus combined skin needling and platelet rich plasma in the treatment of atrophic acne scars: a comparative study, Dermatologic SurgeryDermatol Surg, 40, 864-73, 2014 **Ref Id** 869821 **Country/ies where the study was carried out** Egypt **Study type** Randomised controlled trial **Aim of the study** To evaluate the efficacy and safety of intradermal injection of PRP, 100% focal TCA, and combined skin needling plus topical PRP in the treatment of atrophic acne scars.	**Sample size** N=45 PRP: n=15 TCA CROSS : n=15 Needling + topical PRP: n=15 **Characteristics** Mean age (years)- Mean (±SD) PRP: 25.1 (3.7) TCA CROSS: 25.5 (5.6) Needling + topical PRP: 25.8 (5.3) Gender- Female- Number (%) PRP: 10 (66.7) TCA CROSS: 10 (66.7) Needling + topical PRP: 11 (73.3) Gender- Male- Number (%) PRP: 5 (33.3) TCA CROSS: 5 (33.3) Needling + topical PRP: 4 (26.7)	**Interventions** PRP: local anaesthetic cream was applied to the face before treatment, area of intervention was sterilised with alcohol, 0.1 to 0.3 mL intradermal injection of PRP, followed by gentle massage after treatment and topical antibiotic 3 days after. TCA CROSS: skin cleansed and degreased with acetone, CROSS technique with TCA 100%, followed by application of antibiotic cream and sunscreen after intervention. Needling + topical PRP: local anaesthetic cream was applied to the face before treatment, area of intervention was sterilised with alcohol, 0.1 to 0.3 mL intradermal injection of PRP, followed by skin needling using a dermaroller, followed by application of antibiotic cream and sunscreen after intervention. Each participant underwent 3 sessions at 2-week interval.	**Details** **Power analysis** Not mentioned. **Statistical analyses** Chi-square (X^2) or Fisher exact test analysis of variance (F test) and McNemar X^2 test were used when appropriate. $p<0.05$ was considered statistically significant.	**Results** **Primary outcomes** **Improvement in scarring – investigator assessed** Investigator assessed improvement- Grade 1- Number (%) PRP: 0 TCA CROSS: 0 Needling + topical PRP: 1 (6.7) Investigator assessed improvement- Grade 2- Number (%) PRP: 6 (40) TCA CROSS: 5 (33.3) Needling + topical PRP: 6 (40) Investigator assessed improvement- Grade 3- Number (%) PRP: 5 (33.3) TCA CROSS: 6 (40)	**Limitations** **Cochrance RoB Tool v2.0** Selection bias: Some concerns (no details provided) Performance bias: Some concerns (not feasible to blind participants or personnel delivering interventions due to study design) Attrition bias: Low risk of bias (high retention rate and no reported loss to follow up) Detection bias: Low risk of bias (photographs taken at baseline, at each session, 2 weeks after the last session, and at the end of follow-up. Results assessed by 2 blinded dermatologists) Reporting bias: Some concerns (no intervention protocol provided)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates December 2011 to October 2012. **Source of funding** Not mentioned.	Scar duration- Mean (±SD) PRP: 5.9 (2.0) TCA CROSS: 6.3 (2.1) Needling + topical PRP: 5.7 (1.9) Investigator assessed scarring grade- Grade 2- Number (%) PRP: 2 (13.3) TCA CROSS: 1 (6.7) Needling + topical PRP: 2 (13.3) Investigator assessed scarring grade- Grade 3- Number (%) PRP: 1 (6.7) TCA CROSS: 2 (13.3) Needling + topical PRP: 3 (20) Investigator assessed scarring grade- Grade 4- Number (%) PRP: 12 (80) TCA CROSS: 12 (80) Needling + topical PRP: 10 (66.7) **Inclusion criteria**			Needling + topical PRP: 5 (33.3) Investigator assessed improvement- Grade 4- Number (%) PRP: 4 (26.7) TCA CROSS: 4 (26.7) Needling + topical PRP: 3 (20) p=0.87 Participant reported improvement- Poor- Number (%) PRP: 5 (33.3) TCA CROSS: 6 (40) Needling + topical PRP: 4 (26.7) Participant reported improvement- Good- Number (%) PRP: 3 (20) TCA CROSS: 5 (33.3) Needling + topical PRP: 2 (13.3) Participant reported	Other bias: no other bias detected Overall risk of bias: Some concerns Outcomes reported at 2 months follow-up from baseline. Goodman and Baron scarring grading system used. Participant reported improvement and participant satisfaction measured by: excellent (>75%), very good (50%–74%), good (25%–49%), and poor (<25%). Pain was graded on a scale of 0 (none) to 9 (maximum).

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• People with mild, moderate and severe atrophic acne scars of different durations, types and severity. **Exclusion criteria** • Participants with active acne, herpes labialis, or bacterial infection; • Warts on the face, actinic keratosis, or skin cancer; • Systemic retinoids intake in the previous 6 months, diabetes, pregnancy, history of keloidal scarring; • Particpants with severe systemic illness or malignancy; • Participants on anticoagulant therapy or aspirin, participants with haemoglobin <10 g/dL, or platelets <105/mL were excluded from PRP injection and combined needling and PRP groups.			<u>improvement- Very good- Number (%)</u> PRP: 4 (26.7) TCA CROSS: 4 (26.7) Needling + topical PRP: 7 (46.7) <u>Participant reported improvement- Excellent- Number (%)</u> PRP: 3 (20) TCA CROSS: 0 Needling + topical PRP: 2 (13.3) p=0.49 **<u>Secondary outcomes</u>** **Participant satisfaction with treatment** <u>Participant satisfaction- Poor- Number (%)</u> PRP: 0 TCA CROSS: 0 Needling + topical PRP: 0	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Participant satisfaction- Good- Number (%) PRP: 5 (33.3) TCA CROSS: 6 (40) Needling + topical PRP: 5 (33.3) Participant satisfaction- Very good- Number (%) PRP: 7 (46.7) TCA CROSS: 3 (20) Needling + topical PRP: 5 (33.3) Participant satisfaction- Excellent- Number (%) PRP: 3 (20) TCA CROSS: 6 (40) Needling + topical PRP: 5 (33.3) **Side effects** No reported adverse effects- Number (%) PRP: 14 (93.3) TCA CROSS: 11	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				(73.3) Needling + topical PRP: 0 <u>Mild bruises- Number (%)</u> PRP: 1 (6.7) TCA CROSS: 0 Needling + topical PRP: 0 <u>Hyperpigmentation- Number (%)</u> PRP: 0 TCA CROSS: 4 (26.7) Needling + topical PRP: 0 <u>Erythema and edema- Number (%)</u> PRP: 0 TCA CROSS: 0 Needling + topical PRP: 15 (100) <u>Pain- Mild- Number (%)</u> PRP: 6 (40) TCA CROSS: 15 (100)1	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				Needling + topical PRP: 2 (13.3) Pain- Moderate- Number (%) PRP: 3 (20) TCA CROSS: 0 Needling + topical PRP: 7 (46.7) Pain- Severe- Number (%) PRP: 6 (40) TCA CROSS: 0 Needling + topical PRP: 6 (40)	

Appendix E– Forest plots

Forest plots for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

This section includes forest plots only for outcomes that are meta-analysed. No meta-analysis was conducted for this review question and so there are no forest plots. The quality assessment for the outcomes is provided in the GRADE profiles in appendix F.

Appendix F – GRADE tables

GRADE tables for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

Atrophic acne vulgaris scars

Split-face studies

Table 9: Clinical evidence profile for comparison of 10600-nm CO2 laser plus topical stem cell-conditioned medium versus 10600-nm CO2 laser plus topical saline in participants with moderate to severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10600-nm CO2 laser + SC-CM topical	10600-nm CO2 laser + saline topical	Relative (95% CI)	Absolute		
Overall improvement in scarring after the final treatment (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	17	17	-	MD 2.64 lower (5.1 to 0.18 lower)	⊕⊕OO LOW	CRITICAL
Participant satisfaction with treatment assessed at the final follow up visit- Very satisfied/satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	13/17 (76.5%)	10/17 (58.8%)	RR 1.3 (0.81 to 2.09)	176 more per 1000 (from 112 fewer to 641 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment assessed at the final follow up visit - Slightly satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/17 (17.6%)	6/17 (35.3%)	RR 0.5 (0.15 to 1.68)	176 fewer per 1000 (from 300 fewer to 240	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10600-nm CO2 laser + SC-CM topical	10600-nm CO2 laser + saline topical	Relative (95% CI)	Absolute		
										more)		
Participant satisfaction with treatment assessed at the final follow up visit - Unsatisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	1/17 (5.9%)	1/17 (5.9%)	RR 1 (0.07 to 14.72)	0 fewer per 1000 (from 55 fewer to 807 more)	⊕⊕OO LOW	IMPORTANT
Side effects short-term post-treatment - Acne activation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	6/17 (35.3%)	6/17 (35.3%)	RR 1 (0.4 to 2.48)	0 fewer per 1000 (from 212 fewer to 522 more)	⊕⊕OO LOW	IMPORTANT
Side effects short-term post-treatment - Crust formation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/17 (100%)	17/17 (100%)	RR 1 (0.9 to 1.12)	0 fewer per 1000 (from 100 fewer to 120 more)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment - Oedema												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/17 (100%)	17/17 (100%)	RR 1 (0.9 to 1.12)	0 fewer per 1000 (from 100 fewer to 120 more)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment - Erythema												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10600-nm CO2 laser + SC-CM topical	10600-nm CO2 laser + saline topical	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/17 (100%)	17/17 (100%)	RR 1 (0.9 to 1.12)	0 fewer per 1000 (from 100 fewer to 120 more)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment - Persistent pixel stamping marks												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/17 (17.6%)	4/17 (23.5%)	RR 0.75 (0.2 to 2.86)	59 fewer per 1000 (from 188 fewer to 438 more)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Post-inflammatory hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	1/17 (5.9%)	1/17 (5.9%)	RR 1 (0.07 to 14.72)	0 fewer per 1000 (from 55 fewer to 807 more)	⊕⊕OO LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; ECCA: echelle d'e´valuation clinique des cicatrices d'acne´ [clinical evaluation scale for acne scarring]; MD: mean difference; MID: minimally important difference; SC-CM: stem cell-conditioned medium; RR: relative risk
[1] Abdel-Maguid 2019
[2] Overall risk of bias judgement: some concerns as no information provided about allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
MID was calculated for continuous outcome of improvement in scarring: +/-2.5.

Table 10: Clinical evidence profile for comparison of 10600-nm CO2 laser plus topical stem cell-conditioned medium versus 10600-nm CO2 laser plus topical saline in participants with moderate to severe facial acne scars by acne scar type

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**10600-nm CO2 laser + SC-CM topical**	**10600-nm CO2 laser + saline topical**	**Relative (95% CI)**	**Absolute**		
Improvement in scarring after the final treatment – Icepick (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	13	13	-	MD 3.47 lower (5 to 1.94 lower)	⊕⊕⊕O MODERATE	CRITICAL
Improvement in scarring after the final treatment – Boxcar (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	7	8	-	MD 2.38 higher (1.75 lower to 6.51 higher)	⊕⊕OO LOW	CRITICAL
Improvement in scarring after the final treatment – Rolling (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	17	17	-	MD 2.94 lower (5.3 to 0.58 lower)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; CO2: carbon dioxide laser; ECCA: echelle d'e´valuation clinique des cicatrices d'acne´ [clinical evaluation scale for acne scarring]; MD: mean difference; MID: minimally important difference; SC-CM: stem cell-conditioned medium
[1] Abdel-Maguid 2019
[2] Overall risk of bias judgement: some concerns as no information provided about allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
MIDs were calculated for continuous outcome of improvement in scarring and were as follows: for icepick +/-0.8, for boxcar +/-1.9, for rolling scar +/-2.2.

Table 11: Clinical evidence profile for comparison of 10600-nm CO2 laser plus topical platelet-rich plasma versus 10600-nm CO2 laser plus topical stem cell-conditioned medium in participants with moderate to severe facial acne scars

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10600-nm CO2 laser + PRP topical	10600-nm CO2 laser + SC-CM topical	Relative (95% CI)	Absolute		
Overall improvement in scarring after the final treatment (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16	16	-	MD 15.35 lower (18.74 to 11.96 lower)	⊕⊕⊕O MODERATE	CRITICAL
Participant satisfaction with treatment assessed at the final follow up visit - Very satisfied/satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	13/16 (81.3%)	10/16 (62.5%)	RR 1.3 (0.83 to 2.03)	187 more per 1000 (from 106 fewer to 644 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment assessed at the final follow up visit - Slightly satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/16 (18.8%)	6/16 (37.5%)	RR 0.5 (0.15 to 1.66)	188 fewer per 1000 (from 319 fewer to 247 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment assessed at the final follow up visit - Unsatisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Acne activation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/16 (6.3%)	2/16 (12.5%)	RR 0.5 (0.05 to 4.98)	62 fewer per 1000 (from 119 fewer to 498 more)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Crust formation												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10600-nm CO2 laser + PRP topical	10600-nm CO2 laser + SC-CM topical	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/16 (100%)	16/16 (100%)	RR 1 (0.89 to 1.12)	0 fewer per 1000 (from 110 fewer to 120 more)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment - Oedema												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/16 (100%)	16/16 (100%)	RR 1 (0.89 to 1.12)	0 fewer per 1000 (from 110 fewer to 120 more)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment - Erythema												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/16 (100%)	16/16 (100%)	RR 1 (0.89 to 1.12)	0 fewer per 1000 (from 110 fewer to 120 more)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment - Persistent pixel stamping marks												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	0/16 (0%)	3/16 (18.8%)	POR 0.12 (0.01 to 1.22)	161 fewer per 1000 (from 185 fewer to 32 more)	⊕⊕OO LOW	IMPORTANT
Side effects short-term post-treatment - Post-inflammatory hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; MD: mean difference; ECCA: echelle d'e´valuation clinique des cicatrices d'acne´ [clinical evaluation scale for acne scarring]; MID: minimally important difference; POR: Peto odds ratio; PRP: platelet-rich plasma; SC-CM: stem cell-conditioned medium; RD: risk difference; RR: relative risk
[1] Abdel-Maguid 2019
[2] Overall risk of bias judgement: some concerns as no information provided about allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[5] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
MID was calculated for continuous outcome of improvement in scarring: +/-3.2.

Table 12: Clinical evidence profile for comparison of 10600-nm CO2 laser plus topical platelet-rich plasma versus 10600-nm CO2 laser plus topical stem cell-conditioned medium in participants with moderate to severe facial acne scars by acne scar type

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10600-nm CO2 laser + PRP topical	10600-nm CO2 laser + SC-CM topical	Relative (95% CI)	Absolute		
Improvement in scarring after the final treatment – Icepick (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	13	13	-	MD 3.61 lower (5.14 to 2.08 lower)	⊕⊕⊕O MODERATE	CRITICAL
Improvement in scarring after the final treatment – Boxcar (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12	13	-	MD 12.12 lower (14.62 to 9.62 lower)	⊕⊕⊕O MODERATE	CRITICAL
Improvement in scarring after the final treatment – Rolling (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	16	16	-	MD 5.58 lower (8.04 to 3.12 lower)	⊕⊕⊕O MODERATE	CRITICAL

CI: confidence interval; CO2: carbon dioxide laser; ECCA: echelle d'e´valuation clinique des cicatrices d'acne´ [clinical evaluation scale for acne scarring]; MD: mean difference; MID: minimally important difference; PRP: platelet-rich plasma SC-CM: stem cell-conditioned medium
[1] Abdel-Maguid 2019

[2] Overall risk of bias judgement: some concerns as no information provided about allocation concealment.
MIDs were calculated for continuous outcome of improvement in scarring and are as follows: for icepick +/-1.2, for boxcar +/-1.8, for rolling +/-2.5.

Table 13: Clinical evidence profile for comparison of 1550-nm erbium-doped fractional photothermolysis laser versus 10600-nm CO2 laser in participants with mild to severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1550-nm erbium-doped fractional photothermolysis laser	10600-nm CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring 3 months after treatment (investigator assessed; measured with: a categorical scale from minimal/no improvement to near-total improvement; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	8	8	-	MD 0.5 lower (1.15 lower to 0.15 higher)	⊕⊕OO LOW	CRITICAL
Participant satisfaction with treatment 3 months after final treatment – Very satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/8 (0%)	2/8 (25%)	POR (0.2 (0.01 to 3.61))	200 fewer per 1000 (from 248 fewer to 652 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment 3 months after final treatment – Slightly satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/8 (62.5%)	1/8 (12.5%)	RR 5 (0.74 to 33.78)	500 more per 1000 (from 32 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment 3 months after final treatment – Satisfied												
1[1]	randomised	serious[2]	no serious	no serious	very serious[4]	none	2/8 (25%)	4/8	RR 0.5	250 fewer per	⊕OOO	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1550-nm erbium-doped fractional photothermolysis laser	10600-nm CO2 laser	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness				(50%)	(0.13 to 2)	1000 (from 435 fewer to 500 more)	VERY LOW	
Participant satisfaction with treatment 3 months after final treatment – Unsatisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/8 (12.5%)	1/8 (12.5%)	RR 1 (0.07 to 13.37)	0 fewer per 1000 (from 116 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Hypopigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/8 (0%)	0/8 (0%)	RD 0 (-0.21 to 0.21)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Post-therapy hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/8 (12.5%)	1/8 (12.5%)	RR 1 (0.07 to 13.37)	0 fewer per 1000 (from 116 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Post-therapy blister formation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/8 (0%)	0/8 (0%)	RD 0 (-0.21 to 0.21)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term postreatment - Scarring												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1550-nm erbium-doped fractional photothermolysis laser	10600-nm CO2 laser	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/8 (0%)	0/8 (0%)	RD 0 (-0.21 to 0.21)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Secondary bacterial/viral infection												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/8 (0%)	0/8 (0%)	RD 0 (-0.21 to 0.21)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Transient pinpoint bleeding												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/8 (0%)	1/8 (12.5%)	POR 0.14 (0 to 6.82)	108 fewer per 1000 (from 125 fewer to 728 more)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Treatment-associated pain (measured with: a visual analogue scale (0=no pain and 10=extremely painful); better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	8	8	-	MD 3.1 lower (5.06 to 1.14 lower)	⊕⊕⊕O MODERATE	IMPORTANT

CO2: carbon dioxide laser; CI: confidence interval; MD: mean difference; MID: minimally important difference; POR: Peto odds ratio; RD: risk difference
[1] Cho 2010
[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence intervals crosses 2 default MIDs for dichotomous outcomes.
[5] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events. MIDs were calculated for continuous outcomes and were as follows: for scaring improvement +/-0.4, for pain +/-1.

Table 14: Clinical evidence profile for comparison of 10600-nm CO2 laser plus punch elevation versus 10600-nm CO2 laser in participants with moderate to severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10600-nm CO2 laser+ punch elevation	10600-nm CO2 laser	Relative (95% CI)	Absolute		
Excellent improvement in scarring 4 months after treatment (investigator assessed)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	12/42 (28.6%)	2/42 (4.8%)	RR 6 (1.43 to 25.19)	238 more per 1000 (from 20 more to 1000 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Good improvement in scarring 4 months after treatment (investigator assessed)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	19/42 (45.2%)	24/42 (57.1%)	RR 0.79 (0.52 to 1.21)	120 fewer per 1000 (from 274 fewer to 120 more)	⊕⊕⊕O MODERATE	CRITICAL
Moderate improvement in scarring 4 months after treatment (investigator assessed)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	11/42 (26.2%)	14/42 (33.3%)	RR 0.79 (0.4 to 1.53)	70 fewer per 1000 (from 200 fewer to 177 more)	⊕⊕OO LOW	CRITICAL
Minimal improvement in scarring 4 months after treatment (investigator assessed)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	0/42 (0%)	2/42 (4.8%)	POR 0.13 (0.01 to 2.15)	41 fewer per 1000 (from 47 fewer to 49 more)	⊕⊕OO LOW	CRITICAL
Participant satisfaction with treatment 4 months after treatment (measured with: a visual analogue scale (0=no satisfaction, 10=the best possible satisfaction); better												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10600-nm CO2 laser+ punch elevation	10600-nm CO2 laser	Relative (95% CI)	Absolute		
indicated by higher values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[5]	none	42	42	-	MD 1 higher (0.25 to 1.75 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment - Erythema												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	42/42 (100%)	42/42 (100%)	RR 1 (0.96 to 1.05)	0 fewer per 1000 (from 40 fewer to 50 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Side effects short-term post-treatment - Hypopigmentation												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/42 (0%)	0/42 (0%)	RD 0 (-0.05 to 0.05)	-	⊕⊕OO LOW	IMPORTANT
Side effects short-term post-treatment – Post-treatment burning												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	42/42 (100%)	42/42 (100%)	RR 1 (0.96 to 1.05)	0 fewer per 1000 (from 40 fewer to 50 more)	⊕⊕⊕⊕ HIGH	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; MID: minimally important difference; POR: Peto odds ratio; RD: risk difference; RR: relative risk
[1] Faghihi 2015
[2] Evidence downgraded by 1 level due to risk of very serious imprecision as 95% confidence intervals cross 1 default MID for dichotomous outcomes.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence intervals crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

[5] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes. MID was calculated for continuous outcome of participant satisfaction with treatment: +/-0.95.

Table 15: Clinical evidence profile for comparison of CO2 laser plus autologous platelet-rich plasma injection versus CO2 laser plus saline injection in participants with moderate to severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + PRP injection	CO2 laser + saline injection	Relative (95% CI)	Absolute		
Excellent improvement in scarring 4 months after treatment (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⨁◯◯◯ VERY LOW	CRITICAL
Fair/good improvement in scarring 4 months after treatment (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	14/16 (87.5%)	11/16 (68.8%)	RR 1.27 (0.87 to 1.86)	186 more per 1000 (from 89 fewer to 591 more)	⨁⨁◯◯ LOW	CRITICAL
Poor improvement in scarring 4 months after treatment (investigator assessed)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + PRP injection	CO2 laser + saline injection	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	2/16 (12.5%)	5/16 (31.3%)	RR 0.4 (0.09 to 1.77)	188 fewer per 1000 (from 284 fewer to 241 more)	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment 4 months after treatment - Satisfied/very satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	9/16 (56.3%)	7/16 (43.8%)	RR 1.29 (0.64 to 2.6)	127 more per 1000 (from 157 fewer to 700 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment 4 months after treatment - Slightly satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	7/16 (43.8%)	5/16 (31.3%)	RR 1.4 (0.56 to 3.49)	125 more per 1000 (from 138 fewer to 778 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment 4 months after treatment - Unsatisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	0/16 (0%)	4/16 (25%)	POR 0.11 (0.01 to 0.86)	215 fewer per 1000 (from 27 fewer to 247 fewer)	⊕⊕OO LOW	IMPORTANT
Side effects short-term post-treatment - Acneiform eruption												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + PRP injection	CO2 laser + saline injection	Relative (95% CI)	Absolute		
Side effects short-term post-treatment - Dyschromia												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Scar formation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Secondary infection												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/16 (0%)	0/16 (0%)	RD 0 (-0.11 to 0.11)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; MID: minimally important difference; POR: Peto odds ratio; PRP: autologous platelet-rich plasma; RD: risk difference; RR: relative risk
[1] Faghihi 2016
[2] Overall risk of bias judgement: some concerns as no information provided about allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

Table 16: Clinical evidence profile for comparison of fractionated microneedle frequency plus subcision versus fractionated microneedle frequency in participants with moderate to severe facial acne scars

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Fractionated microneedle frequency + subcision**	**Fractionated microneedle frequency**	**Relative (95% CI)**	**Absolute**		
Excellent improvement in scarring at the end of study (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/25 (0%)	0/25 (0%)	RD 0 (-0.07 to 0.07)	-	⊕OOO VERY LOW	CRITICAL
Good improvement in scarring at the end of study (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	13/25 (52%)	8/25 (32%)	RR 1.62 (0.82 to 3.22)	198 more per 1000 (from 58 fewer to 710 more)	⊕⊕OO LOW	CRITICAL
Fair improvement in scarring at the end of study (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	7/25 (28%)	12/25 (48%)	RR 0.58 (0.28 to 1.23)	202 fewer per 1000 (from 346 fewer to 110 more)	⊕⊕OO LOW	CRITICAL
Poor improvement in scarring at the end of study (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	5/25 (20%)	5/25 (20%)	RR 1 (0.33 to 3.03)	0 fewer per 1000 (from 134 fewer to 406 more)	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment at the end of study (measured with: a visual analogue scale (0=no satisfaction, 10=the best possible satisfaction); better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	25	25	-	MD 0.9 higher (0.17 lower to 1.97 higher)	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fractionated microneedle frequency + subcision	Fractionated microneedle frequency	Relative (95% CI)	Absolute		
Side effects short-term post-treatment – Infection												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/25 (0%)	0/25 (0%)	-	RD 0 (-0.07 to 0.07)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Persistent erythema												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/25 (0%)	0/25 (0%)	-	RD 0 (-0.07 to 0.07)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Ulceration												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/25 (0%)	0/25 (0%)	-	RD 0 (-0.07 to 0.07)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Scar formation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/25 (0%)	0/25 (0%)	-	RD 0 (-0.07 to 0.07)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Transient bilateral submandibular lymphadenopathy												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/25 (4%)	0/25 (0%)	POR 7.39 (0.15 to 372.38)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MID: minimally important difference; POR: Peto odds ratio; RD: risk difference; RR: relative risk
[1] Faghihi 2017

[2] Overall risk of bias judgement: some concerns as no information provided about allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[6] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for continuous outcomes.
MID was calculated for continuous outcome of participant satisfaction: +/-0.8.

Table 17: Clinical evidence profile for comparison of CO2 laser plus autologous platelet-rich plasma injection versus CO2 laser in participants with atrophic facial acne scar lesions[#]

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + PRP injection	CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring 3 months after treatment (investigator assessed; measured with: Quantitative Global Acne Scarring Grading Scale adopted by Goodman and Baron; better indicated by higher values)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 1.1 lower (3.1 lower to 0.9 higher)	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment 3 months after treatment – Very satisfied												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15/30 (50%)	1/30 (3.3%)	RR 15 (2.11 to 106.49)	467 more per 1000 (from 37 more to 1000 more)	⊕⊕OO LOW	IMPORTANT
Side effects short-term post-treatment - Hyperpigmentation												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/30 (0%)	0/30 (0%)	RD 0 (-0.06 to 0.06)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; MD: mean difference; MID: minimally important difference; PRP: autologous platelet-rich plasma; RD: risk difference; RR: relative risk
[#] Severity of scarring not specified

[1] Galal 2019
[2] Overall risk of bias judgement: high risk of bias as randomisation was done by tossing a coin, no information provided about allocation concealment and whether outcome assessors were blinded.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
MID was calculated for continuous outcome of improvement in scarring: +/-2.8.

Table 18: Clinical evidence profile for comparison of CO2 laser plus autologous platelet-rich plasma injection versus CO2 laser plus saline injection in participants with mild, moderate and severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + PRP injection	CO2 laser + saline injection	Relative (95% CI)	Absolute		
Improvement in scar depth (µm) 3 months after treatment (investigator assessed, better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15	15	-	MD 19.9 lower (27.65 to 12.15 lower)	⊕⊕⊕O MODERATE	CRITICAL
Side effects short-term post-treatment - Acneiform eruption												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Post-inflammatory hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/15 (0%)	2/15 (13.3%)	POR 0.13 (0.01 to 2.12)	114 fewer per 1000 (from 132 fewer to 113 more)	⊕OOO VERY LOW	IMPORTANT
Side effects – Treatment-associated pain (short-term post-treatment, a mean value for the three sessions of each treated area was calculated; measured with: a scale of 0 (none) to 9 (maximum); better indicated by lower values)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + PRP injection	CO2 laser + saline injection	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15	15	-	MD 4.1 higher (3.40 to 4.80 higher)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; MD: mean difference; MID: minimally important difference; POR: Peto odds ratio; PRP: autologous platelet-rich plasma; RD: risk difference

[1] Gawdat 2014

[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.

[3] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 1 default MIDs for dichotomous outcomes. MIDs were calculated for continuous outcomes and were as follows: for improvement in scar depth +/-7.6, for treatment-associated pain +/-0.4.

Table 19: Clinical evidence profile for comparison of CO2 laser plus autologous platelet-rich plasma (PRP) injection versus CO2 laser plus PRP topical in participants with mild, moderate and severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + PRP injection	CO2 laser+ PRP topical	Relative (95% CI)	Absolute		
Improvement in scar depth (μm) 3 months after treatment (investigator assessed, better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	15	15	-	MD 0.9 lower (8.37 lower to 6.57 higher)	⊕⊕OO LOW	CRITICAL
Side effects short-term post-treatment – Acneiform eruption												
1[1]	randomised	serious[2]	no serious	no serious	very serious[4]	none	0/15	0/15	RD 0 (-	-	⊕OOO	IMPORTANT

	trials		inconsistency	indirectness			(0%)	(0%)	0.12 to 0.12)		VERY LOW	
Side effects short-term post-treatment – Post-inflammatory hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Side effects – Treatment-associated pain (short-term post-treatment, a mean value for the three sessions of each treated area was calculated; measured with: a scale of 0 (none) to 9 (maximum); better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15	15	-	MD 4.3 higher (3.62 to 4.98 higher)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; MD: mean difference; MID: minimally important difference; PRP: autologous platelet-rich plasma; RD: risk difference
[1] Gawdat 2014
[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
MIDs were calculated for continuous outcomes and were as follows: for improvement in scar depth +/-7.6, for treatment-associated pain +/-0.3.

Table 20: Clinical evidence profile for comparison of subcision plus autologous platelet-rich plasma injection versus autologous platelet-rich plasma injection in participants with moderate to severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Subcision + PRP injection**	**PRP injection**	**Relative (95% CI)**	**Absolute**		
Excellent improvement in scarring 6 months after treatment (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/20 (25%)	6/20 (30%)	RR 0.83 (0.3 to 2.29)	51 fewer per 1000 (from 210 fewer to 387	⊕OOO VERY LOW	CRITICAL

										more)		
Marked improvement in scarring 6 months after treatment (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/20 (25%)	6/20 (30%)	RR 0.83 (0.3 to 2.29)	51 fewer per 1000 (from 210 fewer to 387 more)	⊕OOO VERY LOW	CRITICAL
Moderate improvement in scarring 6 months after treatment (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/20 (25%)	8/20 (40%)	RR 0.62 (0.25 to 1.58)	152 fewer per 1000 (from 300 fewer to 232 more)	⊕OOO VERY LOW	CRITICAL
Mild improvement in scarring 6 months after treatment (investigator assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	5/20 (25%)	0/20 (0%)	POR 9.29 (1.46 to 59.09)	-	⊕⊕⊕O MODERATE	CRITICAL

CI: confidence interval; MID: minimally important difference; PRP: autologous platelet-rich plasma; POR: Peto odds ratio; RR: relative risk
[1] Hassan 2019
[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

Table 21: Clinical evidence profile for comparison of CO2 laser versus no treatment in participants with moderate to severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**CO2 laser**	**No treatment**	**Relative (95% CI)**	**Absolute**		
Improvement in scar skin texture 6 months after treatment (investigator assessed; measured with: a numerical scale ranging from 0 (even skin texture without scarring/atrophy) to 10 (worst possible scarring/atrophy); better indicated by higher values)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser	No treatment	Relative (95% CI)	Absolute		
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	12	12	-	MD 1.33 lower (2.35 to 0.31 lower)	⊕⊕⊕O MODERATE	CRITICAL
Improvement in scar skin atrophy 6 months after treatment (investigator assessed; measured with: a numerical scale ranging from 0 (even skin texture without scarring/atrophy) to 10 (worst possible scarring/atrophy); better indicated by higher values)												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	12	12	-	MD 1.33 lower (2.31 to 0.35 lower)	⊕⊕⊕O MODERATE	CRITICAL

CO2: carbon dioxide laser; CI: confidence interval; MD: mean difference; MID: minimally important difference
[1] Hedelund 2012
[2] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
MIDs were calculated for continuous outcomes and are as follows: for improvement in scar skin texture +/-0.6, for improvement in scar skin atrophy +/-0.7.

Table 22: Clinical evidence profile for comparison of 2940-nm Er:YAG laser plus silicone gel versus 2940-nm Er:YAG laser plus hydrophilic cream in participants with moderate to severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	2940-nm Er:YAG + silicone gel	2940-nm Er:YAG + hydrophilic cream	Relative (95% CI)	Absolute		
Excellent improvement in scarring 4 weeks after last treatment (participant assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	3/19 (15.8%)	2/19 (10.5%)	RR 1.5 (0.28 to	53 more per 1000 (from 76	⊕OOO VERY	CRITICAL

									7.99)	fewer to 736 more)	LOW	
Good improvement in scarring 4 weeks after last treatment (participant assessed)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	7/19 (36.8%)	6/19 (31.6%)	RR 1.17 (0.48 to 2.83)	54 more per 1000 (from 164 fewer to 578 more)	⊕OOO VERY LOW	CRITICAL
Side effects short-term post-treatment – Post-laser hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/19 (0%)	0/19 (0%)	RD 0.00 (-0.10 to 0.10)	–	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; Er:YAG: ablative erbium-doped yttrium aluminum garnet laser; MID: minimally important difference; RD: risk difference; RR: relative risk
[1] Khamthara 2018
[2] Overall risk of bias judgement: some concerns as no information provided about allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence intervals crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

Table 23: Clinical evidence profile for comparison of 585-nm pulsed dye laser versus 1064-nm long-pulsed Nd:YAG laser in participants with mild to moderate facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**585-nm pulsed dye laser**	**1064-nm long-pulsed Nd:YAG laser**	**Relative (95% CI)**	**Absolute**		
Improvement in scarring 8 weeks after final treatment (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	18	18	-	MD 2.5 higher (1.44 lower to 6.44 higher)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; ECCA: echelle d'e´valuation clinique des cicatrices d'acne´ [clinical evaluation scale for acne scarring]; MD: mean difference; Nd:YAG: long-pulsed neodymium:yttrium-aluminum-garnet laser; MID: minimally important difference
[1] Lee 2009
[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
MID was calculated for continuous outcome of improvement: +/-4.2.

Table 24: Clinical evidence profile for comparison of 2940-nm Er:YAG laser versus CO2 laser in participants with shallow or deep boxcar facial acne scars[#]

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	2940-nm Er:YAG laser	CO2 laser	Relative (95% CI)	Absolute		
More than 50% improvement in scarring 6 months after final treatment												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	11/20 (55%)	13/20 (65%)	RR 0.85 (0.51 to 1.41)	97 fewer per 1000 (from 318 fewer to 266 more)	⊕OOO VERY LOW	CRITICAL
Side effects short-term post-treatment - Contact dermatitis												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/20 (0%)	0/20 (0%)	RD 0 (-0.09 to 0.09)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Difference in skin colour												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/20 (0%)	0/20 (0%)	RD 0 (-0.09 to 0.09)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Mild post-inflammatory hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	7/20 (35%)	10/20 (50%)	RR 0.7 (0.33 to	150 fewer per 1000 (from 335 fewer to	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	2940-nm Er:YAG laser	CO2 laser	Relative (95% CI)	Absolute		
									1.47)	235 more)		
Side effects short-term post-treatment - Scarring												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/20 (0%)	0/20 (0%)	RD 0 (-0.09 to 0.09)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Wound infection												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/20 (0%)	0/20 (0%)	RD 0 (-0.09 to 0.09)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Treatment-associated pain (measured with: a 10-point pain scale (0 = no pain, 10 = severe pain); better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20	20	-	MD 2.6 lower (3.67 to 1.53 lower)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; Er:YAG: fractional ablative erbium-doped yttrium aluminum garnet laser; MID: minimally important difference; RD: risk difference; RR: relative risk
[#] Severity of scarring not specified
[1] Manuskiatti 2012
[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence intervals crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
MID was calculated for continuous outcome of pain: +/-1.

Table 25: Clinical evidence profile for comparison of 1550-nm fraxel laser with subcision plus CO2 laser versus CO2 laser in participants with atrophic facial acne scars[#]

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**1550-nm fraxel laser with subcision + CO2 laser**	**CO2 laser**	**Relative (95% CI)**	**Absolute**		
Participant satisfaction with treatment 6 months after last treatment (measured with: a visual analogue scale score (no details given); better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	30	30	-	MD 1.4 higher (0.63 to 2.17 higher)	⊕⊕OO LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; MD: mean difference; MID: minimally important difference
[#] Severity of scarring not specified
[1] Nilforoushzadeh 2017
[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
MID was calculated for continuous outcome of participant satisfaction with treatment: +/-0.9.

Table 26: Clinical evidence profile for comparison of 2940-nm ER:YAG laser versus microneedling in participants with mild, moderate and severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**2940-nm Er:YAG laser**	**Micro-needling**	**Relative (95% CI)**	**Absolute**		
Participant satisfaction with treatment 3 months after final treatment - Excellent												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	10/30 (33.3%)	5/30 (16.7%)	RR 2 (0.78 to 5.15)	167 more per 1000 (from 37 fewer to 692 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment 3 months after final treatment - Good												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	2940-nm Er:YAG laser	Micro-needling	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	12/30 (40%)	7/30 (23.3%)	RR 1.71 (0.78 to 3.75)	166 more per 1000 (from 51 fewer to 642 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment 3 months after final treatment - Fair												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/30 (20%)	12/30 (40%)	RR 0.5 (0.22 to 1.16)	200 fewer per 1000 (from 312 fewer to 64 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment 3 months after final treatment - Poor												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/30 (6.7%)	6/30 (20%)	RR 0.33 (0.07 to 1.52)	134 fewer per 1000 (from 186 fewer to 104 more)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Post-inflammatory hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/30 (3.3%)	0/30 (0%)	POR 7.39 (0.15 to 372.38)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment – Treatment-associated pain (measured with: a 10-point pain scale (0 = no pain to 10 = severe pain); better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	30	-	MD 2.33 lower (3.16 to 1.50 lower)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; Er:YAG: fractional ablative erbium-doped yttrium aluminum garnet laser; MID: minimally important difference; POR: Peto odds ratio; RR: relative risk
[1] Osman 2017

[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes. MID was calculated for continuous outcome of pain: +/-0.8.

Table 27: Clinical evidence profile for comparison of 2940-nm Er:YAG laser versus 10600-nm CO2 laser in participants with severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	2940-nm Er:YAG laser	10600-nm CO2 laser	Relative (95% CI)	Absolute		
Improvement in scar depth (mm) 4 weeks after last treatment (investigator assessed, better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	14	14	-	MD 0.26 higher (0.14 lower to 0.66 higher)	⊕⊕OO LOW	CRITICAL
Change in satisfaction with treatment at 4 weeks after last treatment (participant and investigator assessed; measured with: POSAS scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14	14	-	MD 0.8 higher (0.64 to 0.96 higher)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment – Erythema												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14/14 (100%)	14/14 (100%)	RR 1 (0.88 to 1.14)	0 fewer per 1000 (from 120 fewer to 140 more)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects short-term post-treatment – Incrustation/scab formation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious	none	2/14 (14.3%)	5/14 (35.7%)	RR 0.4 (0.09 to 1.73)	214 fewer per 1000 (from 325 fewer to 261	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	2940-nm Er:YAG laser	10600-nm CO2 laser	Relative (95% CI)	Absolute		
										more)		
Side effects short-term post-treatment – Treatment-associated pain (measured with: a visual analogue scale (10-point rating scale from 0 (no pain) to 10); better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	14	14	-	MD 1.1 lower (2.77 lower to 0.57 higher)	⊕⊕OO LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide laser; Er:YAG: fractional ablative erbium-doped yttrium aluminum garnet laser; POSAS: Patient and Observer Scar Assessment Scale. This scale is divided into the 2 sections of participant and observer, and provides a comprehensive estimation of the aesthetic outcome. Both scales contain 6 items rated on a 10-point scale from 0 (participant is not affected) to 10, as well as an extra category "overall opinion" that is rated likewise; MD: mean difference; MID: minimally important difference
[1] Reinholz 2015
[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 1 default MID for continuous outcomes.
MIDs were calculated for continuous outcomes and were as follows: for improvement in scar depth +/-0.4, for change in satisfaction +/-0.2, for pain +/-1.1.

Table 28: Clinical evidence profile for comparison of fractional bipolar radiofrequency versus 1550-nm fractional erbium-doped glass laser in participants with facial atrophic acne scars[#]

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fractional bipolar radiofrequency	1550-nm fractional erbium-doped glass laser	Relative (95% CI)	Absolute		
Participant satisfaction with treatment 1 month after last treatment - Most satisfied												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fractional bipolar radiofrequency	1550-nm fractional erbium-doped glass laser	Relative (95% CI)	Absolute		
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	3/19 (15.8%)	1/20 (5%)	RR 3.16 (0.36 to 27.78)	108 more per 1000 (from 32 fewer to 1000 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment 1 month after last treatment - Very satisfied												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	10/19 (52.6%)	13/20 (65%)	RR 0.81 (0.47 to 1.38)	123 fewer per 1000 (from 344 fewer to 247 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment 1 month after last treatment - Moderately satisfied												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	6/19 (31.6%)	5/20 (25%)	RR 1.26 (0.46 to 3.46)	65 more per 1000 (from 135 fewer to 615 more)	⊕⊕OO LOW	IMPORTANT
Side effects short-term post-treatment - Erythema												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/19 (0%)	1/20 (5%)	POR 0.14 (0 to 7.18)	43 fewer per 1000 (from 50 fewer to 224 more)	⊕⊕OO LOW	IMPORTANT
Side effects short-term post-treatment – Treatment-associated pain (measured with: a scale (0=no pain to 10=the most pain); better indicated by lower values)												
1[1]	randomised trials	no serious risk of	no serious inconsistency	no serious indirectness	no serious imprecision	none	19	20	-	MD 1.85 lower (2.66 to 1.04 lower)	⊕⊕⊕⊕ HIGH	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fractional bipolar radiofrequency	1550-nm fractional erbium-doped glass laser	Relative (95% CI)	Absolute		
		bias										

CI: confidence interval; MID: minimally important difference; POR: Peto odds ratio; RR: relative risk
[#] Severity of scarring not specified
[1] Rongsaard 2014
[2] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes. MID was calculated for continuous outcome of pain: +/-0.7.

Table 29: Clinical evidence profile for comparison of subcision versus collagen filler injection in participants with depressed and rolling types of facial acne scars[#]

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Subcision	Collagen filler injection	Relative (95% CI)	Absolute		
Side effects short-term post-treatment - Post-inflammatory dyspigmentation												
1[1]	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/9 (0%)	0/9 (0%)	RD 0 (-0.19 to 0.19)	-	⊕⊕OO LOW	IMPORTANT

CI: confidence interval; RD: risk difference
[#] Severity of scarring not specified
[1] Sage 2011
[2] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events

Table 30: Clinical evidence profile for comparison of 1320-nm Nd:YAG laser versus 1450-nm diode laser in participants with mild to moderate facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	1320-nm Nd:YAG	1450-nm diode laser	Relative (95% CI)	Absolute		
Side effects short-term post-treatment - Hypertrophic scarring												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/20 (0%)	0/20 (0%)	RD 0 (-0.09 to 0.09)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Hypopigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/20 (0%)	0/20 (0%)	RD 0 (-0.09 to 0.09)	-	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Post-inflammatory hyperpigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/20 (10%)	4/20 (20%)	RR 0.5 (0.1 to 2.43)	100 fewer per 1000 (from 180 fewer to 286 more)	⊕OOO VERY LOW	IMPORTANT
Side effects short-term post-treatment - Post-treatment erythema												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20/20 (100%)	20/20 (100%)	RD 0 (-0.09 to 0.09)	0 fewer per 1000 (from 90 fewer to 100 more)	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; MID: minimally important difference; Nd:YAG: non-ablative long-pulsed neodymium-doped yttrium aluminum garnet laser; RD: risk difference; RR: relative risk

[1] Tanzi 2004

[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.

[3] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

Table 31: Clinical evidence profile for comparison of fractional micro-plasma radiofrequency versus 10600-nm CO2 laser in participants with mild to severe facial acne scars

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fractional micro-plasma radiofrequency	10600-nm CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring 6 months after final treatment (investigator assessed; measured with: ECCA scale; better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	33	33	-	MD 0.1 higher (4.78 lower to 4.98 higher)	⊕⊕⊕O MODERATE	CRITICAL
Participant satisfaction with treatment 6 months after final treatment - Very satisfied/satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	22/33 (66.7%)	20/33 (60.6%)	RR 1.1 (0.76 to 1.59)	61 more per 1000 (from 145 fewer to 358 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment 6 months after final treatment - Slightly satisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	9/33 (27.3%)	10/33 (30.3%)	RR 0.9 (0.42 to 1.93)	30 fewer per 1000 (from 176 fewer to 282 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment 6 months after final treatment - Unsatisfied												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/33 (6.1%)	3/33 (9.1%)	RR 0.67 (0.12 to 3.73)	30 fewer per 1000 (from 80 fewer to 248 more)	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Fractional micro-plasma radiofrequency	10600-nm CO2 laser	Relative (95% CI)	Absolute		
Side effects short-term post-treatment - post-inflammatory pigmentation												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/33 (0%)	12/33 (36.4%)	POR 0.09 (0.03 to 0.31)	315 fewer per 1000 (from 213 fewer to 347 fewer)	⊕⊕⊕O MODERATE	IMPORTANT

CO2: carbon dioxide laser; CI: confidence interval; ECCA: echelle d'e´valuation clinique des cicatrices d'acne´ [clinical evaluation scale for acne scarring]; MD: mean difference; MID: minimally important difference; POR: Peto odds ratio; RR: relative risk
[1] Zhang 2013
[2] Overall risk of bias judgement: some concerns as no information provided about randomisation and allocation concealment.
[3] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
MID was calculated for continuous outcome of improvement in scarring: +/-7.6.

Parallel-group studies

Table 32: Clinical evidence profile for comparison of TCA CROSS versus CO2 laser in participants with ice pick acne scarring (severity of acne not specified)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TCA CROSS	CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring- Percent of scar reduction (excellent)- Invest. assessed (follow-up 6 months; assessed with: Qualitative scarring grading system)												
1[1]	randomised	serious[2]	no serious	no serious	very serious[3]	none	0/14	0/14	RD 0 (-0.13 to	-	⊕OOO	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TCA CROSS	CO2 laser	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness			(0%)	(0%)	0.13)		VERY LOW	
Improvement in scarring - Percent of scar reduction (good)- Invest. assessed (follow-up 6 months; assessed with: Qualitative scarring grading system)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/14 (21.4%)	5/14 (35.7%)	RR 0.6 (0.18 to 2.04)	143 fewer per 1000 (from 293 fewer to 371 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Percent of scar reduction (fair)- Invest. assessed (follow-up 6 months; assessed with: Qualitative scarring grading system)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	7/14 (50%)	6/14 (42.9%)	RR 1.17 (0.52 to 2.6)	73 more per 1000 (from 206 fewer to 686 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Percent of scar reduction (poor)- Invest. assessed (follow-up 6 months; assessed with: Qualitative scarring grading system)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/14 (28.6%)	3/14 (21.4%)	RR 1.33 (0.36 to 4.9)	71 more per 1000 (from 137 fewer to 836 more)	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment - Well (follow-up 6 months; assessed with: Three point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	9/14 (64.3%)	12/14 (85.7%)	RR 0.75 (0.48 to 1.17)	214 fewer per 1000 (from 446 fewer to 146 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment - Fair (follow-up 6 months; assessed with: Three point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/14 (28.6%)	2/14 (14.3%)	RR 2 (0.43 to 9.21)	143 more per 1000 (from 81 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Poor (follow-up 6 months; assessed with: Three point scale)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TCA CROSS	CO2 laser	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/14 (7.1%)	0/14 (0%)	POR 7.93 (-0.15 to 372.38	-	⨁◯◯◯ VERY LOW	IMPORTANT
Side effects - No complications (follow-up 6 months; assessed with: Survey)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/14 (0%)	0/14 (0%)	RD 0 (-01.13 to 0.13)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Side effects - Persistent swelling (follow-up 6 months; assessed with: Survey)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/14 (0%)	5/14 (35.7%)	POR 0.10 (0.01 to 0.64)	321 fewer per 1000 (from 129 fewer to 354 fewer)	⨁⨁⨁◯ MODERATE	IMPORTANT
Side effects - Temporary post procedure hypo-pigmentation (non-event) (follow-up 6 months; assessed with: Survey)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/14 (0%)	0/14 (0%)	RD 0 (-01.13 to 0.13)	-	⨁◯◯◯ VERY LOW	IMPORTANT
Side effects - Temporary post procedure hyper-pigmentation (follow-up 6 months; assessed with: Survey)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	9/14 (64.3%)	2/14 (14.3%)	RR 4.5 (1.18 to 17.21)	500 more per 1000 (from 26 more to 1000 more)	⨁⨁◯◯ LOW	IMPORTANT
Side effects - Infection (follow-up 6 months; assessed with: Survey)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	6/14 (42.9%)	2/14 (14.3%)	RR 3 (0.73 to 12.39)	286 more per 1000 (from 39 fewer to 1000 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Side effects - Itching (picking at scabs) (follow-up 6 months; assessed with: Survey)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TCA CROSS	CO2 laser	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/14 (7.1%)	0/14 (0%)	POR 7.39	-	⊕OOO VERY LOW	IMPORTANT
Side effects - Contact dermatitis (follow-up 6 months; assessed with: Survey)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/14 (0%)	0/14 (0%)	RD 0 (-0.13 to 0.13)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide; POR:Peto odds ratio; RD: risk difference; RR: risk ratio; TCA CROSS: trichloroacetic acid chemical reconstruction of skin scars
1 Ahmed 2014
2 Overall risk of bias judgement: some concerns as no details on allocation concealment provided.
3 Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
4 Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
5 Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.

Table 33: Clinical evidence profile for comparison of CO2 laser + Subcision versus CO2 laser in participants with mild, moderate, and severe atrophic acne scarring

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + Subcision	CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring - Goodman and Baron grading scale (grade 4)- Invest. assesed (follow-up 4 weeks; assessed with: Goodman and Baron grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/23 (17.4%)	2/21 (9.5%)	RR 1.83 (0.37 to 8.96)	79 more per 1000 (from 60 fewer to 758 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + Subcision	CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring - Goodman and Baron grading scale (grade 3)- Invest. assesed (follow-up 4 weeks; assessed with: Goodman and Baron grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	14/23 (60.9%)	16/21 (76.2%)	RR 0.8 (0.53 to 1.2)	152 fewer per 1000 (from 358 fewer to 152 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron grading scale (grade 2)- Invest. assesed (follow-up 4 weeks; assessed with: Goodman and Baron grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/23 (21.7%)	3/21 (14.3%)	RR 1.52 (0.41 to 5.6)	74 more per 1000 (from 84 fewer to 657 more)	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment - Excellent (follow-up 4 weeks; assessed with: 10 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	16/23 (69.6%)	8/21 (38.1%)	RR 1.83 (1.1 to 3.04)[5]	316 more per 1000 (from 38 more to 777 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment - Good (follow-up 4 weeks; assessed with: 10 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/23 (17.4%)	8/21 (38.1%)	RR 0.46 (0.16 to 1.3)	206 fewer per 1000 (from 320 fewer to 114 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Poor (follow-up 4 weeks; assessed with: 10 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	3/23 (13%)	5/21 (23.8%)	RR 0.55 (0.15 to 2.02)	107 fewer per 1000 (from 202 fewer to 243 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide; RR: risk ratio
[1] Anupama 2016
[2] Overall risk of bias judgement: some concerns due to no information provided for sequence randomisation or allocation concealment.

[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] 90% CI used

Table 34: Clinical evidence profile for comparison of Nd:YAG laser versus CO2 laser in participants with moderate to severe atrophic acne scarring

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nd:YAG laser	CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring - Clinical improvement (mild)- Invest. assessed (follow-up 6 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	8/32 (25%)	6/32 (18.8%)	RR 1.33 (0.52 to 3.41)	62 more per 1000 (from 90 fewer to 452 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Clinical improvement (moderate)- Invest. assessed (follow-up 6 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	20/32 (62.5%)	14/32 (43.8%)	RR 1.43 (0.89 to 2.3)	188 more per 1000 (from 48 fewer to 569 more)	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Clinical improvement (good)- Invest. assessed (follow-up 6 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	4/32 (12.5%)	11/32 (34.4%)	RR 0.36 (0.15 to 0.87)[5]	220 fewer per 1000 (from 45 fewer to 292 fewer)	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Clinical improvement (excellent)- Invest. assessed (follow-up 6 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/32 (0%)	1/32 (3.1%)	POR 0.14 (0 to 6.82)	27 fewer per 1000 (from 31 fewer to 182 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nd:YAG laser	CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring - Clinical improvement (mild)- Participant reported (follow-up 6 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	8/32 (25%)	4/32 (12.5%)	RR 2 (0.67 to 5.98)	125 more per 1000 (from 41 fewer to 623 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Clinical improvement (moderate)- Participant reported (follow-up 6 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	21/32 (65.6%)	16/32 (50%)	RR 1.31 (0.86 to 2.01)	155 more per 1000 (from 70 fewer to 505 more)	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Clinical improvement (good)- Participant reported (follow-up 6 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	3/32 (9.4%)	11/32 (34.4%)	RR 0.27 (0.08 to 0.89)	251 fewer per 1000 (from 38 fewer to 316 fewer)	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Clinical improvement (excellent)- Participant reported (follow-up 6 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/32 (0%)	1/32 (3.1%)	POR 0.14 (0 to 6.82)	27 fewer per 1000 (from 31 fewer to 182 more)	⊕OOO VERY LOW	CRITICAL
Side effects- Mild post - inflammatory hyperpigmentation (follow-up 6 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/32 (18.8%)	10/32 (31.3%)	RR 0.6 (0.25 to 1.45)	125 fewer per 1000 (from 234 fewer to 141 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide; Nd:YAG: neodymium-doped yttrium aluminium garnet; POR: Peto odds ratio: RR: risk ratio

[1] Asilian 2011

[2] Overall risk of bias judgement: some concerns due to no details provided on allocation concealment or blinding of personnel or outcomes.

[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] 90% CI usesd.

Table 35: Clinical evidence profile for comparison of Subcision + needling + PRP versus Subcision + needling in participants with severe atrophic acne scarring

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Subcision + needling + PRP	Subcision + needling	Relative (95% CI)	Absolute		
Improvement in scarring - Goodman and Baron scale rating (level 4)- Invest. assessed (follow-up 3 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/15 (0%)	1/15 (6.7%)	POR 0.14 (0 to 6.82)	57 fewer per 1000 (from 67 fewer to 388 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale rating (level 3)- Invest. assessed (follow-up 3 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	10/15 (66.7%)	12/15 (80%)	RR 0.83 (0.54 to 1.29)	136 fewer per 1000 (from 368 fewer to 232 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale rating (level 2)- Invest. assessed (follow-up 3 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	2/15 (13.3%)	RR 2.5 (0.57 to 10.93)	200 more per 1000 (from 57 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Poor (0-24% improvement)- Participant reported (follow-up 3 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/15 (0%)	1/15 (6.7%)	POR 0.14 (0 to 6.82)	57 fewer per 1000 (from 67 fewer to	⊕OOO VERY	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Subcision + needling + PRP	Subcision + needling	Relative (95% CI)	Absolute		
										388 more)	LOW	
Improvement in scarring - Good (25-49% improvement)- Participant reported (follow-up 3 months; assessed with: Quartile grading system)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	3/15 (20%)	9/15 (60%)	RR 0.33 (0.11 to 0.99)	402 fewer per 1000 (from 6 fewer to 534 fewer)	⊕⊕OO LOW	IMPORTANT
Improvement in scarring - Very good (50-74% improvement)- Participant reported (follow-up 3 months; assessed with: Quartile grading system)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	10/15 (66.7%)	4/15 (26.7%)	RR 2.5 (1.16 to 5.38)[5]	400 more per 1000 (from 43 more to 1000 more)	⊕⊕OO LOW	IMPORTANT
Improvement in scarring - Excellent (75-100% improvement)- Participant reported (follow-up 3 months; assessed with: Quartile grading system)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/15 (13.3%)	1/15 (6.7%)	RR 2 (0.2 to 19.78)	67 more per 1000 (from 53 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; POR: Peto odds ratio; PRP: platelet rich plasma; RR: risk ratio
[1] Bhargava 2019
[2] Overall risk of bias judgement: some concerns due to no details provided on sequence randomisation, allocation concealment and blinding of personnel and outcomes.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] 90% CI used.

Table 36: Clinical evidence profile for comparison of Erbium laser versus Microneedling in participants with moderate to severe atrophic acne scarring

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Erbium laser	Microneedling	Relative (95% CI)	Absolute		
Improvement in scarring - Change score from baseline on QGGSPS scale- Invest. assessed (follow-up 6 months; measured with: Brazilian Portuguese Quantitative Global Grading System for Postacne Scarring Instrument ; range of scores: 0-84; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	22	20	-	MD 0.64 lower (1.01 to 0.27 lower)	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Improvement noticed after first treatment- Participant assessed (follow-up 6 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	19/22 (86.4%)	13/20 (65%)	RR 1.33 (0.93 to 1.91)	215 more per 1000 (from 45 fewer to 591 more)	⊕⊕OO LOW	CRITICAL
Participant satisfaction with treatment - Degree of improvement (follow-up 6 months; measured with: 10 point scale ; range of scores: 0-10; Better indicated by higher values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	22	20	-	MD 0.3 higher (0.67 lower to 1.27 higher)	⊕⊕OO LOW	IMPORTANT
Side effects - Crusts (follow-up 6 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	8/20 (40%)	7/20 (35%)	RR 1.14 (0.51 to 2.55)	49 more per 1000 (from 171 fewer to 542 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - Pustules (follow-up 6 months)												
1[1]	randomised	serious[2]	no serious	no serious	very serious[5]	none	1/20	1/20	RR 1.00	0 fewer per	⊕OOO	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Erbium laser	Microneedling	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness			(5%)	(5%)	(0.07 to 14.9)	1000 (from 47 fewer to 695 more)	VERY LOW	
Side effects - Bullae (follow-up 6 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	5/20 (25%)	0/20 (0%)	POR 9.29 (1.46 to 59.09)	-	⊕⊕⊕O MODERATE	IMPORTANT
Side effects - Pain after session (>/=2 hours) (follow-up 6 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/20 (15%)	1/20 (5%)	RR 3 (0.34 to 26.45)	100 more per 1000 (from 33 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - Post-inflammatory hyperpigmentation (follow-up 6 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	3/20 (15%)	0/20 (0%)	POR 8.23 (0.81 to 84.07)	-	⊕⊕OO LOW	IMPORTANT

CI: confidence interval; MD: mean difference; POR: Peto odds ratio: RR: risk ratio
[1] Cachafeiro 2016
[2] Overall risk of bias judgement: some concerns due to no details provided on allocation concealment.
[3] 95% CI crosses 1 MID (0.5x control group SD, for outcome: improvement in scarring =0.48, Satisfaction with treatment= 0.96, Side effects= 0.20).
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

Table 37: Clinical evidence profile for comparison of Er:Glass laser versus Microneedling in participants with atrophic acne scarring (severity of acne not specified)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Er:Glass laser	Microneedling	Relative (95% CI)	Absolute		
Improvement in scarring - Acne scar improvement on ECCA after 1st treatment- Invest. assessed (measured with: ECCA grading scale ; range of scores: 0-540; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	20	20	-	MD 2.5 higher (13.83 lower to 18.83 higher)	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Acne scar improvement on ECCA after 2nd treatment- Invest. assessed (measured with: ECCA grading scale ; range of scores: 0-540; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	20	20	-	MD 1 higher (14.08 lower to 16.08 higher)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Acne scar improvement on ECCA after 3rd treatment- Invest. assessed (measured with: ECCA grading scale ; range of scores: 0-540; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	20	20	-	MD 0.5 lower (14.82 lower to 13.82 higher)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Physician's global assessment (none)- Invest. assessed (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/20 (5%)	2/20 (10%)	RR 0.5 (0.05 to 5.08)	50 fewer per 1000 (from 95 fewer to 408 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Physician's global assessment (slight)- Invest. assessed (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/20 (15%)	5/20 (25%)	RR 0.6 (0.17 to 2.18)	100 fewer per 1000 (from 207 fewer to	⊕OOO VERY	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Er:Glass laser	Microneedling	Relative (95% CI)	Absolute		
										295 more)	LOW	
Improvement in scarring - Physician's global assessment (average)- Invest. assessed (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	5/20 (25%)	5/20 (25%)	RR 1 (0.34 to 2.93)	0 fewer per 1000 (from 165 fewer to 483 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Physician's global assessment (good)- Invest. assessed (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[5]	none	8/20 (40%)	7/20 (35%)	RR 1.14 (0.51 to 2.55)	49 more per 1000 (from 171 fewer to 542 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Physician's global assessment (very good)- Invest. assessed (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/20 (15%)	1/20 (5%)	RR 3 (0.34 to 26.45)	100 more per 1000 (from 33 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment - Improvement (none) (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/20 (5%)	1/20 (5%)	RR 1 (0.07 to 14.9)	0 fewer per 1000 (from 47 fewer to 695 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Improvement (slight) (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[5]	none	4/20 (20%)	8/20 (40%)	RR 0.5 (0.18 to 1.4)	200 fewer per 1000 (from 328 fewer to 160 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Improvement (average) (follow-up 8 weeks; assessed with: 5 point scale)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Er:Glass laser	Microneedling	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	8/20 (40%)	6/20 (30%)	RR 1.33 (0.57 to 3.14)	99 more per 1000 (from 129 fewer to 642 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Improvement (good) (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	5/20 (25%)	4/20 (20%)	RR 1.25 (0.39 to 3.99)	50 more per 1000 (from 122 fewer to 598 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Improvement (very good) (follow-up 8 weeks; assessed with: 5 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	2/20 (10%)	1/20 (5%)	RR 2 (0.2 to 20.33)	50 more per 1000 (from 40 fewer to 966 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - Temporary erythema >5 days (follow-up 8 weeks)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[5]	none	5/20 (25%)	3/20 (15%)	RR 1.67 (0.46 to 6.06)	100 more per 1000 (from 81 fewer to 759 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - Temporary edema >5 days (follow-up 8 weeks)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/20 (15%)	1/20 (5%)	RR 3 (0.34 to 26.45)	100 more per 1000 (from 33 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - Temporary dryness >5 days (follow-up 8 weeks)												
1[5]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	2/20 (10%)	2/20 (10%)	RR 1 (0.16 to 6.42)	0 fewer per 1000 (from 84 fewer to 542 more)	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Er:Glass laser	Microneedling	Relative (95% CI)	Absolute		
Side effects- Induction of acne vulgaris (follow-up 8 weeks)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	2/20 (10%)	0/20 (0%)	POR 7.79 (0.47 to 129.11)	-	⊕OOO VERY LOW	IMPORTANT
Side effects - Temporary post-inflammatory hyperpigmentation (follow-up 8 weeks)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	2/20 (10%)	0/20 (0%)	POR 7.79 (0.47 to 129.11)	-	⊕OOO VERY LOW	IMPORTANT
Side effects - Hypertrophic scars (non-event) (follow-up 8 weeks)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	0/20 (0%)	0/20 (0%)	RD 0 (-0.09 to 0.09)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; ECCA: échelle d'évaluation clinique des cicatrices d'acné; Er: erbium; MD: mean difference; POR: Peto odds ratio; RD: risk difference; RR: risk ratio
[1] Chae 2015
[2] Overall risk of bias judgement: some concerns due to no details provided on sequence randomisation or allocation concealment.
[3] 95% CI crosses 1 MID (0.5x control group SD, for outcome: ECAA 1st treatment= 13.95, Pain during treatment= 0.54).
[4] 95% CI crosses 2 MIDs (0.5x control group SD, for outcome: ECCA 2nd treatment= 13.41, ECCA 3rd treatment= 11.20).
[5] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[6] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

Table 38: Clinical evidence profile for comparison of Glycolic acid peel versus Placebo in participants with mild, moderate, and severe atrophic acne scarring

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Glycolic acid peel**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Improvement in scarring- Good response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/16 (37.5%)	0/14 (0%)	POR 9.64 (1.65 to 56.19)	-	⊕⊕OO LOW	IMPORTANT
Improvement in scarring - Partial response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	9/16 (56.3%)	5/14 (35.7%)	RR 1.57 (0.69 to 3.59)	204 more per 1000 (from 111 fewer to 925 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Minor response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	1/16 (6.3%)	6/14 (42.9%)	RR 0.15 (0.03 to 0.78)[5]	364 fewer per 1000 (from 94 fewer to 416 fewer)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - No response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/16 (0%)	6/14 (42.9%)	POR 0.08 (0.01 to 0.44)	394 fewer per 1000 (from 240 fewer to 424 fewer)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; POR: Peto odds ratio; RR: risk ratio
[1] Erbagci 2000
[2] Overall risk of bias judgement: high risk of bias due to no details provided on sequence randomisation, allocation concealment and many participants lost to follow up.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] 90% CI used.

Table 39: Clinical evidence profile for comparison of Glycolic acid cream versus Placebo in participants with mild, moderate, and severe atrophic acne scarring

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Glycolic acid cream	Placebo	Relative (95% CI)	Absolute		
Improvement in scarring - Good response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/18 (0%)	0/14 (0%)	RD 0 (-0.12 to 0.12)	-	⨁◯◯◯ VERY LOW	CRITICAL
Improvement in scarring - Partial response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	13/18 (72.2%)	5/14 (35.7%)	RR 2.02 (1.07 to 3.82)[5]	364 more per 1000 (from 25 more to 1000 more)	⨁◯◯◯ VERY LOW	CRITICAL
Improvement in scarring - Minor response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	5/18 (27.8%)	6/14 (42.9%)	RR 0.65 (0.25 to 1.69)	150 fewer per 1000 (from 321 fewer to 296 more)	⨁◯◯◯ VERY LOW	CRITICAL
Improvement in scarring - No response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/18 (0%)	6/14 (42.9%)	POR 0.07 (0.01 to 0.38)	399 fewer per 1000 (from 266 fewer to 424 fewer)	⨁⨁◯◯ LOW	CRITICAL

CI: confidence interval; POR: Peto odds ratio; RD: risk difference; RR: risk ratio
[1] Erbagci 2000
[2] Overall risk of bias judgement: high risk of bias due to no details provided on sequence randomisation, allocation concealment and many participants lost to follow up.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
[4] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.
[5] 90% CI used.
[6] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.

Table 40: Clinical evidence profile for comparison of Glycolic acid peel versus Glycolic acid cream in participants with mild, moderate, and severe atrophic acne scarring

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Glycolic acid peel	Glycolic acid cream	Relative (95% CI)	Absolute		
Improvement in scarring - Good response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/16 (37.5%)	0/18 (0%)	POR 12.24 (2.15 to 69.74)	-	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Partial response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	9/16 (56.3%)	13/18 (72.2%)	RR 0.78 (0.46 to 1.31)	159 fewer per 1000 (from 390 fewer to 224 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Minor response- Invest. assessed (assessed with: 10 point scale)												
1	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/16 (6.3%)	5/18 (27.8%)	RR 0.23 (0.03 to 1.73)	214 fewer per 1000 (from 269 fewer to 203 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - No response- Invest. assessed (assessed with: 10 point scale)												
1[1]	randomised trials	very serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/16 (0%)	0/18 (0%)	RD 0 (-0.11 to 0.11)	-	⊕OOO VERY LOW	CRITICAL

CI: confidence interval; POR: Peto odds ratio; RD: risk difference; RR: risk ratio
[1] Erbagci 2000
[2] Overall risk of bias judgement: high risk of bias due to no details provided on sequence randomisation, allocation concealment and many participants lost to follow up.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

Table 41: Clinical evidence profile for comparison of Percutaneous collagen induction versus TCA CROSS in participants with atrophic acne scarring (severity of acne not specified)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Percutaneous collagen induction	TCA CROSS	Relative (95% CI)	Absolute		
Improvement in scarring - Change in scar severity score from baseline- Invest. assessed (follow-up 4 weeks; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	15	12	-	MD 10.30 higher (7.99 lower to 28.59 higher)	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Significant improvement- Invest. assessed (follow-up 4 weeks; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	7/15 (46.7%)	8/12 (66.7%)	RR 0.7 (0.36 to 1.37)	200 fewer per 1000 (from 427 fewer to 247 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Moderate improvement- Invest. assessed (follow-up 4 weeks; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/15 (33.3%)	3/12 (25%)	RR 1.33 (0.4 to 4.49)	83 more per 1000 (from 150 fewer to 872 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Mild improvement- Invest. assessed (follow-up 4 weeks; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/15 (13.3%)	1/12 (8.3%)	RR 1.6 (0.16 to 15.6)	50 more per 1000 (from 70 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Minimal improvement- Invest. assessed (follow-up 4 weeks; assessed with: Quartile grading scale)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Percutaneous collagen induction	TCA CROSS	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/15 (6.7%)	0/12 (0%)	POR 6.05 (0.12 to 312.42)	-	⊕OOO VERY LOW	CRITICAL
Side effects - Report of pain (follow-up 4 weeks; measured with: 10 point scale; range of scores: 0-9; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	15	12	-	MD 1.6 higher (0.28 to 2.92 higher)	⊕⊕OO LOW	IMPORTANT
Side effects - Transient post-inflammatory hyperpigmentation lasting 2 to 6 months (follow-up 4 weeks; assessed with: Survey)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/15 (0%)	6/12 (50%)	POR 0.06 (0.01 to 0.37)	470 fewer per 1000 (from 315 fewer to 495 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects - Second infection (non-event) (follow-up 8 weeks)												
1[6]	randomised trials	serious[7]	no serious inconsistency	no serious indirectness	very serious[8]	none	0/20 (0%)	0/20 (0%)	RD 0 (-0.09 to 0.09)	-	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; MD: mean difference; POR: Peto odds ratio; RD: risk difference; RR: risk ratio; TCA CROSS: trichloroacetic acid chemical reconstruction of skin scars
[1] Leheta 2011
[2] Overall risk of bias judgement: some concerns due to no details provided on sequence randomisation and allocation concealment.
[3] 95% CI crosses 1 MID (0.5x control group SD, for scar severity score= 16.40).
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[5] 95% CI crosses 1 MID (0.5x control group SD, for report of pain= 0.8).
[6] Chae 2015
[7] Overall risk of bias judgement: some concerns due to no details provided on sequence randomisation or allocation concealment.
[8] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

Table 42: Clinical evidence profile for comparison of Percutaneous collagen induction + TCA 20% versus Photothermolysis in participants with atrophic acne scarring (severity of acne not specified)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Percutaneous collagen induction + TCA 20%	Photothermolysis	Relative (95% CI)	Absolute		
Improvement in scarring - Scar severity score (follow-up 12 months; measured with: Acne scar severity scale; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision[3]	none	13	13	-	MD 4.77 lower (18.99 lower to 9.45 higher)	⊕⊕⊕O MODERATE	CRITICAL
Improvement in scarring - Change in scar severity score from baseline (follow-up 12 months; measured with: Acne scar severity scale; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	13	13	-	MD 4.07 higher (17.66 lower to 25.8 higher)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; MD: mean difference; TCA: trichloroacetic acid
[1] Leheta 2014
[2] Overall risk of bias judgement: some concerns due to no details provided on allocation concealment.
[3] MID= 0.5xSD of control at baseline: +/-21.23.
[4] 95% CI crosses 1 MID (0.5x control group SD, for scar severity= 21.23).

Table 43: Clinical evidence profile for comparison of Alternating PCI-TCA + Laser versus Percutaneous collagen induction + TCA 20% in participants with atrophic acne scarring (severity of acne not specified)

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alternating PCI-TCA + Laser	Percutaneous collagen induction + TCA 20%	Relative (95% CI)	Absolute		
Improvement in scarring - Scar severity score (follow-up 12 months; measured with: Acne scar severity scale; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision[3]	none	13	13	-	MD 7.93 lower (18.74 lower to 2.88 higher)	⊕⊕⊕O MODERATE	CRITICAL
Improvement in scarring - Change in scar severity score from baseline (follow-up 12 months; measured with: Acne scar severity scale; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[4]	none	13	13	-	MD 16.7 lower (37.95 lower to 4.55 higher)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; MD: mean difference; PCI: percutaneous collagen induction; TCA: trichloroacetic acid
[1] Leheta 2014
[2] Overall risk of bias judgement: some concerns due to no details provided on allocation concealment.
[3] MID= 0.5xSD of control at baseline: +/-18.88.
[4] 95% CI crosses 1 MID (0.5x control group SD, for scar severity= 18.88).

Table 44: Clinical evidence profile for comparison of Alternating PCI-TCA + Laser versus Photothermolysis in participants with atrophic acne scarring (severity of acne not specified)

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alternating PCI-TCA + Laser	Photothermolysis	Relative (95% CI)	Absolute		
Improvement in scarring - Scar severity score (follow-up 12 months; measured with: Acne scar severity scale; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	13	13	-	MD 12.7 lower (25.09 to 0.31	⊕⊕OO	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Alternating PCI-TCA + Laser	Photothermolysis	Relative (95% CI)	Absolute		
										lower)	LOW	
Improvement in scarring - Change in scar severity score from baseline (follow-up 12 months; measured with: Acne scar severity scale; Better indicated by lower values)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	13	13	-	MD 12.63 lower (35.26 lower to 10 higher)	⊕⊕OO LOW	CRITICAL

CI: confidence interval; MD: mean difference; PCI: percutaneous collagen induction; TCA: trichloroacetic acid
[1] Leheta 2014
[2] Overall risk of bias judgement: some concerns due to no details provided on allocation concealment.
[3] 95% CI crosses 1 MID (0.5x control group SD, for scar severity= 21.23).

Table 45: Clinical evidence profile for comparison of CO2 laser + Needling versus CO2 laser in participants with moderate to severe ice pick acne scarring

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + Needling	CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring - Acne scar severity index (healed)- Invest. assessed (follow-up 3 months; assessed with: Acne scar severity index)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	9/30 (30%)	9/30 (30%)	RR 1 (0.46 to 2.17)	0 fewer per 1000 (from 162 fewer to 351 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Acne scar severity index (mild)- Invest. assessed (follow-up 3 months; assessed with: Acne scar severity index)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + Needling	CO2 laser	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	11/30 (36.7%)	14/30 (46.7%)	RR 0.79 (0.43 to 1.44)	98 fewer per 1000 (from 266 fewer to 205 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Acne scars severity index (moderate)- Invest. assessed (follow-up 3 months; assessed with: Acne scar severity index)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	10/30 (33.3%)	7/30 (23.3%)	RR 1.43 (0.63 to 3.25)	100 more per 1000 (from 86 fewer to 525 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Acne scars severity index (severe)- Invest. assessed (follow-up 3 months; assessed with: Acne scar severity index)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/30 (0%)	0/30 (0%)	RD 0 (-0.06 to 0.06)	-	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron grading scale (macular)- Invest. assessed (follow-up 3 months; assessed with: Goodman and Baron grading scale)												
1[1]	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	9/30 (30%)	10/30 (33.3%)	RR 0.9 (0.43 to 1.9)	33 fewer per 1000 (from 190 fewer to 300 more)	⊕⊕OO LOW	CRITICAL
Improvement in scarring - Goodman and Baron grading scale (mild)- Invest. assessed (follow-up 3 months; assessed with: Goodman and Baron grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	11/30 (36.7%)	13/30 (43.3%)	RR 0.85 (0.45 to 1.58)	65 fewer per 1000 (from 238 fewer to 251 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron grading scale (moderate)- Invest. assessed (follow-up 3 months; assessed with: Goodman and Baron grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	10/30 (33.3%)	7/30 (23.3%)	RR 1.43 (0.63 to 3.25)	100 more per 1000 (from 86 fewer to 525 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CO2 laser + Needling	CO2 laser	Relative (95% CI)	Absolute		
Improvement in scarring - Goodman and Baron grading scale (severe)- Invest. assessed (follow-up 3 months; assessed with: Goodman and Baron grading scale)												
1	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/30 (0%)	0/30 (0%)	RD 0 (-0.06 to 0.06)	-	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment - Excellent improvement (assessed with: 4 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	21/30 (70%)	24/30 (80%)	RR 0.88 (0.65 to 1.17)	96 fewer per 1000 (from 280 fewer to 136 more)	⊕⊕OO LOW	IMPORTANT
Participant satisfaction with treatment - Good improvement (assessed with: 4 point scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	9/30 (30%)	6/30 (20%)	RR 1.5 (0.61 to 3.69)	100 more per 1000 (from 78 fewer to 538 more)	⊕OOO VERY LOW	IMPORTANT

CI: confidence interval; CO2: carbon dioxide; RD: risk difference; RR: risk ratio
[1] Mohammed 2013
[2] Overall risk of bias judgement: some concerns due to no details provided on sequence randomisation or allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
[5] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.

Table 46: Clinical evidence profile for comparison of Intradermal PRP versus TCA CROSS in participants with mild, moderate, and severe atrophic acne scarring

Quality assessment	No of participants	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intradermal PRP	TCA CROSS	Relative (95% CI)	Absolute		
Improvement in scarring - Goodman and Baron scale (grade 1)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 2)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	6/15 (40%)	5/15 (33.3%)	RR 1.2 (0.47 to 3.09)	67 more per 1000 (from 177 fewer to 697 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 3)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/15 (33.3%)	6/15 (40%)	RR 0.83 (0.32 to 2.15)	68 fewer per 1000 (from 272 fewer to 460 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 4)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/15 (26.7%)	4/15 (26.7%)	RR 1 (0.31 to 3.28)	0 fewer per 1000 (from 184 fewer to 608 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Poor improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/15 (33.3%)	6/15 (40%)	RR 0.83 (0.32 to 2.15)	68 fewer per 1000 (from 272 fewer to 460 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Good improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/15 (20%)	5/15 (33.3%)	RR 0.6 (0.17 to 2.07)	133 fewer per 1000 (from 277 fewer to 357 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intradermal PRP	TCA CROSS	Relative (95% CI)	Absolute		
Improvement in scarring - Very good improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/15 (26.7%)	4/15 (26.7%)	RR 1 (0.31 to 3.28)	0 fewer per 1000 (from 184 fewer to 608 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Excellent improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	3/15 (20%)	0/15 (0%)	POR 8.57 (0.82 to 89.45)	-	⊕⊕OO LOW	CRITICAL
Participant satisfaction with treatment- Poor (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Good (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	6/15 (40%)	RR 0.83 (0.32 to 2.15)	68 fewer per 1000 (from 272 fewer to 460 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Very good (assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	7/15 (46.7%)	3/15 (20%)	RR 2.33 (0.74 to 7.35)	266 more per 1000 (from 52 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Excellent (follow-up 2 months; assessed with: Quartile grading scale)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intradermal PRP	TCA CROSS	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/15 (20%)	6/15 (40%)	RR 0.5 (0.15 to 1.64)	200 fewer per 1000 (from 340 fewer to 256 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - No reported adverse effects (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	14/15 (93.3%)	11/15 (73.3%)	RR 1.27 (0.91 to 1.78)	198 more per 1000 (from 66 fewer to 572 more)	⊕⊕OO LOW	IMPORTANT
Side effects - Mild bruises (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/15 (6.7%)	0/15 (0%)	POR 7.39 (0.15 to 372.38)	-	⊕OOO VERY LOW	IMPORTANT
Side effects - Hyperpigmentation (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	0/15 (0%)	4/15 (26.7%)	POR 0.11 (0.01 to 0.85)	237 fewer per 1000 (from 40 fewer to 264 fewer)	⊕⊕OO LOW	IMPORTANT
Side effects - Erythema and edema (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Side effects - Pain (mild) (follow-up 2 months)												
1[1]	randomised	serious[2]	no serious	no serious	no serious	none	6/15	15/15	RR 0.42	580 fewer per	⊕⊕⊕O	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intradermal PRP	TCA CROSS	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness	imprecision		(40%)	(100%)	(0.23 to 0.76)	1000 (from 240 fewer to 770 fewer)	MODERATE	
Side effects - Pain (moderate) (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	3/15 (20%)	0/15 (0%)	POR 8.57 (0.82 to 89.45)	-	⊕⊕OO LOW	IMPORTANT
Side effects - Pain (severe) (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/15 (40%)	0/15 (0%)	POR 11.21 (1.93 to 65.09)	-	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; POR: Peto odds ratio; PRP: platelet rich plasma; RD: risk difference; RR: risk ratio; TCA CROSS: trichloroacetic acid chemical reconstruction of skin scars
[1] Nofal 2014
[2] Overall risk of bias judgement: some concerns due to no details provided on sequence randomisation and allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[5] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.

Table 47: Clinical evidence profile for comparison of Needling + topical PRP versus TCA CROSS in participants with mild, moderate, and severe atrophic acne scarring

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	TCA CROSS	Relative (95% CI)	Absolute		
Improvement in scarring- Goodman and Baron scale (grade 1)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	TCA CROSS	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/15 (6.7%)	0/15 (0%)	POR 7.39 (0.15 to 372.38)	-	⨁◯◯◯ VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 2)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/15 (40%)	5/15 (33.3%)	RR 1.2 (0.47 to 3.09)	67 more per 1000 (from 177 fewer to 697 more)	⨁◯◯◯ VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 3)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	6/15 (40%)	RR 0.83 (0.32 to 2.15)	68 fewer per 1000 (from 272 fewer to 460 more)	⨁◯◯◯ VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 4)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	3/15 (20%)	4/15 (26.7%)	RR 0.75 (0.2 to 2.79)	67 fewer per 1000 (from 213 fewer to 477 more)	⨁◯◯◯ VERY LOW	CRITICAL
Improvement in scarring - Poor improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/15 (26.7%)	6/15 (40%)	RR 0.67 (0.23 to 1.89)	132 fewer per 1000 (from 308 fewer to 356 more)	⨁◯◯◯ VERY LOW	CRITICAL
Improvement in scarring - Good improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/15 (13.3%)	5/15 (33.3%)	RR 0.4 (0.09 to 1.75)	200 fewer per 1000 (from 303 fewer to 250 more)	⨁◯◯◯ VERY LOW	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	TCA CROSS	Relative (95% CI)	Absolute		
Improvement in scarring - Very good improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	7/15 (46.7%)	4/15 (26.7%)	RR 1.75 (0.64 to 4.75)	200 more per 1000 (from 96 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Excellent improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/15 (13.3%)	0/15 (0%)	POR 7.94 (0.47 to 133.26)	-	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment - Poor (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Good (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	6/15 (40%)	RR 0.83 (0.32 to 2.15)	68 fewer per 1000 (from 272 fewer to 460 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Very good (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	3/15 (20%)	RR 1.67 (0.48 to 5.76)	134 more per 1000 (from 104 fewer to 952 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Excellent (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	6/15 (40%)	RR 0.83 (0.32 to	68 fewer per 1000 (from 272 fewer to	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	TCA CROSS	Relative (95% CI)	Absolute		
									2.15)	460 more)		
Side effects - No reported adverse effects (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/15 (0%)	11/15 (73.3%)	POR 0.05 (0.01 to 0.2)	697 fewer per 1000 (from 587 fewer to 726 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects - Mild bruises (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Side effects - Hyperpigmentation (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[5]	none	0/15 (0%)	4/15 (26.7%)	POR 0.11 (0.01 to 0.85)	237 fewer per 1000 (from 40 fewer to 264 fewer)	⊕⊕OO LOW	IMPORTANT
Side effects - Erythema and edema (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15/15 (100%)	0/15 (0%)	POR 47.78 (11.7 to 195.19)	-	⊕⊕⊕O MODERATE	IMPORTANT
Side effects - Pain (mild) (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/15 (13.3%)	15/15 (100%)	RR 0.16 (0.05 to 0.51)	840 fewer per 1000 (from 490 fewer to 950 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects - Pain (moderate) (follow-up 2 months)												
1[1]	randomised	serious[2]	no serious	no serious	no serious	none	7/15	0/15	POR 12.45	-	⊕⊕⊕O	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	TCA CROSS	Relative (95% CI)	Absolute		
	trials		inconsistency	indirectness	imprecision		(46.7%)	(0%)	(2.36 to 65.72)		MODERATE	
Side effects - Pain (severe) (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/15 (40%)	0/15 (0%)	POR 11.21 (1.93 to 65.09)	-	⊕⊕⊕O MODERATE	IMPORTANT

CI: confidence interval; POR: Peto odds ratio; PRP: platelet rich plasma; RD: risk difference; RR: risk ratio; TCA CROSS: trichloroacetic acid chemical reconstruction of skin scars
[1] Nofal 2014
[2] Overall risk of bias judgement: some concerns due to no details provided on sequence randomisation and allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.
[5] Evidence downgraded by 1 level due to risk of serious imprecision as 95% confidence interval crosses 1 default MID for dichotomous outcomes.

Table 48: Clinical evidence profile for comparison of Needling + topical PRP versus Intradermal PRP in participants with mild, moderate, and severe atrophic acne scarring

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	Intradermal PRP	Relative (95% CI)	Absolute		
Improvement in scarring - Goodman and Baron scale (grade 1)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/15 (6.7%)	0/15 (0%)	POR 7.39 (0.15 to 372.38)	-	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 2)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	Intradermal PRP	Relative (95% CI)	Absolute		
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/15 (40%)	6/15 (40%)	RR 1 (0.42 to 2.4)	0 fewer per 1000 (from 232 fewer to 560 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 3)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	5/15 (33.3%)	RR 1 (0.36 to 2.75)	0 fewer per 1000 (from 213 fewer to 583 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Goodman and Baron scale (grade 4)- Invest. assessed (follow-up 2 months; assessed with: Goodman and Baron scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	3/15 (20%)	4/15 (26.7%)	RR 0.75 (0.2 to 2.79)	67 fewer per 1000 (from 213 fewer to 477 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Poor improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/15 (26.7%)	5/15 (33.3%)	RR 0.8 (0.27 to 2.41)	67 fewer per 1000 (from 243 fewer to 470 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Good improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/15 (13.3%)	3/15 (20%)	RR 0.67 (0.13 to 3.44)	66 fewer per 1000 (from 174 fewer to 488 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	Intradermal PRP	Relative (95% CI)	Absolute		
Improvement in scarring - Very good improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	7/15 (46.7%)	4/15 (26.7%)	RR 1.75 (0.64 to 4.75)	200 more per 1000 (from 96 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Improvement in scarring - Excellent improvement- Participant assessed (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/15 (13.3%)	3/15 (20%)	RR 0.67 (0.13 to 3.44)	66 fewer per 1000 (from 174 fewer to 488 more)	⊕OOO VERY LOW	CRITICAL
Participant satisfaction with treatment - Poor (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Good (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	5/15 (33.3%)	RR 1 (0.36 to 2.75)	0 fewer per 1000 (from 213 fewer to 583 more)	⊕OOO VERY LOW	IMPORTANT
Participant satisfaction with treatment - Very good (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	7/15 (46.7%)	RR 0.71 (0.29 to 1.75)	135 fewer per 1000 (from 331 fewer to 350 more)	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	Intradermal PRP	Relative (95% CI)	Absolute		
Participant satisfaction with treatment - Excellent (follow-up 2 months; assessed with: Quartile grading scale)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/15 (33.3%)	3/15 (20%)	RR 1.67 (0.48 to 5.76)	134 more per 1000 (from 104 fewer to 952 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - No reported adverse effects (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/15 (0%)	14/15 (93.3%)	POR 0.03 (0.01 to 0.11)	905 fewer per 1000 (from 831 fewer to 924 fewer)	⊕⊕⊕O MODERATE	IMPORTANT
Side effects - Mild bruises (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/15 (0%)	1/15 (6.7%)	POR 0.14 (0 to 6.82)	57 fewer per 1000 (from 67 fewer to 388 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - Hyperpigmentation (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/15 (0%)	0/15 (0%)	RD 0 (-0.12 to 0.12)	-	⊕OOO VERY LOW	IMPORTANT
Side effects - Erythema and edema (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	15/15 (100%)	0/15 (0%)	POR 47.78 (11.7 to 195.19)	-	⊕⊕⊕O MODERATE	IMPORTANT

Quality assessment							No of participants		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Needling + topical PRP	Intradermal PRP	Relative (95% CI)	Absolute		
Side effects - Pain (mild) (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/15 (13.3%)	6/15 (40%)	RR 0.33 (0.08 to 1.39)	268 fewer per 1000 (from 368 fewer to 156 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - Pain (moderate) (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	7/15 (46.7%)	3/15 (20%)	POR 3.19 (0.72 to 14.19)	438 more per 1000 (from 56 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT
Side effects - Pain (severe) (follow-up 2 months)												
1[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	6/15 (40%)	6/15 (40%)	RR 1 (0.42 to 2.4)	0 fewer per 1000 (from 232 fewer to 560 more)	⊕OOO VERY LOW	IMPORTANT

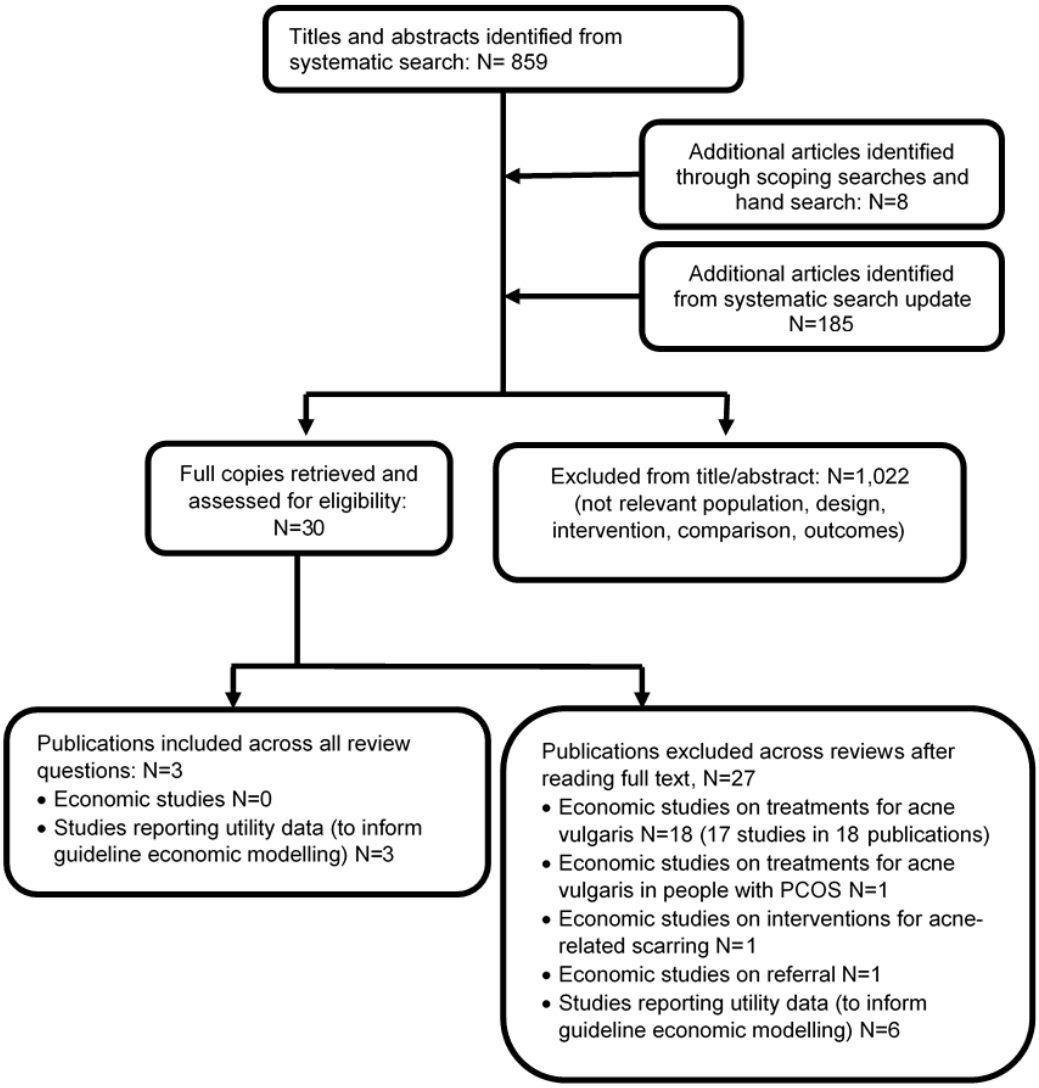
CI: confidence interval; POR: Peto odds ratio; PRP: platelet rich plasma; RD: risk difference; RR: risk ratio; TCA CROSS: trichloroacetic acid chemical reconstruction of skin scars
[1] Nofal 2014
[2] Overall risk of bias judgement: some concerns due to no details provided on sequence randomisation and allocation concealment.
[3] Evidence downgraded by 2 levels due to risk of very serious imprecision as 95% confidence interval crosses 2 default MIDs for dichotomous outcomes.
[4] Evidence downgraded by 2 levels due to risk of very serious imprecision due to small number of events.

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

A global health economics search was undertaken for all areas covered in the guideline. Figure 2 shows the flow diagram of the selection process for economic evaluations of interventions and strategies associated with the care of people with acne vulgaris and studies reporting acne vulgaris-related health state utility data.

Figure 2. Flow diagram of selection process for economic evaluations of interventions and strategies associated with the care of people with acne vulgaris and studies reporting acne vulgaris-related health state utility data



Appendix H – Economic evidence tables

Economic evidence tables for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

No economic evidence was identified which was applicable to this review question.

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

No economic evidence was identified which was applicable to this review question.

Appendix J– Economic analysis

Economic analysis for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

No economic analysis was conducted for this review question**.**

Appendix K – Excluded studies

Excluded clinical and economic studies for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

Clinical studies

Table 49: Excluded clinical studies and reasons for their exclusion

Study	Reason for Exclusion
Randomized, Double-Blind, Split-Face Study Evaluating Fractional Ablative Erbium: YAG Laser-Mediated Trans-Epidermal Delivery of Cosmetic Actives and a Novel Acoustic Pressure Wave Ultrasound Technology for the Treatment of Skin Aging, Melasma, and Acne Scars, Journal of drugs in dermatology : JDD. 14 (11) (pp 1191-1198), 2015. Date of publication: 01 nov 2015., 2015	The intervention did not match the protocol
Comparative study of the efficacy of Platelet-rich plasma combined with carboxytherapy vs its use with fractional carbon dioxide laser in atrophic acne scars, Journal of Cosmetic Dermatology, 2018	No relevant study design - not RCT
Aalami Harandi, S., Balighi, K., Lajevardi, V., Akbari, E., Subcision-suction method: A new successful combination therapy in treatment of atrophic acne scars and other depressed scars, Journal of the European Academy of Dermatology and Venereology, 25, 92-99, 2011	No relevant study design - not RCT
Aamir, S., Ali Rafique Mirza, M., Iqbal, Z., CROSS treatment of acne scars with trichloroacetic acid, Journal of Pakistan Association of Dermatologists, 23, 180-183, 2013	No relevant study design - not RCT
Abdel Aal, A. M., Ibrahim, I. M., Sami, N. A., Abdel Kareem, I. M., Evaluation of autologous platelet-rich plasma plus ablative carbon dioxide fractional laser in the treatment of acne scars, Journal of Cosmetic and Laser Therapy, 20, 106-113, 2018	No relevant study design - not RCT
Abdel Kareem, I. M., Fouad, M. A., Ibrahim, M. K., Effectiveness of subcision using carboxytherapy plus fractional carbon dioxide laser resurfacing in the treatment of atrophic acne scars: comparative split face study, Journal of Dermatological Treatment., 2019	No relevant study design - not RCT
Abou Eitta, R. S., Ismail, A. A., Abdelmaksoud, R. A., Ghezlan, N. A., Mehanna, R. A., Evaluation of autologous adipose-derived stem cells vs. fractional carbon dioxide laser in the treatment of post acne scars: a split-face study, International Journal of Dermatology., 2019	No relevant study design - not RCT
Afra, T. P., Narang, T., Dogra, S., Muhammed Razmi, T., Topical tazarotene as a useful alternative to microneedling in atrophic postacne scarring: a randomized clinical trial, British journal of dermatology. Conference: 98th annual meeting of the british association of dermatologists. United kingdom, 179, 67, 2018	Conference abstract

Afra, T. P., Razmi, T. M., Narang, T., Dogra, S., Kumar, A., Topical Tazarotene Gel, 0.1%, as a Novel Treatment Approach for Atrophic Postacne Scars: A Randomized Active-Controlled Clinical Trial, JAMA facial plastic surgery, 15, 15, 2018	The intervention did not match the protocol
Agarwal, N., Gupta, L. K., Khare, A. K., Kuldeep, C. M., Mittal, A., Therapeutic response of 70% trichloroacetic acid CROSS in atrophic acne scars, Dermatologic surgery, 41, 597-604, 2015	No relevant study design - not RCT
Ahmad, T. J., Muzaffar, F., Nabi, H., Malik, S., Noreen, A., Hayat, R., Efficacy and safety of ablative fractional carbon dioxide laser for acne scars, Journal of Pakistan Association of Dermatologists, 22, 41-44, 2012	No relevant study design - not RCT
Al Qarqaz, F., Al-Yousef, A., Skin microneedling for acne scars associated with pigmentation in patients with dark skin, Journal of Cosmetic Dermatology, 17, 390-395, 2018	No relevant study design - not RCT
Al Taweel, A. A. I., Al Refae, A. A. A. S., Hamed, A. M., Kamal, A. M., Comparative study of the efficacy of Platelet-rich plasma combined with carboxytherapy vs its use with fractional carbon dioxide laser in atrophic acne scars, Journal of Cosmetic Dermatology, 18, 150-155, 2019	No relevant study design - not RCT
Alam, M., Han, S., Pongprutthipan, M., Disphanurat, W., Kakar, R., Nodzenski, M., Pace, N., Kim, N., Yoo, S., Veledar, E., Poon, E., West, D. P., Efficacy of a needling device for the treatment of acne scars: a randomized clinical trial, JAMA DermatologyJAMA Dermatol, 150, 844-9, 2014	Includes both atrophic and hypertrophic acne scars but reported no subgroup analysis
Alam, M., Omura, N., Kaminer, M. S., Subcision for acne scarring: technique and outcomes in 40 patients, Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al.], 31, 310-317; discussion 317, 2005	No relevant study design - not RCT
Al-Dhalimi, M. A., Arnoos, A. A., Subcision for treatment of rolling acne scars in Iraqi patients: A clinical study, Journal of Cosmetic Dermatology, 11, 144-150, 2012	No relevant study design - not RCT
Al-Dhalimi, M., Jaber, A., Treatment of atrophic facial acne scars with fractional Er:Yag laser, Journal of Cosmetic and Laser Therapy, 17, 184-188, 2015	Participants are randomly selected and not randomly assigned to intervention group.
Alexis, A. F., Fractional laser resurfacing for acne scarring in patients with Fitzpatrick skin types IV-VI, Journal of Drugs in Dermatology, 10, s6-s7, 2011	Short summary of a study about the use of fractional laser resurfasing for acne vulgaris scars
Alexis, A. F., Coley, M. K., Nijhawan, R. I., Luke, J. D., Shah, S. K., Argobi, Y. A., Nodzenski, M., Veledar, E., Alam, M., Nonablative Fractional Laser Resurfacing for Acne Scarring in Patients With Fitzpatrick Skin Phototypes IV-VI, Dermatologic SurgeryDermatol Surg, 42, 392-402, 2016	The study assessed the efficacy and safety of 1 intervention, that is lower versus higher density laser setting
Alexis, A., Coley, M., Alam, M., Luke, J., Shah, S., Argobi, Y., A prospective randomized split-face	Conference abstract

comparison study of non-ablative fractional laser resurfacing in the treatment of acne scarring in fitzpatrick skin phototypes IV-VI, Lasers in Surgery and Medicine, 23), 939, 2011	
Alser, O. H., Goutos, I., The evidence behind the use of platelet-rich plasma (PRP) in scar management: a literature review, Scars, Burns & HealingScars Burn Heal, 4, 2059513118808773, 2018	Descriptive review of the use of platelet-rich plasma in scar management
Alster, T. S., McMeekin, T. O., Improvement of facial acne scars by the 585 nm flashlamp-pumped pulsed dye laser, Journal of the American Academy of DermatologyJ Am Acad Dermatol, 35, 79-81, 1996	No relevant study design - not RCT
Alster, T. S., Tanzi, E. L., Lazarus, M., The use of fractional laser photothermolysis for the treatment of atrophic scars, Dermatologic Surgery, 33, 295-299, 2007	No relevant study design - not RCT
Alster, T. S., West, T. B., Resurfacing of atrophic facial acne scars with a high-energy, pulsed carbon dioxide laser, Dermatologic Surgery, 22, 151-155, 1996	No relevant study design - not RCT
Alster, T., Hirsch, R., Single-pass CO2 laser skin resurfacing of light and dark skin: extended experience with 52 patients, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 5, 39-42, 2003	No relevant study design - not RCT
Al-Waiz, M. M., Al-Sharqi, A. I., Medium-depth chemical peels in the treatment of acne scars in dark-skinned individuals, Dermatologic Surgery, 28, 383-387, 2002	No relevant study design - not RCT
Anupama, Y. G., Wahab, A. J., Effectiveness of CO2 laser with subcision in patients with acne scars, Journal of Cosmetic and Laser Therapy, 18, 367â€• 371, 2016	Duplicate.
Apfelberg, D. B., A critical appraisal of high-energy pulsed carbon dioxide laser facial resurfacing for acne scars, Annals of plastic surgery, 38, 95-100, 1997	No relevant study design - not RCT
Arora, S., Bhandaree Gupta, P., Automated microneedling device - A new tool in dermatologist's kit - A review, Journal of Pakistan Association of Dermatologists, 22, 354-357, 2012	Short summary of the use of microneedling for acne scars, hair loss and wrinkles
Arsiwala, S. Z., Subcision with CROSS TCA peels for moderate to severe acne scars, Indian Dermatology Online JournalIndian dermatol, 5, 97-8, 2014	Letter to the Editor
Arsiwala, S., Desai, S., Fractional carbon dioxide laser: Optimizing treatment outcomes for pigmented atrophic acne scars in skin of color, Journal of Cutaneous and Aesthetic Surgery, 12, 85-94, 2019	Article is about the acne scars morphology, pathogenesis, assessment and management options
Artzi, O., Cohen, S., Koren, A., Niv, R., Friedman, O., Dual-plane hyaluronic acid treatment for atrophic acne scars, Journal of Cosmetic Dermatology., 2019	No relevant study design - not RCT
Asif, M., Kanodia, S., Singh, K., Combined autologous platelet-rich plasma with microneedling verses microneedling with distilled water in the treatment of atrophic acne scars: a concurrent split-face study, Journal of Cosmetic Dermatology, 15, 434-443, 2016	No relevant study design - not RCT
Asilian, A., Faghihi, G., Asemi Esfahani, A., Mokhtari, F., Nilforoushzadeh, M., Mozafarpoor, S., Comparison of two	Not reported if participants were not on oral isotretinoin

methods of subcision Nokor and blunt blade in acne scars treatment, Journal of Cosmetic Dermatology., 2019	treatment for at least 6 months before the beginning of the study
Asilian, A., Faghihi, G., Shamoradi, Z., Saber, M., Pourvahedi, B., Hafezi, H., Evaluating the effectiveness of acne scar peeling with salicylic acid 30% in polyethylene glycol vehicle, Journal of isfahan medical school, 36, 1116â€• 1121, 2018	Not in English language
Azzam, O. A., Atta, A. T., Sobhi, R. M., Mostafa, P. I., Fractional CO(2) laser treatment vs autologous fat transfer in the treatment of acne scars: a comparative study, Journal of Drugs in Dermatology: JDD, 12, e7-e13, 2013	No relevant study design - not RCT
Balighi, K., Robati, R. M., Moslehi, H., Robati, A. M., Subcision in acne scar with and without subdermal implant: a clinical trial, Journal of the European Academy of Dermatology & VenereologyJ Eur Acad Dermatol Venereol, 22, 707-11, 2008	No relevant study design - not RCT
Bansal, R., Erbium-glass laser in the treatment of facial scars in patients with dark skin types, British Journal of Dermatology, 177 (Supplement 1), 113-114, 2017	Conference abstract
Battle, F., Battle, S., Clinical Evaluation of Safety and Efficacy of Fractional Radiofrequency Facial Treatment of Skin Type VI Patients, Journal of drugs in dermatology : JDD, 17, 1169 - 1172, 2018	No relevant study design - not RCT
Beer,K., A single-center, open-label study on the use of injectable poly-L-lactic acid for the treatment of moderate to severe scarring from acne or varicella, Dermatologic Surgery, 33 Suppl 2, S159-S167, 2007	No relevant study design - not RCT
Bencini, P. L., Tourlaki, A., Galimberti, M., Longo, C., Pellacani, G., De Giorgi, V., Guerriero, G., Nonablative fractional photothermolysis for acne scars: Clinical and in vivo microscopic documentation of treatment efficacy, Dermatologic Therapy, 25, 463-467, 2012	The study design is a cohort study.
Bernstein, E. F., Double-pass, low-fluence laser treatment using a large spot-size 1,450 nm laser improves acne, Lasers in Surgery and Medicine, 41, 116-121, 2009	No relevant study design - not RCT
Bernstein, E. F., Ferreira, M., Anderson, D., A pilot investigation to subjectively measure treatment effect and side-effect profile of non-ablative skin remodeling using a 532 nm, 2 ms pulse-duration laser, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 3, 137-41, 2001	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Bernstein, E. F., Schomacker, K. T., Basilavecchio, L. D., Plugis, J. M., Bhawalkar, J. D., Treatment of acne scarring with a novel fractionated, dual-wavelength, picosecond-domain laser incorporating a novel holographic beam-splitter, Lasers in Surgery & MedicineLasers Surg Med, 49, 796-802, 2017	The study design is a prospective cohort study
Bhardwaj, D., Khunger, N., An Assessment of the Efficacy and Safety of CROSS Technique with 100% TCA in the Management of Ice Pick Acne Scars, Journal of Cutaneous & Aestheic SurgeryJ, 3, 93-6, 2010	No relevant study design - not RCT

Bhargava, S., Cunha, P. R., Lee, J., Kroumpouzos, G., Acne Scarring Management: Systematic Review and Evaluation of the Evidence, American Journal of Clinical DermatologyAm J Clin Dermatol, 09, 09, 2018	Included studies were checked for a potential inclusion in this review
Biesman, B. S., Cohen, J. L., DiBernardo, B. E., Emer, J. J., Geronemus, R. G., Gold, M. H., Lehman, A. S., Pilcher, B. K., Monheit, G. D., Schlesinger, T. E., Teller, C. F., Treatment of Atrophic Facial Acne Scars With Microneedling Followed by Polymethylmethacrylate-Collagen Gel Dermal Filler, Dermatologic Surgery, 20, 20, 2019	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Bjorn, M., Stausbol-Gron, B., Braae Olesen, A., Hedelund, L., Treatment of acne scars with fractional CO2 laser at 1-month versus 3-month intervals: an intra-individual randomized controlled trial, Lasers in Surgery & MedicineLasers Surg Med, 46, 89-93, 2014	The study assessed the efficacy and safety of 1 intervention, that is fractional CO laser at 1-month versus 3-month intervals
Bonati, L. M., Epstein, G. K., Strugar, T. L., Microneedling in All Skin Types: A Review, Journal of Drugs in Dermatology: JDDJ Drugs Dermatol, 16, 308-313, 2017	Included studies were checked for a potential inclusion in this review
Brauer, J. A., Kazlouskaya, V., Alabdulrazzaq, H., Bae, Y. S., Bernstein, L. J., Anolik, R., Heller, P. A., Geronemus, R. G., Use of a picosecond pulse duration laser with specialized optic for treatment of facial acne scarring, JAMA Dermatology, 151, 278-284, 2015	No relevant study design - not RCT
Bulbul Baskan, E., Akin Belli, A., Evaluation of the efficacy of microneedle fractional radiofrequency in Turkish patients with atrophic facial acne scars, Journal of Cosmetic Dermatology, 11, 11, 2018	No relevant study design - not RCT
Cameli, N., Mariano, M., Serio, M., Ardigo, M., Preliminary comparison of fractional laser with fractional laser plus radiofrequency for the treatment of acne scars and photoaging, Dermatologic SurgeryDermatol Surg, 40, 553-61, 2014	No relevant study design - not RCT
Casabona, G., Combined use of microfocused ultrasound and a calcium hydroxylapatite dermal filler for treating atrophic acne scars: A pilot study, Journal of Cosmetic and Laser Therapy, 20, 301-306, 2018	No relevant study design - not RCT
Chae, W. S., Suh, H. S., Choi, Y. S., A Comparative Study of the Efficacy and Safety of 100% TCA CROSS and Phenol CROSS for Atrophic Acne Scarring, Korean j dermatol, 52, 293â€• 301, 2014	Not in English language
Chan, N. P. Y., Ho, S. G. Y., Yeung, C. K., Shek, S. Y. N., Chan, H. H., The use of non-ablative fractional resurfacing in Asian acne scar patients, Lasers in Surgery and Medicine, 42, 710-715, 2010	No relevant study design - not RCT
Chan, N. P., Ho, S. G., Yeung, C. K., Shek, S. Y., Chan, H. H., Fractional ablative carbon dioxide laser resurfacing for skin rejuvenation and acne scars in Asians, Lasers in Surgery & MedicineLasers Surg Med, 42, 615-23, 2010	No relevant study design - not RCT
Chandrashekar, B. S., Sriram, R., Mysore, R., Bhaskar, S., Shetty, A., Evaluation of microneedling fractional radiofrequency device for treatment of acne scars,	No relevant study design - not RCT

Journal of Cutaneous & Aestheic SurgeryJ, 7, 93-7, 2014	
Chang, H. C., Sung, C. W., Lin, M. H., Efficacy of Autologous Platelet-Rich Plasma Combined With Ablative Fractional Carbon Dioxide Laser for Acne Scars: A Systematic Review and Meta-Analysis, Aesthetic Surgery Journal, 27, 27, 2019	Included studies were checked for a potential inclusion in this review
Chapas, A. M., Brightman, L., Sukal, S., Hale, E., Daniel, D., Bernstein, L. J., Geronemus, R. G., Successful treatment of acneiform scarring with CO2 ablative fractional resurfacing, Lasers in Surgery & MedicineLasers Surg Med, 40, 381-6, 2008	No relevant study design - not RCT
Chathra, N., Mysore, V., Resurfacing of facial acne scars with a new variable-pulsed Er:YAG laser in Fitzpatrick skin types IV and v, Journal of Cutaneous and Aesthetic Surgery, 11, 20-25, 2018	No relevant study design - not RCT
Chawla, S., Split Face Comparative Study of Microneedling with PRP Versus Microneedling with Vitamin C in Treating Atrophic Post Acne Scars, Journal of Cutaneous & Aestheic SurgeryJ, 7, 209-12, 2014	No relevant study design - not RCT
Cho, S. B., Lee, S. J., Kang, J. M., Kim, Y. K., Chung, W. S., Oh, S. H., The efficacy and safety of 10,600-nm carbon dioxide fractional laser for acne scars in Asian patients, Dermatologic Surgery, 35, 1955-1961, 2009	No relevant study design - not RCT
Cho, S. I., Chung, B. Y., Choi, M. G., Baek, J. H., Cho, H. J., Park, C. W., Lee, C. H., Kim, H. O., Evaluation of the clinical efficacy of fractional radiofrequency microneedle treatment in acne scars and large facial pores, Dermatologic Surgery, 38, 1017-1024, 2012	No relevant study design - not RCT
Cohen, B. E., Brauer, J. A., Geronemus, R. G., Acne scarring: A review of available therapeutic lasers, Lasers in Surgery and Medicine, 48, 95-115, 2016	Included studies were checked for a potential inclusion in this review
Dai, R., Xie, H., Hua, W., Li, X. H., Li, L., The efficacy and safety of the fractional radiofrequency technique for the treatment of atrophic acne scar in Asians: A meta-analysis, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 19, 337-344, 2017	Included studies were checked for a potential inclusion in this review
Davari, P., Gorouhi, F., Jafarian, S., Dowlati, Y., Firooz, A., A randomized investigator-blind trial of different passes of microdermabrasion therapy and their effects on skin biophysical characteristics, International Journal of Dermatology, 47, 508-513, 2008	One participant out of 10 had acne vulgaris scars
Deng, H., Yuan, D., Yan, C., Lin, X., Ding, X., A 2940 nm fractional photothermolysis laser in the treatment of acne scarring: A pilot study in China, Journal of Drugs in Dermatology, 8, 978-980, 2009	No relevant study design - not RCT
Deshmukh, N. S., Belgaumkar, V. A., Platelet-Rich Plasma Augments Subcision in Atrophic Acne Scars: A Split-Face Comparative Study, Dermatologic Surgery, 45, 90-98, 2019	No relevant study design - not RCT
Dierickx, C., Larsson, M. K., Blomster, S., Effectiveness and Safety of Acne Scar Treatment With Nonanimal Stabilized Hyaluronic Acid Gel, Dermatologic surgery :	No relevant study design - not RCT

official publication for American Society for Dermatologic Surgery [et al.], 44, S10-S18, 2018	
Dogra, S., Yadav, S., Sarangal, R., Microneedling for acne scars in Asian skin type: an effective low cost treatment modality, Journal of Cosmetic DermatologyJ, 13, 180-7, 2014	No relevant study design - not RCT
Dreno, B., Katsambas, A., Pelfini, C., Plantier, D., Jancovici, E., Ribet, V., Nocera, T., Morinet, P., Khammari, A., Combined 0.1% retinaldehyde/6% glycolic acid cream in prophylaxis and treatment of acne scarring, Dermatology, 214, 260-267, 2007	Not relevant intervention
Elcin, G., Yalici-Armagan, B., Fractional carbon dioxide laser for the treatment of facial atrophic acne scars: prospective clinical trial with short and long-term evaluation, Lasers in Medical ScienceLasers Med Sci, 32, 2047-2054, 2017	No relevant study design - not RCT
El-Domyati, M., Abdel-Wahab, H., Hossam, A., Microneedling combined with platelet-rich plasma or trichloroacetic acid peeling for management of acne scarring: A split-face clinical and histologic comparison, Journal of Cosmetic DermatologyJ, 17, 73-83, 2018	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
El-Domyati, M., Barakat, M., Awad, S., Medhat, W., El-Fakahany, H., Farag, H., Microneedling therapy for atrophic acne scars an objective evaluation, Journal of Clinical and Aesthetic Dermatology, 8, 36-42, 2015	No relevant study design - not RCT
Elsaie, M. L., Ibrahim, S. M., Saudi, W., Ablative Fractional 10 600 nm Carbon Dioxide Laser Versus Non-ablative Fractional 1540 nm Erbium-Glass Laser in Egyptian Post-acne Scar patients, 9, 32-35, 2018	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Engin, B., Kutlubay, Z., Karakus, O., Yardimci, G., Dogan, Z., Tuzun, Y., Serdaroglu, S., Evaluation of effectiveness of erbium:yttrium-aluminum-garnet laser on atrophic facial acne scars with 22-MHz digital ultrasonography in a Turkish population, Journal of Dermatology, 39, 982-988, 2012	No relevant study design - not RCT
Epstein, R. E., Spencer, J. M., Correction of atrophic scars with artefill: An open-label pilot study, Journal of Drugs in Dermatology, 9, 1062-1064, 2010	No relevant study design - not RCT
Erdmann, C. M., Lasers, peels, injections and masks. An overview of treatment modalities for scars, Advance for Nurse PractitionersAdv Nurse Pract, 15, 45-46, 49-4650, 52, 2007	Narrative review on treatment options for acne-related scars
Erol, O.O., Gurlek, A., Agaoglu, G., Topcuoglu, E., Oz, H. Treatment of hypertrophic scars and keloids using intense pulsed light (IPL). Aesthetic Plast Surg, 32(6):902-9, 2008	No relevant study design - not RCT
Fabbrocini, G., Fardella, N., Monfrecola, A., Proietti, I., Innocenzi, D., Acne scarring treatment using skin needling, Clinical and Experimental Dermatology, 34, 874-879, 2009	No relevant study design - not RCT

Fabbrocini, G., Marasca, C., Ammad, S., Brazzini, B., Izzo, R., Donnarumma, M., Monfrecola, G., Assessment of the combined efficacy of needling and the use of silicone gel in the treatment of C-section and other surgical hypertrophic scars and keloids, Advances in skin & wound care, 29, 408â€• 411, 2016	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Firooz, A., Rajabi-Estarabadi, A., Nassiri-Kashani, M. H., Treatment of atrophic facial acne scars with fractional Er:YAG laser in skin phototype III-IV: A pilot study, Journal of Cosmetic and Laser Therapy, 18, 204-207, 2016	No relevant study design - not RCT
Fitzpatrick, R. E., Treatment of inflamed hypertrophic scars using intralesional 5-FU, Dermatologic Surgery, 25, 224-32, 1999	No relevant study design - not RCT
Fliegelman, M. T., Loveman, A. B., Dermabrasion in the treatment of acneform and other types of scarring, The Journal of the Kentucky State Medical AssociationJ Ky State Med Assoc, 56, 367-9, 1958	Short summary about the dermabrasion technique for acne and other scars
Forbat, E., Al-Niaimi, F., Fractional radiofrequency treatment in acne scars: Systematic review of current evidence, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 18, 442-447, 2016	Included studies were checked for a potential inclusion in this review
Friedman, P. M., Jih, M. H., Skover, G. R., Payonk, G. S., Kimyai-Asadi, A., Geronemus, R. G., Treatment of atrophic facial acne scars with the 1064-nm Q-switched Nd:YAG laser: Six-month follow-up study, Archives of Dermatology, 140, 1337-1341, 2004	No relevant study design - not RCT
Gadkari, R., Nayak, C., A split-face comparative study to evaluate efficacy of combined subcision and dermaroller against combined subcision and cryoroller in treatment of acne scars, Journal of Cosmetic DermatologyJ, 13, 38-43, 2014	Participants were excluded if they used oral isotretinoin 3 months before the study and not 6 months
Garg, S., Baveja, S., Combination therapy in the management of atrophic acne scars, Journal of Cutaneous & Aestheic SurgeryJ, 7, 18-23, 2014	No relevant study design - not RCT
Garret, A. B., Dufresne Jr, R. G., Ratz, J. L., Berlin, A. J., Carbon dioxide laser treatment of pitted acne scarring, Journal of Dermatologic Surgery and Oncology, 16, 737-740, 1990	No relevant study design - not RCT
Gheisari, M., Iranmanesh, B., Saghi, B., Blunt cannula subcision is more effective than Nokor needle subcision for acne scars treatment, Journal of Cosmetic Dermatology, 18, 192-196, 2019	No relevant study design - not RCT
Gold, M. H., Biron, J. A., Treatment of acne scars by fractional bipolar radiofrequency energy, Journal of Cosmetic and Laser Therapy, 14, 172-178, 2012	No relevant study design - not RCT
Gold, M. H., Heath, A. D., Biron, J. A., Clinical evaluation of the SmartSkinTM fractional laser for the treatment of photodamage and acne scars, Journal of Drugs in Dermatology, 8, s4-s8, 2009	No relevant study design - not RCT
Gold, M. H., Wilson, A., Mordon, S. R., Treatment of acne scarring with a novel dual-wavelength laser, Journal of	No relevant study design - not RCT

Cosmetic Dermatology., 2019	
Goldberg, D. J., Amin, S., Hussain, M., Acne scar correction using calcium hydroxylapatite in a carrier-based gel, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 8, 134-6, 2006	No relevant study design - not RCT
Goldman, M. P., Manuskiatti, W., Combined laser resurfacing with the 950-microsec pulsed CO2 + Er:YAG lasers, Dermatologic SurgeryDermatol Surg, 25, 160-3, 1999	Study population are people with photo-damaged skin
Gonzalez, M. J., Sturgill, W. H., Ross, E. V., Uebelhoer, N. S., Treatment of acne scars using the plasma skin regeneration (PSR) system, Lasers in Surgery & MedicineLasers Surg Med, 40, 124-7, 2008	No relevant study design - not RCT
Halachmi, S., Orenstein, A., Meneghel, T., Lapidoth, M., A novel fractional micro-plasma radio-frequency technology for the treatment of facial scars and rhytids: A pilot study, Journal of Cosmetic and Laser Therapy, 12, 208-212, 2010	No relevant study design - not RCT
Harris, A. G., Naidoo, C., Murrell, D. F., Skin needling as a treatment for acne scarring: An up-to-date review of the literature, International Journal Of Women.s DermatologyInt J Womens Dermatol, 1, 77-81, 2015	Included studies were checked for a potential inclusion in this review
Hasegawa, T., Matsukura, T., Mizuno, Y., Suga, Y., Ogawa, H., Ikeda, S., Clinical trial of a laser device called fractional photothermolysis system for acne scars, Journal of DermatologyJ Dermatol, 33, 623-7, 2006	No relevant study design - not RCT
Hayashi, T., Furukawa, H., Oyama, A., Funayama, E., Saito, A., Murao, N., Yamamoto, Y., A new uniform protocol of combined corticosteroid injections and ointment application reduces recurrence rates after surgical keloid/hypertrophic scar excision, Dermatologic Surgery, 38, 893-897, 2012	No relevant study design - not RCT
Hedelund, L., Moreau, K. E., Beyer, D. M., Nymann, P., Haedersdal, M., Fractional nonablative 1,540-nm laser resurfacing of atrophic acne scars. A randomized controlled trial with blinded response evaluation, Lasers in Medical ScienceLasers Med Sci, 25, 749-54, 2010	Main results reported as medians. No results for other outcomes for control group reported
Hedelund, L., Winther, K. V., Beyer, D. M., Nymann, P., Hædersdal, M., Fractional nonablative 1540 nm laser resurfacing for atrophic acne scars: a randomized controlled trial, Lasers in Surgery and Medicine, 41, 87â€• 88, 2009	Conference abstract
Hee, J. K., Tae, G. K., Yeon, S. K., Jin, M. P., Ju, H. L., Comparison of a 1,550nm Erbium:Glass fractional laser and a chemical reconstruction of skin scars (CROSS) method in the treatment of acne scars: A simultaneous split-face trial, Lasers in Surgery and Medicine, 41, 545-549, 2009	Data not useful for an analysis as no standard deviations reported or data reported in figures
Hesseler, M. J., Shyam, N., Platelet-rich plasma and its utility in the treatment of acne scars: A systematic review, Journal of the American Academy of Dermatology, 80, 1730-1745, 2019	Included studies were checked for a potential inclusion in this review

Hsiao, P. F., Lin, Y. C., Huang, C. C., Wu, Y. H., Efficacy and safety of a single treatment using a 10,600-nm carbon dioxide fractional laser for mild-to-moderate atrophic acne scars in Asian skin, Dermatologica Sinica, 31, 59-63, 2013	No relevant study design - not RCT
Hu, S., Chen, M. C., Lee, M. C., Yang, L. C., Keoprasom, N., Fractional resurfacing for the treatment of atrophic facial acne scars in asian skin, Dermatologic surgery, 35, 826-832, 2009	No relevant study design - not RCT
Hu, S., Gold, M. H., Treatment of facial acne scars in asian skin with the single-spot, 2940-nm Er:YAG dual-mode laser, Journal of drugs in dermatology, 9, 1341-1344, 2010	Not an RCT
Hu, S., Hsiao, W. C., Chen, M. C., Huang, Y. L., Chang, S. L., Shih, P. Y., Gold, M. H., Ablative fractional erbium-doped yttrium aluminum garnet laser with coagulation mode for the treatment of atrophic acne scars in Asian skin, Dermatologic Surgery, 37, 939-944, 2011	No relevant study design - not RCT
Huang, C. H., Chern, E., Peng, J. H., Peng, P. H. L., Noninvasive Atrophic Acne Scar Treatment in Asians With a 755-nm Picosecond Laser Using A Diffractive Optic Lens - A Retrospective Photographic Review, Dermatologic Surgery, 45, 195-202, 2019	No relevant study design - not RCT
Huang, L., A new modality for fractional CO2 laser resurfacing for acne scars in Asians, Lasers in Medical Science, 28, 627-632, 2013	No relevant study design - not RCT
Ibrahim, M. K., Ibrahim, S. M., Salem, A. M., Skin microneedling plus platelet-rich plasma versus skin microneedling alone in the treatment of atrophic post acne scars: a split face comparative study, Journal of Dermatological Treatment, 29, 281-286, 2018	No relevant study design - not RCT
Ibrahim, Z. A., El-Ashmawy, A. A., Shora, O. A., Therapeutic effect of microneedling and autologous platelet-rich plasma in the treatment of atrophic scars: A randomized study, Journal of Cosmetic DermatologyJ, 16, 388-399, 2017	Mixed population, that is participants had acne vulgaris, post-chickenpox or post-traumatic scars; no subgroup analysis by acne scar type reported
Isarria, M. J., Cornejo, P., Munoz, E., Royo de la Torre, J., Moraga, J. M., Evaluation of clinical improvement in acne scars and active acne in patients treated with the 1540-nm non-ablative fractional laser, Journal of Drugs in Dermatology: JDDJ Drugs Dermatol, 10, 907-12, 2011	No relevant study design - not RCT
Jordan, R. E., Cummins, C. L., Burls, A. J., Seukeran, D. C., Laser resurfacing for facial acne scars, Cochrane Database of Systematic ReviewsCochrane Database Syst Rev, CD001866, 2001	No randomised controlled trials were identified
Jordan, R., Cummins, C. C., Burls, A., Seukeran, D. D., Laser resurfacing for facial acne scars, Cochrane Database of Systematic Reviews, 2016 (4) (no pagination), 2016	This Cochrane review has been withdrawn as it has been updated by way of a new protocol and then a review, as the scope of the review has substantially expanded (Hay et al. 2016)

Jordan, R., Cummins, C., Burls, A., Laser resurfacing of the skin for the improvement of facial acne scarring: a systematic review of the evidence, British Journal of DermatologyBr J Dermatol, 142, 413-23, 2000	Included studies were checked for a potential inclusion in this review
Joseph, J. H., Shamban, A., Eaton, L., Lehman, A., Cohen, S., Spencer, J., Bruce, S., Grimes, P., Tedaldi, R., Callender, V., Werschler, P., Polymethylmethacrylate Collagen Gel-Injectable Dermal Filler for Full Face Atrophic Acne Scar Correction, Dermatologic Surgery, 15, 15, 2019	No relevant study design - not RCT
Jung, J. Y., Lee, J. H., Ryu, D. J., Lee, S. J., Bang, D., Cho, S. B., Lower-fluence, higher-density versus higher-fluence, lower-density treatment with a 10,600-nm carbon dioxide fractional laser system: A split-face, evaluator-blinded study, Dermatologic Surgery, 36, 2022-2029, 2010	The study assessed the efficacy and safety of 1 intervention, that is lower-fluence, higher-density versus higher-fluence, lower-density treatment with a CO fractional laser
Jung, K. E., Jung, K. H., Park, Y. M., Lee, J. Y., Kim, T. Y., Kim, H. O., Kim, H. S., A Split-face comparison of ablative fractional lasers (CO<inf>2</inf> and Er:YAG) in Asian patients; Postprocedure erythema, pain and patient's satisfaction, Journal of Cosmetic and Laser Therapy, 15, 70-73, 2013	No relevant study design - not RCT
Jurassich, S., Lo Schiavo, A., Pinto, F., Nacca, M., Vacuum skin-abrasion versus glycolic acid peeling in the treatment of atrophic acne scars, Journal of Applied Cosmetology, 14, 127-132, 1996	No relevant study design - not RCT
Kang, W. H., Kim, Y. J., Pyo, W. S., Park, S. J., Kim, J. H., Atrophic acne scar treatment using triple combination therapy: Dot peeling, subcision and fractional laser, Journal of Cosmetic and Laser Therapy, 11, 212-215, 2009	No relevant study design - not RCT
Kar, B. R., Raj, C., Fractional CO₂ Laser vs Fractional CO₂ with Topical Platelet-rich Plasma in the Treatment of Acne Scars: A Split-face Comparison Trial, Journal of Cutaneous & Aestheic SurgeryJ, 10, 136-144, 2017	No relevant study design - not RCT
Karabut, M. M., Gladkova, N. D., Feldchtein, F. I., Fractional laser photothermolysis in the treatment of skin defects: Possibilities and effectiveness (review), Sovremennye Tehnologii v Medicine, 8, 98-107, 2016	Review on fractional laser photothermolysis for improvement of various skin conditions
Karnik, J., Baumann, L., Bruce, S., Callender, V., Cohen, S., Grimes, P., Joseph, J., Shamban, A., Spencer, J., Tedaldi, R., et al.,, A double-blind, randomized, multicenter, controlled trial of suspended polymethylmethacrylate microspheres for the correction of atrophic facial acne scars, Journal of the American Academy of Dermatology, 71, 77â€• 83, 2014	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Katz, B., Efficacy of a new fractional CO2 laser in the treatment of photodamage and acne scarring, Dermatologic Therapy, 23, 403-6, 2010	No relevant study design - not RCT
Kaur, J., Kalsy, J., Subcision plus 50% trichloroacetic acid chemical reconstruction of skin scars in the	Letter to the Editor

management of atrophic acne scars: A cost-effective therapy, Indian Dermatology Online JournalIndian dermatol, 5, 95-7, 2014	
Keller, R., Belda Junior, W., Valente, N. Y., Rodrigues, C. J., Nonablative 1,064-nm Nd:YAG laser for treating atrophic facial acne scars: histologic and clinical analysis, Dermatologic Surgery, 33, 1470-6, 2007	No relevant study design - not RCT
Khunger, N., Bhardwaj, D., Khunger, M., Evaluation of CROSS technique with 100% TCA in the management of ice pick acne scars in darker skin types, Journal of Cosmetic DermatologyJ, 10, 51-7, 2011	No relevant study design - not RCT
Kim, C. N. T., Thi, L. P., Van, T. N., Minh, P. P. T., Nguyet, M. V., Thi, M. L., Huu, N. D., Hau, K. T., Gandolfi, M., Satolli, F., Feliciani, C., Vojvodic, A., Tirant, M., Lotti, T., Successful Treatment of Facial Atrophic Acne Scars by Fractional Radiofrequency Microneedle in Vietnamese Patients, Open Access Macedonian Journal of Medical Sciences, 7, 192-194, 2019	No relevant study design - not RCT
Kim, H. J., Kim, T. G., Kwon, Y. S., Park, J. M., Lee, J. H., Comparison of a 1,550 nm Erbium: glass fractional laser and a chemical reconstruction of skin scars (CROSS) method in the treatment of acne scars: a simultaneous split-face trial, Lasers in Surgery & MedicineLasers Surg Med, 41, 545-9, 2009	Data not useful for an analysis as no standard deviations reported or data reported in figures
Kim, S., Treatment of acne scars in asian patients using a 2,790-nm fractional Yttrium scandium gallium garnet laser, Dermatologic Surgery, 37, 1464-1469, 2011	No relevant study design - not RCT
Kim, S., Cho, K. H., Clinical trial of dual treatment with an ablative fractional laser and a nonablative laser for the treatment of acne scars in Asian patients, Dermatologic SurgeryDermatol Surg, 35, 1089-98, 2009	Participants were excluded if they used isotretinoin within 2 months of the study and not 6 months
Koren, A., Isman, G., Cohen, S., Bar Ilan, E., Salameh, F., Sprecher, E., Artzi, O., Efficacy of a combination of diluted calcium hydroxylapatite-based filler and an energy-based device for the treatment of facial atrophic acne scars, Clinical & Experimental DermatologyClin Exp Dermatol, 21, 21, 2019	No relevant study design - not RCT
Kravvas, G., Al-Niaimi, F., A systematic review of treatments for acne scarring. Part 2: Energy-based techniques, Scars, Burns & HealingScars Burn Heal, 4, 2059513118793420, 2018	Included studies were checked for a potential inclusion in this review
Kravvas, G., Al-Niaimi, F., A systematic review of treatments for acne scarring. Part 1: Non-energy-based techniques, Scars, Burns & HealingScars Burn Heal, 3, 2059513117695312, 2017	Included studies were checked for a potential inclusion in this review
Kurokawa, I., Oiso, N., Kawada, A., Adjuvant alternative treatment with chemical peeling and subsequent iontophoresis for postinflammatory hyperpigmentation, erosion with inflamed red papules and non-inflamed atrophic scars in acne vulgaris, Journal of Dermatology, 44, 401-405, 2017	No relevant study design - not RCT
Kutlubay, Z., Gokdemir, G., Treatment of atrophic facial acne scars with the Er:YAG laser: A Turkish experience,	No relevant study design - not RCT

Journal of Cosmetic and Laser Therapy, 12, 65-72, 2010	
Kwon, H. H., Park, H. Y., Choi, S. C., Bae, Y., Jung, J. Y., Park, G. H., Combined fractional treatment of acne scars involving non-ablative 1,550-nm erbium-glass laser and micro-needling radiofrequency: A 16-week prospective, randomized split-face study, Acta Dermato-Venereologica, 97, 947-951, 2017	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Kwon, H. H., Park, H. Y., Choi, S. C., Bae, Y., Jung, J. Y., Park, G. H., Novel device-based acne treatments: comparison of a 1450-nm diode laser and microneedling radiofrequency on mild-to-moderate acne vulgaris and seborrhoea in Korean patients through a 20-week prospective, randomized, split-face study, Journal of the European Academy of Dermatology & VenereologyJ Eur Acad Dermatol Venereol, 32, 639-644, 2018	Participants were not on oral isotretinoin treatment for 3 and not for at least 6 months before the beginning of the study
Lan, T., Xiao, Y., Tang, L., Hamblin, M. R., Yin, R., Treatment of atrophic acne scarring with fractional micro-plasma radio-frequency in Chinese patients: A prospective study, Lasers in Surgery and Medicine, 50, 844-850, 2018	No relevant study design - not RCT
Layton, A.M., Yip, J. Cunliffe WJ.A comparison of intralesional triamcinolone and cryosurgery in the treatment of acne keloids. Br J Dermatol, 130(4):498-501, 1994	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Lee, H. J., Lee, E. G., Kang, S., Sung, J. H., Chung, H. M., Kim, D. H., Efficacy of microneedling plus human stem cell conditioned medium for skin rejuvenation: a randomized, controlled, blinded split-face study, 26, 584-91, 2014	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Lee, H. S., Lee, J. H., Ahn, G. Y., Lee, D. H., Shin, J. W., Kim, D. H., Chung, J. H., Fractional photothermolysis for the treatment of acne scars: A report of 27 Korean patients, Journal of Dermatological Treatment, 19, 45-49, 2008	No relevant study design - not RCT
Lee, J. B., Chung, W. G., Kwahck, H., Lee, K. H., Focal treatment of acne scars with trichloroacetic acid: chemical reconstruction of skin scars method, Dermatologic Surgery, 28, 1017-21; discussion 1021, 2002	No relevant study design - not RCT
Lee, J. W., Kim, B. J., Kim, M. N., Lee, C. K., Treatment of Acne scars using subdermal minimal surgery technology, Dermatologic Surgery, 36, 1281-1287, 2010	No relevant study design - not RCT
Lee, J. W., Kim, B. J., Kim, M. N., Mun, S. K., The efficacy of autologous platelet rich plasma combined with ablative carbon dioxide fractional resurfacing for acne scars: a simultaneous split-face trial, Dermatologic SurgeryDermatol Surg, 37, 931-8, 2011	Study does not specify the types of acne scars
Lee, S. J., Kang, J. M., Chung, W. S., Kim, Y. K., Kim, H. S., Ablative non-fractional lasers for atrophic facial acne scars: A new modality of erbium:YAG laser resurfacing in Asians, Lasers in Medical Science, 29, 615-619, 2014	No relevant study design - not RCT
Lee, S. J., Suh, D. H., Chang, K. Y., Kim, H. J., Kim, T. I., Jeong, K. H., Shin, M. K., Song, K. Y., The efficacy and	No relevant study design - not RCT

safety of subcision using CO<inf>2</inf> gas combined with fractional laser for acne scars: Clinical and microscopic evaluation, Journal of Cosmetic and Laser Therapy, 18, 417-420, 2016	
Leheta, T. M., Abdel Hay, R. M., El Garem, Y. F., Deep peeling using phenol versus percutaneous collagen induction combined with trichloroacetic acid 20% in atrophic post-acne scars; a randomized controlled trial, Journal of Dermatological TreatmentJ Dermatolog Treat, 25, 130-6, 2014	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Leo, M. S., Kumar, A. S., Kirit, R., Konathan, R., Sivamani, R. K., Systematic review of the use of platelet-rich plasma in aesthetic dermatology, Journal of Cosmetic DermatologyJ, 14, 315-23, 2015	Acne-related studies that were included in this article were checked for a potential inclusion in this review
Linkner, R. V., On, S. J., Haddican, M., Singer, G., Shim-Chang, H., Evaluating the efficacy of photodynamic therapy with 20% aminolevulinic acid and microdermabrasion as a combination treatment regimen for acne scarring: A split-face, randomized, double-blind pilot study, Journal of Clinical and Aesthetic Dermatology, 7, 32-35, 2014	Participants who took all medications, topical and oral, known to alter the course of acne scarring or acne vulgaris taken within 2 weeks and not 6 months of initiation or during the study period were excluded.
Lipper, G. M., Perez, M., Nonablative acne scar reduction after a series of treatments with a short-pulsed 1,064-nm neodymium:YAG laser, Dermatologic SurgeryDermatol Surg, 32, 998-1006, 2006	No relevant study design - not RCT
Maddin, S., Danto, J. L., Stewart, W. D., Dermal abrasion for the removal of acne scars, Canadian Medical Association JournalCan Med Assoc J, 82, 1072-4, 1960	A short summary of the dermal abrasion procedure
Magnani, L. R., Schweiger, E. S., Fractional CO2 lasers for the treatment of atrophic acne scars: A review of the literature, Journal of Cosmetic and Laser Therapy, 16, 48-56, 2014	Included studies were checked for a potential inclusion in this review
Mahmoud, B. H., Srivastava, D., Janiga, J. J., Yang, J. J., Lim, H. W., Ozog, D. M., Safety and efficacy of erbium-doped yttrium aluminum garnet fractionated laser for treatment of acne scars in type IV to VI skin, Dermatologic SurgeryDermatol Surg, 36, 602-9, 2010	The study assessed the efficacy and safety of one intervention, that is 1,550-nm erbium fractionated laser 10 mJ versus 40 mJ
Majid, I., Imran, S., Fractional CO2 Laser Resurfacing as Monotherapy in the Treatment of Atrophic Facial Acne Scars, Journal of Cutaneous & Aestheic SurgeryJ, 7, 87-92, 2014	No relevant study design - not RCT
Manuskiatti, W., Triwongwaranat, D., Varothai, S., Eimpunth, S., Wanitphakdeedecha, R., Efficacy and safety of a carbon-dioxide ablative fractional resurfacing device for treatment of atrophic acne scars in Asians, Journal of the American Academy of Dermatology, 63, 274-283, 2010	No relevant study design - not RCT
Min, S. U., Choi, Y. S., Lee, D. H., Yoon, M. Y., Suh, D. H., Comparison of a long-pulse Nd:YAG laser and a combined 585/1,064-nm laser for the treatment of acne scars: a randomized split-face clinical study, Dermatologic SurgeryDermatol Surg, 35, 1720-7, 2009	Data not useful for an analysis as no standard deviations reported or data reported in figures

Min, S., Park, S. Y., Moon, J., Kwon, H. H., Yoon, J. Y., Suh, D. H., Comparison between Er:YAG laser and bipolar radiofrequency combined with infrared diode laser for the treatment of acne scars: Differential expression of fibrogenetic biomolecules may be associated with differences in efficacy between ablative and non-ablative laser treatment, Lasers in Surgery & MedicineLasers Surg Med, 49, 341-347, 2017	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Min, S., Park, S. Y., Yoon, J. Y., Suh, D. H., Comparison of fractional microneedling radiofrequency and bipolar radiofrequency on acne and acne scar and investigation of mechanism: comparative randomized controlled clinical trial, Archives of Dermatological ResearchArch Dermatol Res, 307, 897-904, 2015	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Min, S., Yoon, J. Y., Park, S. Y., Moon, J., Kwon, H. H., Suh, D. H., Combination of platelet rich plasma in fractional carbon dioxide laser treatment increased clinical efficacy of for acne scar by enhancement of collagen production and modulation of laser-induced inflammation, Lasers in Surgery & MedicineLasers Surg Med, 50, 302-310, 2018	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Moftah, N. H., El Khayyat, M. A. M., Ragai, M. H., Alaa, H., Carboxytherapy versus skin microneedling in treatment of atrophic postacne scars: A comparative clinical, histopathological, and histometrical study, Dermatologic Surgery, 44, 1332-1341, 2018	No relevant study design - not RCT
Mubashir, S., Hassan, I., Sajad, P., Abdullah, Z., Sheikh, G., Efficacy of catgut as a modality of treatment in case of acne scars: A pilot study, Journal of the Saudi Society of Dermatology and Dermatologic Surgery, 17, 17-19, 2013	No relevant study design - not RCT
Mujahid, N., Shareef, F., Maymone, M. B. C., Vashi, N. A., Microneedling as a Treatment for Acne Scarring: A Systematic Review, Dermatologic Surgery, 23, 23, 2019	Included studies were checked for a potential inclusion in this review
Munavalli, G. S., Smith, S., Maslowski, J. M., Weiss, R. A., Successful treatment of depressed, distensible acne scars using autologous fibroblasts: a multi-site, prospective, double blind, placebo-controlled clinical trial, Dermatologic SurgeryDermatol Surg, 39, 1226-36, 2013	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Naouri, M., Atlan, M., Perrodeau, E., Georgesco, G., Khallouf, R., Martin, L., MacHet, L., High-resolution ultrasound imaging to demonstrate and predict efficacy of carbon dioxide fractional resurfacing laser treatment, Dermatologic Surgery, 37, 596-603, 2011	No relevant study design - not RCT
Nilforoushzadeh, M., Lotfi, E., Nickkholgh, E., Salehi, B., Shokrani, M., Can Subcision with the Cannula be an Acceptable Alternative Method in Treatment of Acne Scars?, Medical archives (Sarajevo, Bosnia and Herzegovina), 69, 384-386, 2015	No relevant study design - not RCT
Nirmal, B., Pai, S. B., Sripathi, H., Rao, R., Prabhu, S., Kudur, M. H., Nayak, S. U., Efficacy and safety of erbium-doped yttrium aluminium garnet fractional resurfacing laser for treatment of facial acne scars, Indian Journal of Dermatology, Venereology & LeprologyIndian J Dermatol	No relevant study design - not RCT

Venereol Leprol, 79, 193-8, 2013	
Niwa, A. B., Mello, A. P., Torezan, L. A., Osorio, N., Fractional photothermolysis for the treatment of hypertrophic scars: clinical experience of eight cases, Dermatologic Surgery, 35, 773-7; discussion 777-8, 2009	No relevant study design - not RCT
Okoye, G.A., Rainer, B.M., Leung, S.G., Suh, H.S., Kim, J.H., Nelson, A.M., Garza, L.A., Chien, A.L., Kang, S. Improving acne keloidalis nuchae with targeted ultraviolet B treatment: a prospective, randomized, split-scalp comparison study. Br J Dermatol, 171(5):1156-63, 2014	Not acne disease
Omi, T., Kawana, S., Sato, S., Bonan, P., Naito, Z., Fractional CO2 laser for the treatment of acne scars, Journal of Cosmetic Dermatology, 10, 294-300, 2011	No relevant study design - not RCT
Ong, M. W., Bashir, S. J., Fractional laser resurfacing for acne scars: a review, British Journal of DermatologyBr J Dermatol, 166, 1160-9, 2012	Included studies were checked for a potential inclusion in this review
Ortiz, A. E., Tremaine, A. M., Zachary, C. B., Long-term efficacy of a fractional resurfacing device, Lasers in Surgery and Medicine, 42, 168-170, 2010	No relevant study design - not RCT
Park, G. H., Rhee, D. Y., Bak, H., Chang, S. E., Lee, M. W., Choi, J. H., Moon, K. C., Bang, J. S., Kim, B. J., Kim, M. N., Lee, S. Y., Treatment of atrophic scars with fractional photothermolysis: Short-term follow-up, Journal of Dermatological Treatment, 22, 43-48, 2011	No relevant study design - not RCT; also half of the participants in one arm had acne-related scars, others had scars caused by trauma, herpes zoster, and burns
Park, J. H., Choi, Y. D., Kim, S. W., Kim, Y. C., Park, S. W., Effectiveness of modified phenol peel (Exoderm) on facial wrinkles, acne scars and other skin problems of Asian patients, Journal of Dermatology, 34, 17-24, 2007	Only 11 participants out of 39 were treated for acne vulgaris scars
Park, J. Y., Lee, E. G., Yoon, M. S., Lee, H. J., The efficacy and safety of combined microneedle fractional radiofrequency and sublative fractional radiofrequency for acne scars in Asian skin, Journal of Cosmetic Dermatology, 15, 102-107, 2016	No relevant study design - not RCT
Patel, N., Clement, M., Selective nonablative treatment of acne scarring with 585 nm flashlamp pulsed dye laser, Dermatologic Surgery, 28, 942-945, 2002	No relevant study design - not RCT
Payapvipapong, K., Niumpradit, N., Piriyanand, C., Buranaphalin, S., Nakakes, A., The treatment of keloids and hypertrophic scars with intralesional bleomycin in skin of color, Journal of Cosmetic Dermatology, 14, 83-90, 2015	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Peterson, J. D., Palm, M. D., Kiripolsky, M. G., Guiha, I. C., Goldman, M. P., Evaluation of the effect of fractional laser with radiofrequency and fractionated radiofrequency on the improvement of acne scars, Dermatologic Surgery, 37, 1260-1267, 2011	No relevant study design - not RCT
Petrov, A., Pljakovska, V., Fractional carbon dioxide laser in treatment of acne scars, Macedonian Journal of Medical Sciences, 4, 2016	No relevant study design - not RCT
Phothong, W., Wanitphakdeedecha, R., Sathaworawong, A., Manuskiatti, W., High versus moderate energy use of	The study assessed the efficacy of 1 intervention, that

bipolar fractional radiofrequency in the treatment of acne scars: a split-face double-blinded randomized control trial pilot study, Lasers in Medical ScienceLasers Med Sci, 31, 229-34, 2016	is lower versus moderate energy of bipolar fractional radiofrequency
Politi, Y., Levi, A., Lapidoth, M., Integrated cooling-vacuum-assisted non-fractional 1540 nm erbium: Glass laser is effective in treating acne scars, Journal of Drugs in Dermatology, 15, 1359-1363, 2016	No relevant study design - not RCT
Politi, Y., Levi, A., Snast, I., Ad, El D., Lapidoth, M., Integrated Cooling-Vacuum-Assisted Non-Fractional 1540-nm Erbium:Glass Laser: A New Modality for the Simultaneous Effective Treatment of Acne Lesions and Scars, Journal of drugs in dermatology : JDD, 17, 1173 - 1176, 2018	No relevant study design - not RCT
Porwal, S., Chahar, Y. S., Singh, P. K., A comparative study of combined dermaroller and platelet-rich plasma versus dermaroller alone in acne scars and assessment of quality of life before and after treatment, Indian Journal of Dermatology, 63, 403-408, 2018	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Pudukadan, D., Treatment of acne scars on darker skin types using a noninsulated smooth motion, electronically controlled radiofrequency microneedles treatment system, Dermatologic Surgery, 43, S64-S69, 2017	No relevant study design - not RCT
Puri, N., A study on the efficacy of TCA CROSS for the management of acne scars, Journal of Pakistan Association of Dermatologists, 23, 184-189, 2013	No relevant study design - not RCT
Puri, N., Comparative study of dermaroller therapy versus trichloroacetic acid CROSS for the treatment of atrophic acne scars, Journal of Pakistan Association of Dermatologists, 25, 114-118, 2015	No relevant study design - not RCT
Puri, N., Efficacy of Modified Jessner's Peel and 20% TCA Versus 20% TCA Peel Alone for the Treatment of Acne Scars, Journal of Cutaneous & Aestheic SurgeryJ, 8, 42-5, 2015	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Qian, H., Lu, Z., Ding, H., Yan, S., Xiang, L., Gold, M. H., Treatment of acne scarring with fractional CO2 laser, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 14, 162-5, 2012	No relevant study design - not RCT; also not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Qin, X., Li, H., Jian, X., Yu, B., Evaluation of the efficacy and safety of fractional bipolar radiofrequency with high-energy strategy for treatment of acne scars in Chinese, Journal of Cosmetic and Laser Therapy, 17, 237-245, 2015	No relevant study design - not RCT
Quarles, F. N., Brody, H., Badreshia, S., Vause, S. E., Brauner, G., Breadon, J. Y., Swinehart, J., Epps, R. E., Acne keloidalis nuchae, Dermatologic Therapy, 20, 128-32, 2007	Doctors' opinion on the treatment of people with acne keloidalis nuchae
Rahman, Z., Tanner, H., Jiang, K., Atrophic scar revision using fractional photothermolysis, Cosmetic Dermatology, 20, 593-602, 2007	No relevant study design - not RCT and also a mixed population as not only people

	with acne vulgaris scars included
Ramadan, S. A., El-Komy, M. H., Bassiouny, D. A., El-Tobshy, S. A., Subcision versus 100% trichloroacetic acid in the treatment of rolling acne scars, Dermatologic Surgery, 37, 626-33, 2011	No relevant study design - not RCT
Ramaut, L., Hoeksema, H., Pirayesh, A., Stillaert, F., Monstrey, S., Microneedling: Where do we stand now? A systematic review of the literature, Journal of Plastic, Reconstructive & Aesthetic Surgery: JPRASJ Plast Reconstr Aesthet Surg, 71, 1-14, 2018	Included studies were checked for a potential inclusion in this review
Ramesh, M., Gopal, M., Kumar, S., Talwar, A., Novel Technology in the Treatment of Acne Scars: The Matrix-tunable Radiofrequency Technology, Journal of Cutaneous & Aestheic SurgeryJ, 3, 97-101, 2010	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Rana, S., Mendiratta, V., Chander, R., Efficacy of microneedling with 70% glycolic acid peel vs microneedling alone in treatment of atrophic acne scars-A randomized controlled trial, Journal of Cosmetic DermatologyJ, 16, 454-459, 2017	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Rattner, H., Lazar, P., Dermabrasion for the improvement of acne scars, Journal of the American Medical AssociationJama, 171, 2326-31, 1959	Descriptive article about dermabrasion for the improvement of acne vulgaris scars
Rattner, H., Rein Ch, R., Treatment of acne scars by dermabrasion (Rotary brush method), JAMA (Chicago, Ill.), 159, 1299-1301, 1955	A report on treatment of acne vulgaris scars by dermabrasion
Reiches, A. J., Plastic planing or dermabrasion of acne scars and other skin defects, Clinical Medicine, 3, 135-138, 1956	The full copy of the paper is not available
Rogachefsky, A. S., Hussain, M., Goldberg, D. J., Atrophic and a mixed pattern of acne scars improved with a 1320-nm Nd:YAG laser, Dermatologic Surgery, 29, 904-908, 2003	No relevant study design - not RCT
Ruiz-Esparza, J., Barba Gomez, J. M., Gomez De La Torre, O. L., Huerta Franco, B., Parga Vazquez, E. G., UltraPulse laser skin resurfacing in hispanic patients: A prospective study of 36 individuals, Dermatologic Surgery, 24, 59-62, 1998	No relevant study design - not RCT
Ruiz-Esparza, J., Barba Gomez, J., Avram, M. R., Nonablative radiofrequency for active acne vulgaris: The use of deep dermal heat in the treatment of moderate to severe active acne vulgaris (thermotherapy): A report of 22 patients, Dermatologic Surgery, 29, 333-339, 2003	No relevant study design - not RCT
Rusciani, L., Rossi, G., Bono, R., Use of cryotherapy in the treatment of keloids, Journal of Dermatologic Surgery and Oncology, 19, 529-534, 1993	No relevant study design - not RCT; also a mixed population as various causes (not only acne vulgaris) of keloids included
Saadawi, A. N., Esawy, A. M., Kandeel, A. H., El-Sayed, W., Microneedling by dermapen and glycolic acid peel for	Not reported if participants were not on oral isotretinoin

the treatment of acne scars: Comparative study, Journal of Cosmetic Dermatology, 18, 107-114, 2019	treatment for at least 6 months before the beginning of the study
Sadick, N. S., Cardona, A., Laser treatment for facial acne scars: A review, Journal of Cosmetic and Laser Therapy, 20, 424-435, 2018	Included studies were checked for a potential inclusion in this review
Sadick, N. S., Schecter, A. K., A preliminary study of utilization of the 1320-nm Nd:YAG laser for the treatment of acne scarring, Dermatologic Surgery, 30, 995-1000, 2004	No relevant study design - not RCT
Saluja, S. S., Walker, M. L., Summers, E. M., Tristani-Firouzi, P., Smart, D. R., Safety of non-ablative fractional laser for acne scars within 1 month after treatment with oral isotretinoin: A randomized split-face controlled trial, Lasers in Surgery & MedicineLasers Surg Med, 49, 886-890, 2017	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Saple, D., Tambe, S., Combination modalities of treatment for management of acne scars, Journal of Dermatology, 1), 165, 2012	Conference abstract
Sapra, S., Stewart, J. A., Mraud, K., Schupp, R., A Canadian study of the use of poly-l-lactic acid dermal implant for the treatment of hill and valley acne scarring, Dermatologic Surgery, 41, 587-594, 2015	No relevant study design - not RCT
Sardana, K., Manjhi, M., Garg, V. K., Sagar, V., Which type of atrophic acne scar (ice-pick, boxcar, or rolling) responds to nonablative fractional laser therapy?, Dermatologic surgery, 40, 288-300, 2014	No relevant study design - not RCT
Sarnoff, D., Gotkin, R., Evaluation of the safety and efficacy of dual treatment with an ablative fractional CO2 laser and a non-ablative 1440nm Nd: YAG laser for atrophic facial acne scars, Lasers in Surgery and Medicine., 44, 11â€• 12, 2012	Conference abstract
Savant, S. S., Facial dermabrasion in acne scars and genodermatoses-A study of 65 patients, Indian Journal of Dermatology, Venereology & LeprologyIndian J Dermatol Venereol Leprol, 66, 79-84, 2000	No relevant study design - not RCT
Scrimali, L., Lomeo, G., Nolfo, C., Pompili, G., Tamburino, S., Catalani, A., Sirag, P., Perrotta, R. E., Treatment of hypertrophic scars and keloids with a fractional CO2 laser: A personal experience, Journal of Cosmetic and Laser Therapy, 12, 218-221, 2010	No relevant study design - not RCT
Semchyshyn, N., Prodanovic, E., Varade, R., Treating acne scars in patients with fitzpatrick skin types IV to VI using the 1450-nm diode laser, Cutis, 92, 49-53, 2013	No relevant study design - not RCT
Sharad, J., Combination of microneedling and glycolic acid peels for the treatment of acne scars in dark skin, Journal of Cosmetic DermatologyJ, 10, 317-23, 2011	No relevant study design - not RCT
Shilpa, K., Sacchidanand, S., Leelavathy, B., Shilpashree, P., Divya, G., Ranjitha, R., Lakshmi, D. V., Outcome of Dermal Grafting in the Management of Atrophic Facial Scars, Journal of Cutaneous & Aestheic SurgeryJ, 9, 244-248, 2016	No relevant study design - not RCT and also a mixed population as various causes (not only acne vulgaris) of facial scars included

Shin, J. U., Lee, S. H., Jung, J. Y., Lee, J. H., A split-face comparison of a fractional microneedle radiofrequency device and fractional carbon dioxide laser therapy in acne patients, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 14, 212-7, 2012	Study assesses the efficacy of 2 devices to treat acne vulgaris and not acne scars
Shockman, S., Paghdal, K. V., Cohen, G., Medical and surgical management of keloids: A review, Journal of Drugs in Dermatology, 9, 1249-1257, 2010	Descriptive review about the medical and surgical management of keloids
Tanghetti, E., Tanghetti, M., Is deeper better: A prospective study of deep vs superficial non-ablative fractional laser treatment of acne scars and photo-aging, Lasers in Surgery and Medicine, 25), 4, 2013	Conference abstract
Tanzi, E. L., Alster, T. S., Treatment of atrophic facial acne scars with a dual-mode Er:YAG laser, Dermatologic Surgery, 28, 551-555, 2002	No relevant study design - not RCT
Taub, A. F., Garretson, C. B., Treatment of acne scars of skin types II to V by sublative fractional bipolar radiofrequency and bipolar radiofrequency combined with diode laser, Journal of Clinical and Aesthetic Dermatology, 4, 18-27, 2011	No relevant study design - not RCT
Tawfik, A., Osman, M. A., Rashwan, I., A Novel Treatment of Acne Keloidalis Nuchae by Long-Pulsed Alexandrite Laser, Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al.], 44, 413-420, 2018	No relevant study design - not RCT
Tay, Y. K., Kwok, C., Minimally ablative erbium:YAG laser resurfacing of facial atrophic acne scars in asian skin: A pilot study, Dermatologic Surgery, 34, 681-685, 2008	No relevant study design - not RCT
Taylor, M. B., Zaleski-Larsen, L., McGraw, T. A., Single session treatment of rolling acne scars using tumescent anesthesia, 20% trichloracetic acid extensive subcision, and fractional CO<inf>2</inf> laser, Dermatologic surgery, 43, S70-S74, 2017	No relevant study design - not RCT
Tenna, S., Cogliandro, A., Barone, M., Panasiti, V., Tirindelli, M., Nobile, C., Persichetti, P., Comparative Study Using Autologous Fat Grafts Plus Platelet-Rich Plasma With or Without Fractional CO2 Laser Resurfacing in Treatment of Acne Scars: Analysis of Outcomes and Satisfaction With FACE-Q, Aesthetic plastic surgery, 41, 661-666, 2017	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Tenna, S., Cogliandro, A., Piombino, L., Filoni, A., Persichetti, P., Combined use of fractional CO2 laser and radiofrequency waves to treat acne scars: a pilot study on 15 patients, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 14, 166-71, 2012	No relevant study design - not RCT
Thi Kim, C. N., Thi, L. P., Van, T. N., Thi Minh, P. P., Nguyet, M. V., Thi, M. L., Huu, N. D., Hau, K. T., Gandolfi, M., Satolli, F., Feliciani, C., Vojvodic, A., Tirant, M., Lotti, T., Successful treatment of facial atrophic acne scars by fractional radiofrequency microneedle in Vietnamese patients, Open Access Macedonian Journal of Medical Sciences, 7, 192-194, 2019	No relevant study design - not RCT

Thi Minh, P. P., Dang Bich, D., Thi Hai, V. N., Nguyen Van, T., Tran Cam, V., Hau Khang, T., Gandolfi, M., Satolli, F., Feliciani, C., Tirant, M., Vojvodic, A., Lotti, T., Microneedling therapy for atrophic acne scar: Effectiveness and safety in Vietnamese patients, Open Access Macedonian Journal of Medical Sciences, 7, 293-297, 2019	No relevant study design - not RCT
Thomas, C. L., Kim, B., Lam, J., Richards, S., See, A., Kalouche, S., Paver, R. D., Fernandez Penas, P., Objective severity does not capture the impact of rosacea, acne scarring and photoaging in patients seeking laser therapy, Journal of the European Academy of Dermatology and Venereology, 31, 361-366, 2017	No relevant study design - not RCT
Tierney, E. P., Treatment of acne scarring using a dual-spot-size ablative fractionated carbon dioxide laser: review of the literature, Dermatologic SurgeryDermatol Surg, 37, 945-61, 2011	Included studies were checked for a potential inclusion in this review
Trelles, M. A., Martinez-Carpio, P. A., Attenuation of acne scars using high power fractional ablative unipolar radiofrequency and ultrasound for transepidermal delivery of bioactive compounds through microchannels, Lasers in Surgery and Medicine, 46, 152-159, 2014	No relevant study design - not RCT
Trelles, M. A., Shohat, M., Urdiales, F., Safe and effective one-session fractional skin resurfacing using a carbon dioxide laser device in super-pulse mode: a clinical and histologic study, Aesthetic Plastic SurgeryAesthetic Plast Surg, 35, 31-42, 2011	No relevant study design - not RCT and also only 10 out of 40 had acne scars
Trimas, S. J., Boudreaux, C. E., Metz, R. D., Carbon dioxide laser abrasion. Is it appropriate for all regions of the face?, Archives of facial plastic surgery : official publication for the American Academy of Facial Plastic and Reconstructive Surgery, Inc, and the International Federation of Facial Plastic Surgery Societies. 2, 137-140, 2000	No relevant study design - not RCT
Tsai, R. Y., Wang, C. N., Chan, H. L., Aluminum oxide crystal microdermabrasion. A new technique for treating facial scarring, Dermatologic Surgery, 21, 539-42, 1995	No relevant study design - not RCT and also a mixed population as various causes (not only acne vulgaris) of facial scars included
Uebelhoer, N. S., Bogle, M. A., Dover, J. S., Arndt, K. A., Rohrer, T. E., Comparison of stacked pulses versus double-pass treatments of facial acne with a 1,450-nm laser, Dermatologic SurgeryDermatol Surg, 33, 552-9, 2007	The study assessed the efficacy of a single-pass consisting of stacked double pulses versus a double-pass treatment of single pulses of 1,450-nm diode laser
van Drooge, A. M., Vrijman, C., van der Veen, W., Wolkerstorfer, A., A randomized controlled pilot study on ablative fractional CO2 laser for consecutive patients presenting with various scar types, Dermatologic SurgeryDermatol Surg, 41, 371-7, 2015	52% of the population had atrophic and 48% had hypertrophic scars, however no useful data by scar subgroup was reported
Vanthitha, P. R., Vellaisamy, S. G., Gopalan, K., Nanjappachetty, G., A comparative study of the resurfacing effect of microdermabrasion versus glycolic	Not reported if participants were not on oral isotretinoin treatment for at least 6 months

acid peel in the management of acne scars, Journal of Pakistan Association of Dermatologists, 28, 224-232, 2018	before the beginning of the study
Vejjabhinanta, V., Wanitphakdeedecha, R., Limtanyakul, P., Manuskiatti, W., The efficacy in treatment of facial atrophic acne scars in Asians with a fractional radiofrequency microneedle system, Journal of the European Academy of Dermatology and Venereology, 28, 1219-1225, 2014	No relevant study design - not RCT
Verner, I., Clinical evaluation of the efficacy and safety of fractional bipolar radiofrequency for the treatment of moderate to severe acne scars, Dermatologic Therapy, 29, 24-27, 2016	No relevant study design - not RCT
Wada, T., Kawada, A., Hirao, A., Sasaya, H., Oiso, N., Efficacy and safety of a low-energy double-pass 1450-nm diode laser for the treatment of acne scars, Photomedicine and laser surgery, 30, 107-111, 2012	No relevant study design - not RCT
Walgrave, S. E., Ortiz, A. E., MacFalls, H. T., Elkeeb, L., Truitt, A. K., Tournas, J. A., Zelickson, B. D., Zachary, C. B., Evaluation of a novel fractional resurfacing device for treatment of acne scarring, Lasers in Surgery and Medicine, 41, 122-127, 2009	No relevant study design - not RCT
Walia, S., Alster, T. S., Prolonged clinical and histologic effects from CO2 laser resurfacing of atrophic acne scars, Dermatologic Surgery, 25, 926-30, 1999	No relevant study design - not RCT
Wang, B., Wu, Y., Luo, Y. J., Xu, X. G., Xu, T. H., Chen, J. Z., Gao, X. H., Chen, H. D., Li, Y. H., Combination of intense pulsed light and fractional CO(2) laser treatments for patients with acne with inflammatory and scarring lesions, Clinical & Experimental DermatologyClin Exp Dermatol, 38, 344-51, 2013	No relevant study design - not RCT
Wang, C. M., Huang, C. L. I., Sindy Hu, C. T., Chan, H. L., The effect of glycolic acid on the treatment of acne in Asian skin, Dermatologic Surgery, 23, 23-29, 1997	No relevant study design - not RCT
Wang, Y. S., Tay, Y. K., Kwok, C., Fractional ablative carbon dioxide laser in the treatment of atrophic acne scarring in Asian patients: A pilot study, Journal of Cosmetic and Laser Therapy, 12, 61-64, 2010	No relevant study design - not RCT
Weinstein, A., Koren, A., Sprecher, E., Zur, E., Mehrabi, J. N., Artzi, O., The combined effect of tranilast 8% liposomal gel on the final cosmesis of acne scarring in patients concomitantly treated by isotretinoin: Prospective double blind split-face study, Clinical and experimental dermatology., 01, 2019	17 out of 40 participants were on isotretinoin during the study
Wanitphakdeedecha, R., Manuskiatti, W., Siriphukpong, S., Chen, T. M., Treatment of punched-out atrophic and rolling acne scars in skin phototypes III, IV, and V with variable square pulse erbium:yttrium-aluminum-garnet laser resurfacing, Dermatologic SurgeryDermatol Surg, 35, 1376-83, 2009	Study compares different laser pulse widths, therefore should be excluded according to our protocol.
Whang, K. K., Lee, M., The principle of a three-staged operation in the surgery of acne scars, Journal of the American Academy of Dermatology, 40, 95-97, 1999	No relevant study design - not RCT

Woo, D. K., Treyger, G., Henderson, M., Huggins, R. H., Richards, D. J., Hamzavi, I., Prospective controlled trial for the treatment of acne keloidalis nuchae with a long-pulsed neodymium-doped yttrium-aluminum-garnet laser, Journal of cutaneous medicine and surgery, 22, 236-238, 2018	Not relevant comparison, that is laser versus topical steroids therapy
Woo, S. H., Park, J. H., Kye, Y. C., Resurfacing of Different Types of Facial Acne Scar with Short-Pulsed, Variable-Pulsed, and Dual-Mode Er:YAG Laser, Dermatologic Surgery, 30, 488-493, 2004	No relevant study design - not RCT
Xu, Y., Deng, Y., Ablative Fractional CO2 Laser for Facial Atrophic Acne Scars, Facial Plastic SurgeryFacial Plast Surg, 34, 205-219, 2018	Included studies were checked for a potential inclusion in this review
Yadav, S., Gupta, S., Radiofrequency-assisted subcision for postacne scars, Journal of the American Academy of Dermatology, 78, e9-e10, 2018	Case report
Yaghmai, D., Garden, J. M., Bakus, A. D., Massa, M. C., Comparison of a 1,064 nm laser and a 1,320 nm laser for the nonablative treatment of acne scars, Dermatologic SurgeryDermatol Surg, 31, 903-9, 2005	The study assessed the efficacy and safety of one intervention, that is 2 different wavelengths (1,064nm versus 1,320 nm) of the same non-ablative Nd:Yag laser
Yang, Q., Huang, W., Qian, H., Chen, S., Ma, L., Lu, Z., Efficacy and safety of 1550-nm fractional laser in the treatment of acne scars in Chinese patients: A split-face comparative study, Journal of cosmetic and laser therapy, 18, 312-316, 2016	Not reported if participants were not on oral isotretinoin treatment for at least 6 months before the beginning of the study
Yeung, C. K., Chan, N. P. Y., Shek, S. Y. N., Chan, H. H. L., Evaluation of combined fractional radiofrequency and fractional laser treatment for acne scars in Asians, Lasers in Surgery and Medicine, 44, 622-630, 2012	No relevant study design - not RCT
Yoo, K. H., Ahn, J. Y., Kim, J. Y., Li, K., Seo, S. J., Hong, C. K., The use of 1540 nm fractional photothermolysis for the treatment of acne scars in Asian skin: A pilot study, Photodermatology Photoimmunology and Photomedicine, 25, 138-142, 2009	No relevant study design - not RCT
Yu, J. N., Abat, K., Safety and efficacy of hybrid energy and trifractional technologies in the treatment of acne scars: An open-label clinical trial, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 18, 60-5, 2016	No relevant study design - not RCT
Yuan, X. H., Zhong, S. X., Li, S. S., Comparison study of fractional carbon dioxide laser resurfacing using different fluences and densities for acne scars in Asians: a randomized split-face trial, Dermatologic SurgeryDermatol Surg, 40, 545-52, 2014	The study assessed the efficacy of one intervention, that is the same fractional CO laser using different fluencies and densities
Zhou, B. R., Zhang, T., Bin Jameel, A. A., Xu, Y., Xu, Y., Guo, S. L., Wang, Y., Permatasari, F., Luo, D., The efficacy of conditioned media of adipose-derived stem cells combined with ablative carbon dioxide fractional resurfacing for atrophic acne scars and skin rejuvenation, Journal of Cosmetic & Laser TherapyJ Cosmet Laser Ther, 18, 138-48, 2016	Not relevant intervention, that is autologous platelet-rich plasma combined with erbium fractional laser therapy

Zhu, J. T., Xuan, M., Zhang, Y. N., Liu, H. W., Cai, J. H., Wu, Y. H., Xiang, X. F., Shan, G. Q., Cheng, B., The efficacy of autologous platelet-rich plasma combined with erbium fractional laser therapy for facial acne scars or acne, Molecular Medicine Reports, 8, 233-237, 2013	No data for the comparison between the two study groups reported

Economic studies

Table 50: Excluded economic studies and reasons for their exclusion

Study	Reason for Exclusion
Ansari F, Sadeghi-Ghyassi F, Yaaghoobian B. The clinical effectiveness and cost-effectiveness of fractional CO2 laser in acne scars and skin rejuvenation: A meta-analysis and economic evaluation. J Cosmet Laser Ther 2018; 20(4):248-251.	Only intervention costs (equipment) considered

Appendix L – Research recommendations – full details

Research recommendations for review question: What are the most effective treatment options for acne vulgaris-associated scarring?

The research recommendations were made to apply to both acne management and management of acne associated scaring. Therefore, they feature also in evidence reports E1 and F1.

Research question 1 – physical modalities (excluding chemical peels)

What is the effectiveness of physical modalities (such as light devices) in the treatment of acne vulgaris or persistent acne vulgaris-related scarring?

Why this is important

Physical treatments for acne are popular with people because they have the benefit of treating a local area without systemic effects. They can be used in people with co-morbidities or side effects where other treatments are unsuitable. They are currently available in the private sector but there is no standardisation of treatment modalities or duration. Many different physical therapies have been described for acne including:

- Comedone extraction
- Phototherapy – including UVB, intense pulsed light, blue and red light
- Photochemical therapy (e.g. photodynamic therapy)
- Laser
- Photopneumatic therapy (e.g. intense pulsed light + vacuum)
- Photothermal therapy (eg gold nanoparticles +light or laser)

Physical treatments are also used for acne scarring. These include

- Punch excision
- CO2 laser
- Dermabrasion
- Radiofrequency (e.g. fractional microneedling, bipolar)

Further research is required to determine the most effective physical treatments for acne and acne scarring. This could open the way to wider availability in the NHS

Table 51: Research recommendation rationale

Research question	What is the effectiveness of physical modalities (such as light devices) in the treatment of acne vulgaris or persistent acne vulgaris-related scarring?
Why is this needed	
Importance to 'patients' or the population	Physical treatments for acne are popular with people because they have the benefit of treating a local area without systemic effects. They can be used in people with co-morbidities or side effects where other treatments are unsuitable. There is evidence from small studies that physical therapies including various light sources with or without addition of chemical or physical photosensitiser may be effective in all grades of acne. There is also some evidence to support CO2 laser treatment for acne scarring. However, the studies are too small or of insufficient quality to allow recommendations to be made. .

Research question	What is the effectiveness of physical modalities (such as light devices) in the treatment of acne vulgaris or persistent acne vulgaris-related scarring?
Relevance to NICE guidance	Currently physical treatments for acne vulgaris cannot be recommended. Weak recommendation can be made for CO2 laser for acne scarring, but stronger evidence is required to allow a stronger recommendation. which would lead to wider availability on NHS
Relevance to the NHS	Acne vulgaris is the most common skin condition affecting the majority of teenagers and young adults. Acne scarring leads to lifelong psychological distress for some people. Physical treatments for acne could provide an alternative for people unwilling or unable to use other treatment modalities. With more evidence of effectiveness and cost effectiveness these treatments may become available on the NHS. Physical treatments for acne scarring may benefit the NHS by reducing psychological morbidity.
National priorities	There are 2 national priorities, one is to improve young people's mental health and another is to reduce antibiotic prescribing to prevent resistance. • Improving the mental health of young people is a national priority. Improving acne can have a positive impact on mental health. Rates of depression and suicide are increasing in the under 25-year-old age group, especially amongst men 20-25 years old. (suicides in the UK 2019 ons.gov.uk). In 2018 the government produced a paper 'Transforming children's and young people's mental health provision', including improving services for those 16-25 years old. This aligns with a need to understand support required for young people with acne vulgaris https://www.gov.uk/government/consultations/transforming-children-and-young-peoples-mental-health-provision-a-green-paper/quick-read-transforming-children-and-young-peoples-mental-health-provision • Acne has traditionally been treated with long courses of antibiotics. If any particular type of physical treatment could be identified as having a positive impact on acne vulgaris then it may lead to a decreased need for antibiotics. Antibiotic resistance is rising in the UK and the government wants to optimise antibiotic prescribing to prevent the development of superbugs. Keeping people well informed would therefore help to address this priority (Tackling antimicrobial resistance 2019–2024 The UK's five-year national action plan Published 24 January 2019. HM Government) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/784894/UK_AMR_5_year_national_action_plan.pdf
Current evidence base	It is hard to draw conclusions from the current evidence. There are a lack of existing randomised controlled trials in physical treatments for acne and acne scarring, and those which have been done have been variable quality on small numbers of participants.
Equality	Access to any recommended physical treatments for acne or acne scarring currently differs across the country and according to socioeconomic group. They are mainly available in the private sector.
Feasibility	Physical treatments need to be supervised, even if they are

Research question	What is the effectiveness of physical modalities (such as light devices) in the treatment of acne vulgaris or persistent acne vulgaris-related scarring?
	delivered at home. There would be significant NHS costs associated with setting up provision for physical treatments, but this may be offset by benefits. A time commitment from participants would be required.
Other comments	Not applicable

Table 52: Research recommendation characteristics table - (a) relates to acne management and (b) persistent acne vulgaris-related scarring management

Criterion	Explanation
Population	a) Adults with acne vulgaris. b) Adults with persistent acne vulgaris-related scarring
Intervention	a) any physical intervention (excluding chemical peels) for acne, for example: • A range of light therapies b) any physical intervention for acne scarring, for example • CO2 laser single or multiple treatments
Comparison	a) no treatment or another active treatment. b) no treatment for acne scarring
Outcome	a) Participant reported improvement, clinician reported improvement in lesion count b) Participant reported improvement, clinician reported improvement in scar appearance a) Recurrence a&b) Side effects: participant and clinician reported, including pigmentary changes and scarring
Study design	Randomised controlled trial
Timeframe	a) • 3-6 months (intervention) • 6 month (follow-up) b) • Intervention period • 6 and 12 month follow up
Additional information	Ideally longer term follow-up data collection would also be useful.

Research question 2 – chemical peels

What is the effectiveness of chemical peels in the treatment of acne vulgaris or persistent acne vulgaris-related scarring?

Why this is important

Chemical peels are used to remove the surface of the skin. Peels may be 'superficial' for treatment of acne vulgaris, removing the dead layer of skin, or 'deeper' for atrophic scar management. They are usually applied repeatedly as a course of treatment. Chemical peels are currently not used as standard treatment in the NHS but are available to buy by the

public and can be provided by private aesthetic practitioners. The use of chemical peels has potential to change acne and acne scarring management, as an alternative to those who cannot use, tolerate, or are resistant, to other treatments. Therefore, further research is needed to establish its effectiveness.

Table 53: Research recommendation rationale

Research question	What is the effectiveness of chemical peels in the treatment of acne vulgaris or persistent acne vulgaris-related scarring?
Why is this needed	
Importance to 'patients' or the population	The use of chemical peels has potential to change acne and acne scarring management, as an alternative to those who cannot use, tolerate, or are resistant, to other treatments. Therefore further research is required to increase the robustness of the evidence
Relevance to NICE guidance	Chemical peels are currently not routinely offered as a treatment of acne vulgaris or acne associated scarring in the NHS and there is insufficient evidence to make a strong recommendation.
Relevance to the NHS	Acne vulgaris is the most common skin condition affecting the majority of teenagers and young adults. Acne scarring leads to lifelong psychological distress for some people. Chemical peels for acne could provide an alternative for people unwilling or unable to use other treatment modalities. With more evidence of effectiveness and cost effectiveness these treatments may become available on the NHS. Chemical peels for acne scarring may benefit the NHS by reducing psychological morbidity
National priorities	• Acne has traditionally been treated with long courses of antibiotics. If chemical peels would be effective in the management of acne vulgaris then it may lead to a decreased need for antibiotics. Antibiotic resistance is rising in the UK and the government wants to optimise antibiotic prescribing to prevent the development of superbugs. Keeping people well informed would therefore help to address this priority (Tackling antimicrobial resistance 2019–2024 The UK's five-year national action plan Published 24 January 2019. HM Government) https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/784894/UK_AMR_5_year_national_action_plan.pdf • There are safety concerns about the use of oral retinoids (https://www.gov.uk/government/publications/isotretinoin-for-severe-acne-uses-and-effects) so provision of alternative therapy would be welcome if safe and effective. • Improving the mental health of young people is a national priority. If chemical peels are safe and effective to improve acne it may help improve self-esteem and confidence. Rates of depression and suicide are increasing in the under 25-year-old age group, especially amongst men 20-25 years old. (suicides in the UK 2019 ons.gov.uk). In 2018 the government produced a paper 'Transforming children's and young people's mental health provision', including improving services for those 16-25 years old. More effective acne treatment can have a positive impact on mental wellbeing and therefore addresses this priority. https://www.gov.uk/government/consultations/transforming-children-and-young-peoples-mental-health-provision-a-green-paper/quick-read-transforming-children-and-young-peoples-mental-health-provision
Current evidence base	There was no evidence for the use of chemical peels, either alone or combined, in moderate to severe acne treatment. There was some evidence that chemical peels may be effective in the

Research question	What is the effectiveness of chemical peels in the treatment of acne vulgaris or persistent acne vulgaris-related scarring?
	treatment of mild to moderate acne. However, there was a low number of studies with small sample size. None of the studies compared effectiveness of chemical peels against placebo. The evidence base for chemical peels in treatment of acne associated scarring was low to very low quality with small sample size and limited follow-up time.
Equality	None specified
Feasibility	This research is feasible
Other comments	Not applicable

Table 54: Research recommendation characteristics table – (a) relates to acne management and (b) persistent acne vulgaris-related scarring mangment

Criterion	Explanation
Population	a) Adults with acne vulgaris. b) Adults with persistent acne vulgaris-related scarring
Intervention	a) Chemical peels for the treatment acne b) Chemical peels for the treatment of acne associated scarring
Comparison	Any other peel Any other treatment Placebo
Outcome	a) Patient reported improvement, clinician reported improvement in lesion count b) Patient reported improvement, clinician reported improvement in scar appearance a) Recurrence a&b) Side effects: patient and clinician reported, including pigmentary changes and scarring
Study design	Randomised control trial or split-face trial
Timeframe	Likely treatment over 3 months with follow up to 3 years
Additional information	Not applicable