

Supplementary Material S1: PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page (manuscript title; article type "Systematic Review").
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract (structured: Background, Objectives, Methods, Results, Limitations, Conclusions).
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction, paragraphs 1-3 (epidemiology and burden of acne scarring; current treatment landscape; rationale for evaluating topical insulin, including the scar types in Figure 1 and its molecular mechanisms in Figure 2).
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction, final paragraph ("This systematic review aimed to synthesize the current literature..."); Abstract, Objectives.
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Section 2.2 (Eligibility Criteria); PICO framework in Supplementary Material S3.
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Section 2.1 (Search Strategies): PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus and Google Scholar; initial search 13-27 May 2025, updated search 7 September 2026; no date or year limits; English-language reports only.
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Section 2.1 (controlled vocabulary, MeSH and Emtree, combined with free-text keywords and Boolean operators); full search strings, filters and dates for each database in Supplementary Material S2.
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Section 2.4 (Data Extraction and Synthesis): titles, abstracts and full texts screened independently by two reviewers in Covidence; conflicts resolved by consensus. Figure 3 (PRISMA flow diagram).
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Section 2.4: data extracted independently by two reviewers using a standardized Covidence template; conflicts resolved by consensus. Extraction records in Supplementary Material S5.
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Section 2.3 (Outcomes): primary outcome, physician-reported scar severity on validated scales; secondary outcomes, patient-reported satisfaction, scar-type and skin-type specific response, and safety.
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Section 2.4 and Table 1: study design, country, group names, sample size, withdrawals and reasons, mean age, sex, scar morphology, Fitzpatrick phototype, insulin dose, procedural platform, frequency and duration of treatment. Where a between-group p-value was not reported, statistical significance was treated as undetermined rather than non-significant (Section 3.3.3); where safety data were reported only for a broader study cohort, this is stated (Section 3.6 and Table 5).

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Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Section 2.5 (Risk of Bias Assessment): Cochrane Handbook version 6.5; RoB 2 for randomized trials; ROBINS-I V2 for non-randomized studies; two independent reviewers with conflicts resolved by consensus. Reviewer-level and consensus judgments in Supplementary Material S4.
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Section 2.3 and Tables 2-5: study-reported mean plus or minus SD on validated scar scales, percentage improvement, proportions in response categories, and p-values. No pooled effect measure was calculated.
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Section 2.4: studies grouped by design (randomized vs. non-randomized) and by comparator (placebo or procedure alone, PRP, and other active agents); Section 3.3.
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A: no data conversions or imputations were performed because meta-analysis was not undertaken; values are reported as published.
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Section 2.4; results presented in Tables 1-5 and Figures 3-5.
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Section 2.4: narrative synthesis grouped by comparator and outcome domain. Meta-analysis was not performed because of heterogeneity in scar-grading instruments, insulin doses and procedural platforms.
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Sections 2.3 and 3.4: narrative examination of outcomes by scar morphology and Fitzpatrick phototype (Table 3); no meta-regression was performed.
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A: no sensitivity analyses were undertaken as no quantitative synthesis was performed.
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A: formal assessment of reporting bias (funnel plot, Egger test) was not feasible without a quantitative synthesis. Within-study selective reporting was assessed in RoB 2 domain 5 and ROBINS-I domain 7 (Section 3.2, Figure 4 and Supplementary Material S4).
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A: certainty of the evidence was not formally rated. Methodological quality is described narratively in Section 3.2 and Section 4.
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Section 3, opening paragraph: 572 records retrieved; 62 duplicates removed; 510 records screened; 488 excluded; 22 reports sought for retrieval; 2 not obtained; 20 assessed at full text; 6 excluded; 14 studies included. Figure 3 (PRISMA flow diagram).
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Section 3, opening paragraph and Figure 3: 6 reports excluded at full text, 5 for incorrect study design and 1 for wrong intervention.
Study characteristics	17	Cite each included study and present its characteristics.	Section 3.1 (Demographics, Patient Characteristics, and Study Design); Table 1 (all 14 included studies, references 7 and 23-35). For split-face studies, the unit of analysis and the between-side statistical test used in each study are described in Section 3.1.
Risk of bias in	18	Present assessments of risk of bias for each included study.	Section 3.2 (Risk of Bias Assessment); Figure 4 (RoB 2 for randomized trials;

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studies			ROBINS-I V2 for non-randomized studies); domain-level judgments in Supplementary Material S4.
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 2-5 (comparative efficacy and statistical significance; outcomes by scar type and skin type; qualitative key findings; adverse effects).
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Sections 3.3-3.6: narrative synthesis grouped by comparator and outcome domain, with the risk-of-bias profile of the contributing studies noted; Figure 5.
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Sections 3.3.1-3.3.4 and 3.5, with Tables 2 and 4: study-level results and p-values are reported; no pooled estimate or confidence interval was calculated.
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Section 3.4 and Table 3: narrative examination of results by scar morphology and Fitzpatrick phototype; sources of heterogeneity are discussed in Section 4.
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A: no sensitivity analyses were performed as there was no quantitative synthesis.
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A at the synthesis level (no meta-analysis). Within-study selective reporting is reported in Section 3.2, Figure 4 and Supplementary Material S4.
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A: certainty of the evidence was not formally rated. Section 3.2 and Section 4 summarize the methodological quality of the evidence base.
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Section 4 (Discussion), paragraphs 1-6: interpretation of efficacy against placebo or procedure alone, PRP and other active comparators; scar-type and skin-type response; safety; cost and practicality.
	23b	Discuss any limitations of the evidence included in the review.	Section 4 (limitations paragraph): 7 of 14 studies were randomized; most non-randomized studies were at moderate risk of bias; short follow-up; eight different scar-grading instruments; split-face designs whose paired structure was not consistently accounted for in the original analyses.
	23c	Discuss any limitations of the review processes used.	Section 4 (limitations paragraph): English-language restriction; geographic concentration of the evidence; predominance of Fitzpatrick types III and IV; heterogeneity precluding meta-analysis.
	23d	Discuss implications of the results for practice, policy, and future research.	Section 4 (final paragraphs) and Section 5 (Conclusions): implications for practice, including resource-limited settings, and priorities for future research.
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Section 2, first paragraph: registered on PROSPERO, registration number CRD420251061005.
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Section 2, first paragraph: https://www.crd.york.ac.uk/PROSPERO/view/CRD420251061005
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A: no amendments were made to the information provided at registration or in the protocol.

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Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funding statement: "This research received no external funding."
Competing interests	26	Declare any competing interests of review authors.	Conflicts of Interest statement: "The authors declare no conflicts of interest."
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data Availability Statement and Supplementary Materials: the search strategies (S2), PICO framework (S3), risk-of-bias judgments (S4) and data extraction records (S5) are provided as Supplementary Materials; all included studies are published and cited in the reference list. No new data or analytic code were generated.

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