

Appendix 1:

Preferred Reporting Items for Overviews of Reviews (PRIOR) Checklist (Gates *et al.*, 2022) for “Local injection of botulinum toxin for the prevention of hypertrophic scars and keloids: an overview of reviews”

Section Topic	#	Item	Location reported
Title			
Title	1	Identify the report as an overview of reviews.	Front page.
Abstract			
Abstract	2	Provide a comprehensive and accurate summary of the purpose, methods, and results of the overview of reviews.	Front page, abstract.
Introduction			
Rationale	3	Describe the rationale for conducting the overview of reviews in the context of existing knowledge.	Introduction.
Objectives	4	Provide an explicit statement of the objective(s) or question(s) addressed by the overview of reviews.	Introduction; objective.
Methods			
Eligibility criteria	5a	Specify the inclusion and exclusion criteria for the overview of reviews. If supplemental primary studies were included, this should be stated, with a rationale.	Methods; eligibility criteria.
	5b	Specify the definition of ‘systematic review’ as used in the inclusion criteria for the overview of reviews.	Methods; eligibility criteria.
Information sources	6	Specify all databases, registers, websites, organizations, reference lists, and other sources searched or consulted to identify systematic reviews and supplemental primary studies (if included). Specify the date when each source was last searched or consulted.	Methods; search sources.
Search strategy	7	Present the full search strategies for all databases, registers and websites, such that they could be reproduced. Describe any search filters and limits applied.	Methods; search sources. Appendix 2.
Selection process	8a	Describe the methods used to decide whether a systematic review or supplemental primary study (if included) met the inclusion criteria of the overview of reviews.	Methods; eligibility criteria, selection process.
	8b	Describe how overlap in the populations, interventions, comparators, and/or outcomes of systematic reviews was identified and managed during study selection.	Methods; eligibility criteria, selection process.
Data collection process	9a	Describe the methods used to collect data from reports.	Methods; data collection process.
	9b	If applicable, describe the methods used to identify and manage primary study overlap at the level of the comparison and outcome during data collection. For each outcome, specify the method used to illustrate and/or quantify the degree of primary study overlaps across systematic reviews.	Synthesis methods; comparison between reviews, comparison of primary studies included in the reviews and management of primary studies overlapping.
	9c	If applicable, specify the methods used to manage discrepant data across systematic reviews during data collection.	Methods; data collection process.
Data items	10	List and define all variables and outcomes for which data were sought. Describe any assumptions made and/or measures taken to identify and clarify missing or unclear information.	Methods; data collection process.
Risk of bias assessment	11a	Describe the methods used to assess risk of bias or methodological quality of the included systematic reviews.	Methods; quality assessment.
	11b	Describe the methods used to collect data on (from the systematic reviews) and/or assess the risk of bias of the primary studies included in the systematic reviews. Provide a justification for instances where flawed, incomplete, or missing assessments are identified but not re-assessed.	Methods; data collection process. Results; review characteristics and table 1.
	11c	Describe the methods used to assess the risk of bias of supplemental primary studies (if included).	Not applicable. No additional primary studies were included.
Synthesis methods	12a	Describe the methods used to summarize or synthesize results and provide a rationale for the choice(s).	Synthesis methods.
	12b	Describe any methods used to explore possible causes of heterogeneity among results.	Synthesis methods; comparison between the reviews and comparison of primary studies included in the reviews
	12c	Describe any sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable. No sensitivity analyses were performed.
Reporting bias assessment	13	Describe the methods used to collect data on (from the systematic reviews) and/or assess the risk of bias due to missing results in a summary or synthesis (arising from reporting biases at the levels of the systematic reviews, primary studies, and supplemental primary studies, if included).	Methods; quality assessment.
Certainty assessment	14	Describe the methods used to collect data on (from the systematic reviews) and/or assess certainty (or confidence) in the body of evidence for an outcome.	Methods; data collection process.
Results			
Systematic review and supplemental primary study selection	15a	Describe the results of the search and selection process, including the number of records screened, assessed for eligibility, and included in the overview of reviews, ideally with a flow diagram.	Results; search results and figure 1.
	15b	Provide a list of studies that might appear to meet the inclusion criteria, but were excluded, with the main reason for exclusion.	Appendix 3.

Section Topic	#	Item	Location reported
Characteristics of systematic reviews and supplemental primary studies	16	Cite each included systematic review and supplemental primary study (if included) and present its characteristics.	Table 1.
Primary study overlap	17	Describe the extent of primary study overlaps across the included systematic reviews.	Results; evidence matrix and primary study overlap.
Risk of bias in systematic reviews, primary studies, and supplemental primary studies	18a	Present assessments of risk of bias or methodological quality for each included systematic review.	Results; quality assessment and appendix 5.
	18b	Present assessments (collected from systematic reviews or assessed anew) of the risk of bias of the primary studies included in the systematic reviews.	Not applicable. Risk of bias was not presented at a primary study level.
	18c	Present assessments of the risk of bias of supplemental primary studies (if included).	Not applicable. No additional primary studies were included.
Summary or synthesis of results	19a	For all outcomes, summarize the evidence from the systematic reviews and supplemental primary studies (if included). If meta-analyses were done, present for each the summary estimate and its precision and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Results; prioritized outcomes and table 4.
	19b	If meta-analyses were done, present results of all investigations of possible causes of heterogeneity.	Not applicable. No meta-analysis were conducted.
	19c	If meta-analyses were done, present results of all sensitivity analyses conducted to assess the robustness of synthesized results.	Not applicable. No meta-analysis were conducted.
Reporting biases	20	Present assessments (collected from systematic reviews and/or assessed anew) of the risk of bias due to missing primary studies, analyses, or results in a summary or synthesis (arising from reporting biases at the levels of the systematic reviews, primary studies, and supplemental primary studies, if included) for each summary or synthesis assessed.	Results; table 2, evidence matrix (see notes).
Certainty of evidence	21	Present assessments (collected or assessed anew) of certainty (or confidence) in the body of evidence for each outcome.	Not applicable. Prioritized outcomes were presented narratively.
Discussion			
Discussion	22a	Summarize the main findings, including any discrepancies in findings across the included systematic reviews and supplemental primary studies (if included).	Discussion.
	22b	Provide a general interpretation of the results in the context of other evidence.	Discussion.
	22c	Discuss any limitations of the evidence from systematic reviews, their primary studies, and supplemental primary studies (if included) included in the overview of reviews. Discuss any limitations of the overview of reviews methods used.	Discussion.
	22d	Discuss implications for practice, policy, and future research (both systematic reviews and primary research). Consider the relevance of the findings to the end users of the overview of reviews, e.g., healthcare providers, policymakers, patients, among others.	Discussion
Other information			
Registration and protocol	23a	Provide registration information for the overview of reviews, including register name and registration number, or state that the overview of reviews was not registered.	Methods.
	23b	Indicate where the overview of reviews protocol can be accessed, or state that a protocol was not prepared.	Methods.
	23c	Describe and explain any amendments to information provided at registration or in the protocol. Indicate the stage of the overview of reviews at which amendments were made.	Not applicable.
Support	24	Describe sources of financial or non-financial support for the overview of reviews, and the role of the funders or sponsors in the overview of reviews.	Funding.
Competing interests	25	Declare any competing interests of the overview of reviews' authors.	Declaration of conflict of interest.
Author information	26a	Provide contact information for the corresponding author.	Front page.
	26b	Describe the contributions of individual authors and identify the guarantor of the overview of reviews.	Author contributions.
Availability of data and other materials	27	Report which of the following are available, where they can be found, and under which conditions they may be accessed: template data collection forms; data collected from included systematic reviews and supplemental primary studies; analytic code; any other materials used in the overview of reviews.	Appendix 1-7. Templates are available upon request from the corresponding author.

Notes:

- Gates M, Gates A, Pieper D, Fernandes RM, Tricco AC, Moher D, Brennan SE, Li T, Pollock M, Lunny C, Sepúlveda D, McKenzie JE, Scott SD, Robinson KA, Matthias K, Bougioukas KI, Fusar-Poli P, Whiting P, Moss SJ, & Hartling L. (2022). Reporting guideline for overviews of reviews of healthcare interventions: development of the PRIOR statement. *BMJ* **378**, e070849. <https://doi.org/10.1136/bmj-2022-070849>
- SRs: Systematic reviews

Appendix 2:
Search strategy for Epistemonikos Database

	Search term	Boolean strategy
#1	Scars	scar* OR scarr* OR "scar-related" OR cicatri* OR keloid* OR (incision* AND (surg* OR operat*))
#2	Botulinum toxins	botulinum* OR btx OR botox* OR onabotulinumtoxin* OR abobotulinumtoxin* OR Dysport* OR Azzalure* OR incobotulinumtoxin* OR Xeomin* OR Bocouture* OR Jeuveau* OR prabotulinumtoxin* OR rimabotulinumtoxin* OR Myobloc*
#3	Systematic review	"critical review" OR "electronic search" OR "evidence-based analysis" OR "evidence-based review" OR "literature search" OR "meta analysis" OR "meta synthesis" OR "meta-analyse" OR "meta-analytic review" OR "meta-study" OR "meta-synthesis" OR "metaanalysis" OR "metasynthesis" OR "meta-analysis" OR "pooled effect" OR "random-effects model" OR "systematic quantitative review" OR "systematically searched" OR "systemic review" OR (review AND randomized) OR (systematic AND review) OR MEDLINE OR "literature review" OR PubMed
	Terms combined (with 'AND')	#1 AND #2 AND #3

Appendix 3: List of excluded systematic reviews.

Study	Reference	Reason for exclusion
Austin <i>et al.</i> , 2018	Austin E, Koo E, & Jagdeo J. (2018). The Cellular Response of Keloids and Hypertrophic Scars to Botulinum Toxin A: A Comprehensive Literature Review. <i>Dermatologic surgery: official publication for American Society for Dermatologic Surgery</i> , 44 (2), 149–157. https://doi.org/10.1097/DSS.0000000000001360	Does not include studies carried out in humans.
Bartkowska <i>et al.</i> , 2020	Bartkowska P, Roszak J, Ostrowski H, & Komisarek O. (2020). Botulinum toxin type A as a novel method of preventing cleft lip scar hypertrophy-A literature review. <i>Journal of cosmetic dermatology</i> , 19 (9), 2188–2193. https://doi.org/10.1111/jocd.13614	Narrative review.
Bernabe <i>et al.</i> , 2023	Bernabe RM, Won P, Lin J, Pham C, Madrigal P, Yenikomshian H, & Gillenwater TJ. (2024). Combining scar-modulating agents for the treatment of hypertrophic scars and keloids: A systematic review. <i>Journal of plastic, reconstructive & aesthetic surgery: JPRAS</i> , 88 , 125–140. https://doi.org/10.1016/j.bjps.2023.10.065	Does not meet intervention/comparison criteria (combination of treatments).
Bi <i>et al.</i> , 2019	Bi, M., Sun, P., Li, D., Dong, Z., & Chen, Z. (2019). Intralesional Injection of Botulinum Toxin Type A Compared with Intralesional Injection of Corticosteroid for the Treatment of Hypertrophic Scar and Keloid: A Systematic Review and Meta-Analysis. <i>Medical science monitor: international medical journal of experimental and clinical research</i> , 25 , 2950–2958. https://doi.org/10.12659/MSM.916305	Includes corticosteroids as a comparison.
Bueno <i>et al.</i> , 2023	Bueno, A., Nevado-Sanchez, E., Pardo-Hernández, R., de la Fuente-Anuncibay, R., & González-Bernal, J. J. (2023). Treatment and Improvement of Healing after Surgical Intervention. <i>Healthcare (Basel, Switzerland)</i> , 11 (15), 2213. https://doi.org/10.3390/healthcare11152213	Does not meet intervention/comparison criteria (medications, laser, topical treatment and injectable medications).
Kassir <i>et al.</i> , 2023	Kassir, M., Babaei, M., Hasanzadeh, S., Rezaei Tavirani, M., Razzaghi, Z., & Robati, R. M. (2024). Botulinum toxin applications in the lower face and neck: A comprehensive review. <i>Journal of cosmetic dermatology</i> , 23 (4), 1205–1216. https://doi.org/10.1111/jocd.16116	Includes more diverse populations (not just scars).
Li <i>et al.</i> , 2022	Li, M. Y., Chiu, W. K., Wang, H. J., Chen, I. F., Chen, J. H., Chang, T. P., Ko, Y., & Chen, C. (2022). Effectiveness of Botulinum Toxin Type A Injection on Scars: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. <i>Plastic and reconstructive surgery</i> , 150 (6), 1249e–1258e. https://doi.org/10.1097/PRS.00000000000009742	Does not meet intervention/comparison criteria.
Liu <i>et al.</i> , 2021	Liu, X. G., & Zhang, D. (2021). Evaluation of Efficacy of Corticosteroid and Corticosteroid Combined with Botulinum Toxin Type A in the Treatment of Keloid and Hypertrophic Scars: A Meta-Analysis. <i>Aesthetic plastic surgery</i> , 45 (6), 3037–3044. https://doi.org/10.1007/s00266-021-02426-w	Does not meet intervention/comparison criteria.
Muskat <i>et al.</i> , 2022	Muskat, A., Kost, Y., Balazic, E., Cohen, J. L., & Kobets, K. (2023). Laser-Assisted Drug Delivery in the Treatment of Scars, Rhytids, and Melasma: A Comprehensive Review of the Literature. <i>Aesthetic surgery journal</i> , 43 (3), NP181–NP198. https://doi.org/10.1093/asj/sjac286	Does not meet intervention/comparison criteria.
Pan <i>et al.</i> , 2021	Pan, L., Qin, H., Li, C., Yang, L., Li, M., Kong, J., Zhang, G., & Zhang, L. (2022). Safety and efficacy of botulinum toxin type A in preventing and treating scars in animal models: A systematic review and meta-analysis. <i>International wound journal</i> , 19 (4), 774–781. https://doi.org/10.1111/iwj.13673	Does not include studies carried out in humans.
Pereira & Hassan, 2022	Pereira, I. N., & Hassan, H. (2022). Botulinum toxin A in dentistry and orofacial surgery: an evidence-based review - part 1: therapeutic applications. <i>Evidence-based dentistry</i> . https://doi.org/10.1038/s41432-022-0256-9	Does not meet intervention/comparison criteria.
Prodromidou <i>et al.</i> , 2015	Prodromidou, A., Frountzas, M., Vlachos, D. E., Vlachos, G. D., Bakoyiannis, I., Perrea, D., & Pergialiotis, V. (2015). Botulinum toxin for the prevention and healing of wound scars: A systematic review of literature. <i>Plastic surgery (Oakville, Ont.)</i> , 23 (4), 260–264. https://doi.org/10.4172/plastic-surgery.1000934	Does not meet intervention/comparison criteria.
Siriapaipun <i>et al.</i> , 2016	Siriapaipun K, Prapapan O, Sirithanabadeekul P. (2016). A systematic review of transforming growth factor beta inhibitor treatments on keloid scars. <i>Thai Journal of Pharmaceutical Sciences</i> . 40 :96-99.	Does not include randomized clinical trials as primary studies.
Sohrabi & Goutos, 2020	Sohrabi, C., & Goutos, I. (2020). The use of botulinum toxin in keloid scar management: a literature review. <i>Scars, burns & healing</i> , 6 , 2059513120926628. https://doi.org/10.1177/2059513120926628	Does not include randomized clinical trials as primary studies.
Sun <i>et al.</i> , 2019	Sun, P., Lu, X., Zhang, H., & Hu, Z. (2021). The Efficacy of Drug Injection in the Treatment of Pathological Scar: A Network Meta-analysis. <i>Aesthetic plastic surgery</i> , 45 (2), 791–805. https://doi.org/10.1007/s00266-019-01570-8	Does not meet intervention/comparison criteria.
Wu <i>et al.</i> , 2022	Wu, W., Zhao, Y., Chen, Y., & Zhong, A. (2023). Comparing the Efficacy of Multiple Drugs Injection for the Treatment of Hypertrophic Scars and Keloid: A Network Meta-Analysis. <i>Aesthetic plastic surgery</i> , 47 (1), 465–472. https://doi.org/10.1007/s00266-022-03163-4	Does not meet intervention/comparison criteria.
Xu <i>et al.</i> , 2021	Xu, D., Zhang, D. S., Hu, X. F., & Hu, M. Y. (2021). Evaluation of the efficiency and safety of botulinum toxin A injection on improving facial scars: A protocol for systematic review and meta-analysis. <i>Medicine</i> , 100 (1), e23034. https://doi.org/10.1097/MD.00000000000023034	Does not report data of interest.
Yang <i>et al.</i> , 2021	Yang, S., Luo, Y. J., & Luo, C. (2021). Network Meta-Analysis of Different Clinical Commonly Used Drugs for the Treatment of Hypertrophic Scar and Keloid. <i>Frontiers in medicine</i> , 8 , 691628. https://doi.org/10.3389/fmed.2021.691628	Does not meet intervention/comparison criteria.
Zhuang <i>et al.</i> , 2021	Zhuang, Z., Li, Y., & Wei, X. (2021). The safety and efficacy of intralesional triamcinolone acetonide for keloids and hypertrophic scars: A systematic review and meta-analysis. <i>Burns: journal of the International Society for Burn Injuries</i> , 47 (5), 987–998. https://doi.org/10.1016/j.burns.2021.02.013	Does not meet intervention/comparison criteria.

Appendix 4:
General characteristics of the primary studies as the SRs reported them.

Study/ Year	Intervention (brand)	Control	Number of participants (cases BTX-A/cases control)	Age	Doses	Follow up (longest)	Outcomes
Zhang et al., 2016	BTX-A. Brand not reported	Saline	539 (189/184)	Not reported	Not reported	From 6 months to 1 year	VAS, VSS, scar width, PSAS, OSAS, SBSES, erythema, pliability, itching score and patient satisfaction
Wang et al., 2019a	BTX-A. Brand not reported	Saline or no treatment	385 (not reported)	From 3 months to 88 years	Not reported	From 6 to 60 months	VAS, VSS, scar width and adverse events
Wang et al., 2019b	BTX-A. Brand not reported	Saline or no treatment	Not reported (179/177)	From 3 months to 88 years	From 6U to 80U per participant	From 6 to 27 months	VAS, VSS, scar width, OSAS, PSAS, patient satisfaction, scar discoloration and SBSES
Song et al., 2020	BTX-A. Brand not reported	Saline or no treatment	436 (not reported)	From 3 months to 88 years	From 1.5 to 10U/cm	From 6 to 27 months	VAS, VSS, scar width, OSAS and SBSES
Guo et al., 2020	BTX-A. Botox, Nabota, Hengli and Neuronox	Saline or no treatment	374 (244/242)	Not reported	From 1U/kg to 40U total	From 6 months to 10 years	VAS, VSS, scar width, patient satisfaction and adverse events
Chen et al., 2020	BTX-A. Brand not reported	Placebo	267 (184/182)	Not reported	Not reported	From 6 months to 27 months	VAS, VSS, scar width, PSAS, OSAS and SBSES
Zhang et al., 2020	BTX-A. Botox, Nabota, Hengli and Neuronox	Saline or no treatment	372 (251/246)	Not reported	From 2.5U to 80U	From 6 to 27 months	VAS, VSS, scar width and patient satisfaction
Yang & Li, 2020	BTX-A. Botox, Hengli, Nabota, and Neuronox	Saline or no treatment	915 (537/541)	Not reported	From 1U/kg to 10U/cm total	From 3 to 27 months	VAS, VSS, scar width, SBSES, PSAS, OSAS, effectiveness, color difference and patient satisfaction
Fu et al., 2022	BTX-A. Brand not reported	Saline or no treatment	510 (338/333)	Not reported	From 5U to 65U	From 6 to 27 months	VAS, VSS, scar width, SBSES, mSBSES patient satisfaction, MSS, mMSS, pathology, L^*a^*b value, and adverse events
Qiao et al., 2021	BTX-A. Botox, Xeomin, Nabota	Saline or no treatment	Not reported (352/344)	From 3 months to 59.8 ± 16.63 years	Not reported	From 24 weeks to 12 months	VAS, VSS, scar width, patient self assessment, SBSES, MSS and complications
Ji et al., 2022	BTX-A. Brand not reported	Placebo	161 (83/78)	From 3 months to ≥ 16 years	From 1U/kg to 15U total	6 months	VAS, VSS and scar width
Wang et al., 2022	BTX-A. Brand not reported	Saline or no treatment	210 (109/101)	From 12 to 60 years	From 15U to 50U	From 6 to 27 months	VAS, VSS, scar width, OSAS, PSAS and adverse events
Yue et al., 2022	BTX-A. Brand not reported	Saline or no treatment	Not reported	From 3.13 ± 0.37 months to 62.00 ± 18.20 years	Not reported	From 6 to 12 months	VAS, VSS, scar width, SBSES, OSAS and PSAS
Rammal & Mogharbel, 2023	BTX-A. Brand not reported	Placebo	779 (438/426)	From 3.13 ± 0.37 to 62.0 ± 18.2	From 2.5 to 100 U	From 3 to 27 months	VAS, VSS, scar width, PSAS, SBSES, OSAS and MSS
Martinez et al., 2023	BTX-A. Brand not reported	Saline or no treatment	216 (136/80)	From 3.13 months to 24.7 years	From 1 U/kg to 15 U in 0.6 ml of saline	From 6 to 12 months	VAS, VSS, scar width and adverse events
Notes SRs: Systematic reviews BTX-A: Botulinum toxin type A VAS: Visual Analog Scale VSS: Vancouver Scar Scale SBSES: Stony Brook Scar Evaluation Scale mSBSES: Modified Stony Brook Scar Evaluation Scale OSAS: Observer Scar Assessment Scale PSAS: Patient and Observer Scar Assessment Scale MSS: Manchester Scar Scale mMSS: Modified Manchester Scar Scale L^*a^*b : Cielab color space							

Appendix 5: AMSTAR-2 assessment.

Study	D 1	D 2*	D 3	D 4*	D 5	D 6	D 7*	D 8	D 9*	D 10	D 11*	D 12	D 13*	D 14	D 15*	D 16	AMSTAR-2 Overall Confidence
Zhang <i>et al.</i> , 2016	YES	NO	NO	PARTIAL YES	YES	YES	YES	PARTIAL YES	YES	NO	YES	NO	NO	NO	YES	YES	Critically low
Wang <i>et al.</i> , 2019a	YES	NO	NO	PARTIAL YES	YES	YES	YES	PARTIAL YES	YES	NO	YES	NO	YES	YES	YES	YES	Low
Wang <i>et al.</i> , 2019b	YES	PARTIAL YES	NO	PARTIAL YES	NO	YES	NO	YES	YES	NO	YES	NO	NO	NO	NO	YES	Critically low
Song <i>et al.</i> , 2020	YES	NO	NO	YES	YES	YES	YES	YES	PARTIAL YES	NO	YES	NO	NO	NO	NO	YES	Critically low
Guo <i>et al.</i> , 2020	YES	NO	NO	PARTIAL YES	YES	YES	YES	PARTIAL YES	YES	NO	YES	YES	NO	NO	NO	YES	Critically low
Chen <i>et al.</i> , 2020	YES	NO	NO	PARTIAL YES	YES	YES	NO	NO	PARTIAL YES	NO	YES	NO	NO	YES	NO	YES	Critically low
Zhang <i>et al.</i> , 2020	YES	NO	NO	PARTIAL YES	YES	YES	NO	YES	YES	NO	YES	NO	NO	YES	YES	YES	Critically low
Yang & Li, 2020	YES	NO	NO	PARTIAL YES	YES	YES	NO	YES	YES	NO	YES	NO	NO	YES	NO	NO	Critically low
Fu <i>et al.</i> , 2022	YES	NO	NO	PARTIAL YES	YES	YES	YES	YES	YES	NO	YES	NO	NO	YES	YES	YES	Critically low
Qiao <i>et al.</i> , 2021	YES	YES	NO	PARTIAL YES	YES	YES	NO	PARTIAL YES	YES	NO	YES	NO	NO	NO	YES	YES	Critically low
Ji <i>et al.</i> , 2022	YES	NO	NO	PARTIAL YES	NO	YES	NO	YES	YES	NO	YES	YES	YES	YES	YES	YES	Critically low
Wang <i>et al.</i> , 2022	YES	NO	NO	PARTIAL YES	YES	NO	NO	YES	YES	NO	YES	NO	NO	NO	NO	YES	Critically low
Yue <i>et al.</i> , 2022	YES	PARTIAL YES	NO	PARTIAL YES	NO	YES	NO	PARTIAL YES	YES	NO	YES	YES	YES	YES	YES	YES	Low
Rammal & Mogharbel, 2023	YES	NO	NO	PARTIAL YES	NO	NO	NO	YES	YES	NO	YES	NO	NO	NO	YES	YES	Critically low
Martinez <i>et al.</i> , 2023	YES	NO	NO	PARTIAL YES	YES	YES	NO	YES	YES	NO	NO META-ANALYSIS CONDUCTED	NO META-ANALYSIS CONDUCTED	NO	NO	NO META-ANALYSIS CONDUCTED	YES	Critically low

Notes

- D: Domain
- *: Critical domain
- High confidence: no critical weakness and maximum one non-critical weakness. The systematic review provides an accurate and complete summary of the results of the available studies
- Moderate confidence: no critical weaknesses and more than one non-critical weaknesses. The systematic review has weaknesses, but there are no critical defects, and it can provide an accurate summary of the available studies
- Low confidence: maximum one critical weakness, with or without non-critical weaknesses. The systematic review may not provide an accurate and complete summary of the available studies.
- Critically low confidence: more than one critical weakness, with or without non-critical weaknesses. The confidence of the systematic review is not reliable.

Appendix 6: List of primary studies included in the systematic reviews.

Study	References
Abedini et al., 2020	Abedini, R., Mehdizade Rayeni, N., Haddady Abianeh, S., Rahmati, J., Teymourpour, A., & Nasimi, M. (2020). Botulinum Toxin Type A Injection for Mammoplasty and Abdominoplasty Scar Management: A Split-Scar Double-Blinded Randomized Controlled Study. <i>Aesthetic plastic surgery</i> , 44 (6), 2270–2276. https://doi.org/10.1007/s00266-020-01916-7
Bae et al., 2020	Bae, D. S., Koo, D. H., Kim, J. E., Cho, J. M., & Park, J. O. (2020). Effect of Botulinum Toxin A on Scar Healing after Thyroidectomy: A Prospective Double-blind Randomized Controlled Trial. <i>Journal of clinical medicine</i> , 9 (3), 868. https://doi.org/10.3390/jcm9030868
Chang et al., 2014	Chang, C. S., Wallace, C. G., Hsiao, Y. C., Chang, C. J., & Chen, P. K. (2014). Botulinum toxin to improve results in cleft lip repair. <i>Plastic and reconstructive surgery</i> , 134 (3), 511–516. https://doi.org/10.1097/PRS.0000000000000416
Chang et al., 2014*	Chang, C. S., Wallace, C. G., Hsiao, Y. C., Chang, C. J., & Chen, P. K. (2014). Botulinum toxin to improve results in cleft lip repair: a double-blinded, randomized, vehicle-controlled clinical trial. <i>PloS one</i> , 9 (12), e115690. https://doi.org/10.1371/journal.pone.0115690
Chen et al., 2018	Chen, H., Pan, W., Zhang, J., Cheng, H., & Tan, Q. (2018). The application of W-plasty combined Botox-A injection in treating sunk scar on the face. <i>Medicine</i> , 97 (30), e11427. https://doi.org/10.1097/MD.00000000000011427
Ebrahim et al., 2022	Ebrahim, H., Elardi, A., Khater, S., & Morsi, H. (2022). Successful Topical Application of Botulinum Toxin After Microneedling Versus Microneedling Alone for the Treatment of Atrophic Post Acne Scars: A Prospective, Split-face, Controlled Study. <i>The Journal of clinical and aesthetic dermatology</i> , 15 (7), 26–31.
Elshahed et al., 2020	Elshahed, A. R., Elmanzalawy, K. S., Shehata, H., & ElSaie, M. L. (2020). Effect of botulinum toxin type A for treating hypertrophic scars: A split-scar, double-blind randomized controlled trial. <i>Journal of cosmetic dermatology</i> , 19 (9), 2252–2258. https://doi.org/10.1111/jocd.13627
Guan & Wang, 2018	Guan Qing, Wang Haihong. (2018). A型肉毒毒素防止面部美容切口瘢痕增生的效果观察/ Observation on the effect of botulinum toxin type A in preventing the proliferation of the left scar of facial cosmetic incision. <i>Chinese Journal of Clinical Rational Drug Use</i> . 2018;10:104-105.
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Appendix 7: Adverse events reported as narrative outcomes

Outcome/Study	Adverse events
Zhang et al., 2016	Not reported
Wang et al., 2019a	Presented in MA
Wang et al., 2019b	"Seven of the nine included studies reported that no complications were observed, and only two studies reported adverse events. In one study (Li et al., 2018), no serious complications except local pain (17.6%, 3/17) and pruritus (5.9%, 1/17) occurred after BTXA injection, and the symptoms quickly disappeared without special treatment. Another study (Ziade et al., 2013) reported one complication in the "toxin" group, and the same dosage of BTXA was injected on both sides of the zygomaticus minor (ZM) and the levator labii superioris alaeque nasi muscle (LLSAN) to immobilize a wound on the philtrum. Then, an asymmetrical smile was observed on day 7 postoperatively".
Song et al., 2020	"5 clinical trials reported the occurrence of adverse events (Gassner et al., 2006; Li et al., 2014; Tao et al., 2018; Hu et al., 2018; Xu & Hu, 2019), 11 cases in the experimental group and 1 case in the control group, all of which were temporary adverse events. The symptoms were basically relieved after rest, and no serious adverse events occurred in either group. Not at all the incidence rate of adverse events was 4.12% in the treatment group and 0.04% in the control group ($\chi^2=8.335$, $P=0.004$) The difference is statistically significant. The overall incidence of adverse events in the treatment group was higher than that in the control group".
Guo et al., 2020	"Ten studies reported postoperative adverse events. One study (Ziade et al., 2013) detected an asymmetric smile 7 days after the surgery, 1 study (Li et al., 2018) reported regional complications including pain and pruritus, and 1 study (Gassner et al., 2006) reported 1 case of headache. All reported adverse events resolved without special treatment soon after they were reported. There were no severe adverse events (such as wound dehiscence and infection) during more than 6 months' follow-up".
Chen et al., 2020	Not reported
Zhang et al., 2020	"One study (Ziade et al., 2013) observed an asymmetrical smile on day 7 postoperatively. One study (Li et al., 2018) reported local pain and pruritus in the BTXA group, and the adverse events rapidly disappeared without special treatment. One study (Gassner et al., 2006) reported that 1 patient in the control group had mild headaches during the 6-month follow-up. One study (Huang et al., 2019) reported a mild drooping lid on the third day after BTXA injection. The drooping distance of the eye-lid was approximately 0.5 mm compared with that in the control group; the affected patient was diagnosed with mild blepharoptosis. Symptoms gradually resolved within 6 weeks without any treatment".
Yang & Li, 2020	"Ten of 18 studies reported adverse reactions (Ziade et al., 2013; Wang et al., 2015, 2017; Li et al., 2016; Liu et al., 2018; Tao et al., 2018; Lee et al., 2018; Li et al., 2018; Xu & Hu, 2019; Navarro-Barquín et al., 2019). Besides transient pain, pruritus, and mild headache at the injection point, there were 2 cases of ptosis, 1 case of philtrum fixation wound, 1 case of asymmetrical smile, 1 case of asymmetric oral commissure, 1 case of asymmetric eyebrow, 1 case of abscess, and 1 case of ischemia. The remaining 5 studies reported no adverse events (Chang et al., 2014a, Chang et al., 2014b; Zelken et al., 2016; Hu et al., 2018; Phillips et al., 2019), and 3 studies did not report (Kim et al., 2014; Luan, 2015; Guan & Wang, 2018)".
Fu et al., 2022	Presented in MA
Qiao et al., 2021	Presented in MA
Ji et al., 2022	Not reported
Wang et al., 2022	"Two studies reported two adverse events after the injections of BTA, including mild eyelid ptosis (Lin et al., 2022) and an asymmetrical smile in the BTA group (Ziade et al., 2013). One study reported an adverse event in the control group with a mild headache (Gassner et al., 2006). There were no reports of any severe complications (Ziade et al., 2013; Hu et al., 2018; Lee et al., 2018; Kim et al., 2019)".
Yue et al., 2022	Presented in MA
Rammal & Mogharbel, 2023	Not reported
Martinez et al., 2023	"There were no reports of complications associated with botulinum toxin injection or surgery (Chang et al., 2014a, Chang et al., 2014b; Navarro-Barquín et al., 2019; Sonane et al., 2022; Lu et al., 2022)".

Notes

- BTXA/BTA: botulinum toxin type A
- MA: meta-analysis