

Beyond Wrinkles: A Systematic Review and Meta-Analysis of Off-Label Aesthetic Uses of Botulinum Neurotoxin

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BACKGROUND

- While the FDA-approved cosmetic uses of botulinum neurotoxin include treatment for glabellar lines, crow's feet, and forehead lines, its applications extend far beyond wrinkle reduction.¹⁻⁴
- Many of the most popular botulinum neurotoxin treatments are off-label, yet no systematic review has comprehensively captured the effects and outcomes of these non-wrinkle aesthetic injections.
- Off-label applications raises critical questions about clinical efficacy, safety, and patient satisfaction.
- This study aims to provide a thorough review of neurotoxin's off-label aesthetic applications, focusing on muscle targets, aesthetic outcomes, and patient satisfaction.

METHODS

SEARCH STRATEGY

- MEDLINE, Web of Science, and PUBMED searched for articles in English published between January 1st, 2014 to January 31th, 2024
- Search terms: Botox OR botulinum toxin OR botulinum neurotoxin AND aesthetic OR cosmetic OR esthetic
- PROSPERO 2024 CRD42024590570

STUDY ELIGIBILITY

- Inclusion criteria:
 - Written in English
 - Human subjects aged 18 years or older
 - Address topics related to aesthetic or cosmetic plastic surgery
 - Original research articles, short communications, letters to the editor, case studies, or case series
- Exclusion criteria:
 - Published prior to January 1, 2014
 - involved non-human subjects or participants under 18 years of age
 - Focused on the use of neurotoxin for wrinkles or non-aesthetic purposes
 - Conference proceedings, literature reviews, systematic reviews, and textbook chapters

SCREENING AND REVIEW

Two-stage screening process for relevant study selection by two independent reviewers (KCP & JOK). Any discordance was resolved by a third reviewer (MM).

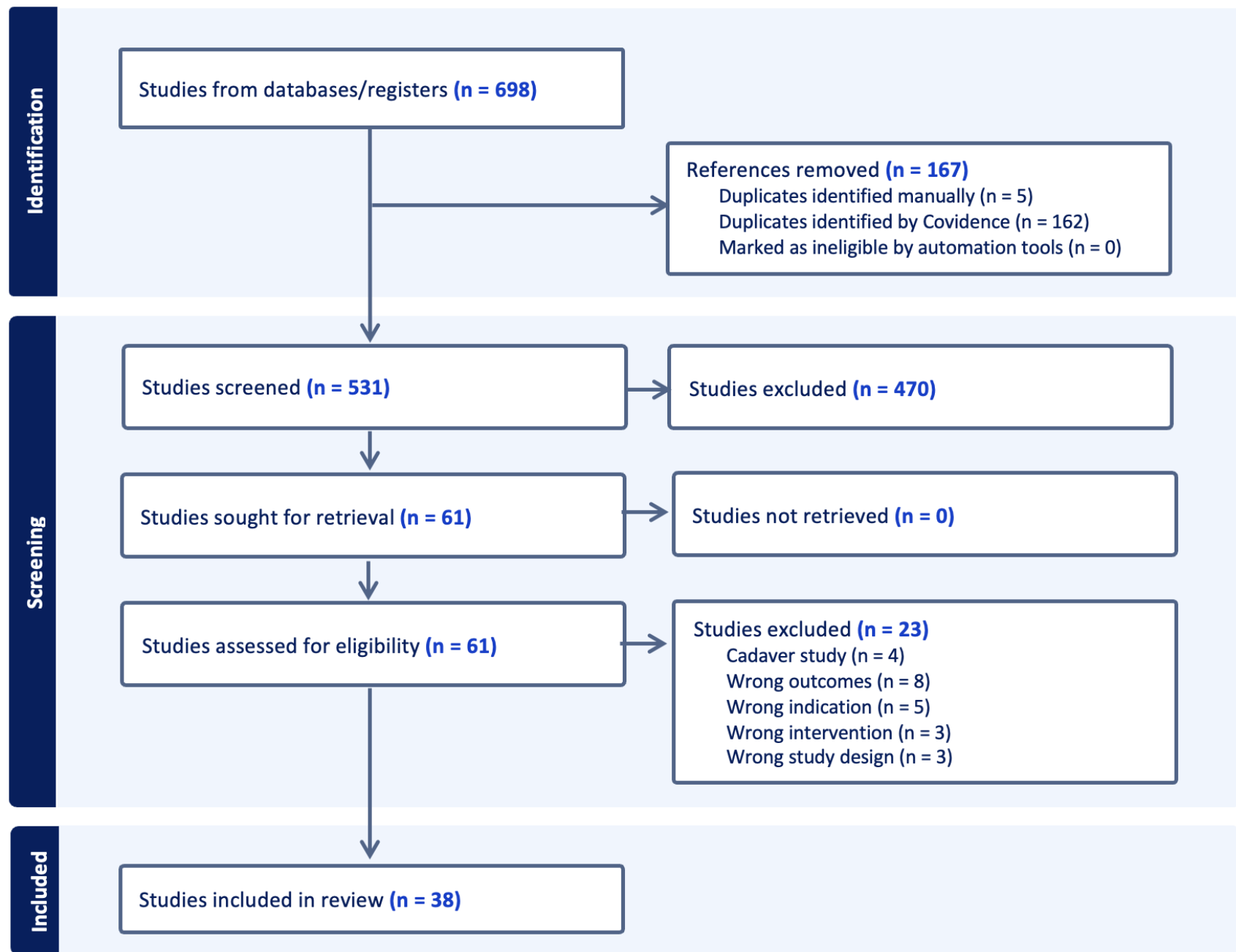


Figure 1. PRISMA flow diagram

RESULTS

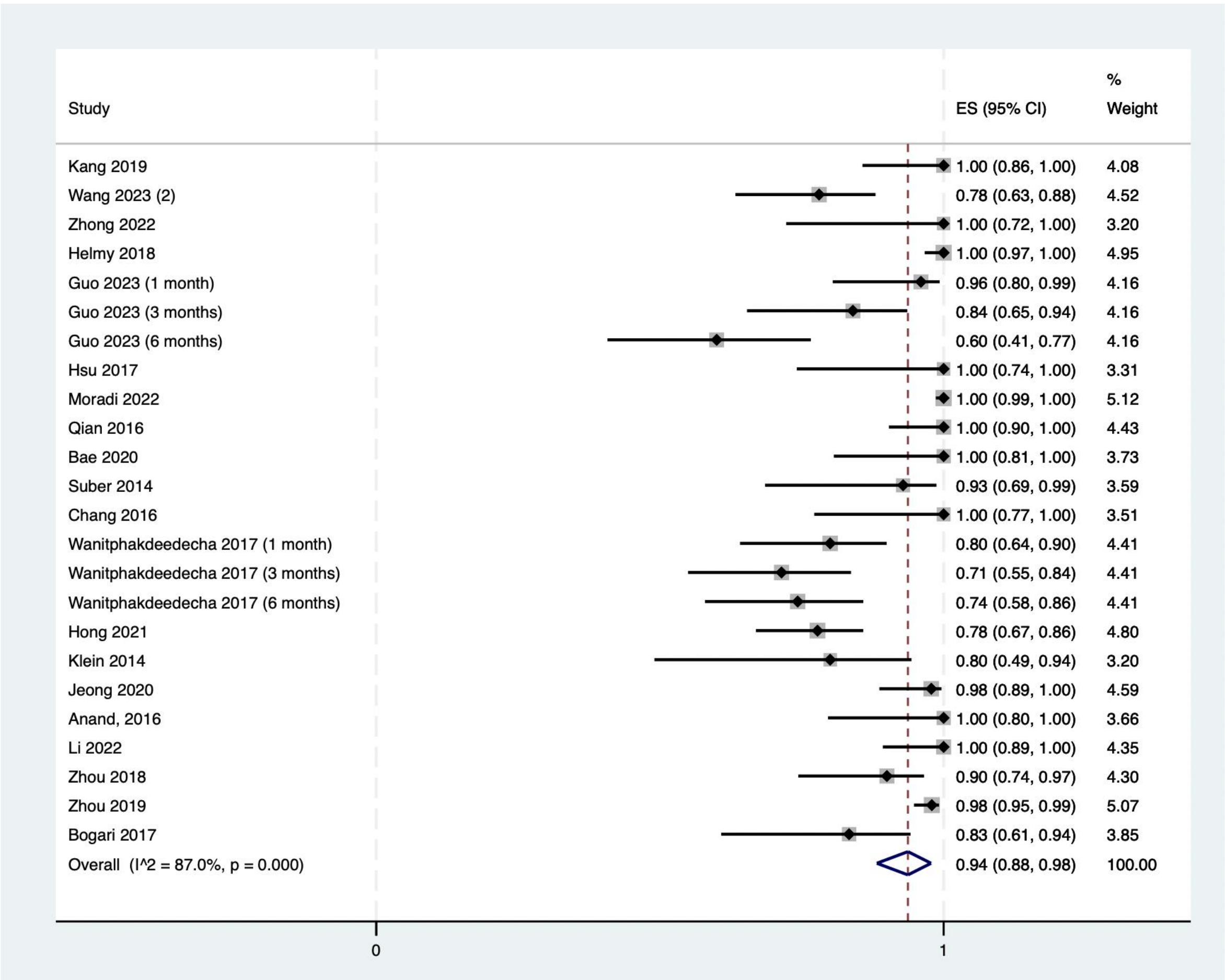


Figure 2. Forest plot summarizing reported patient satisfaction for off-label aesthetic applications of botulinum neurotoxin. Only studies with a sample size of at least 10 participants were included in meta-analysis.

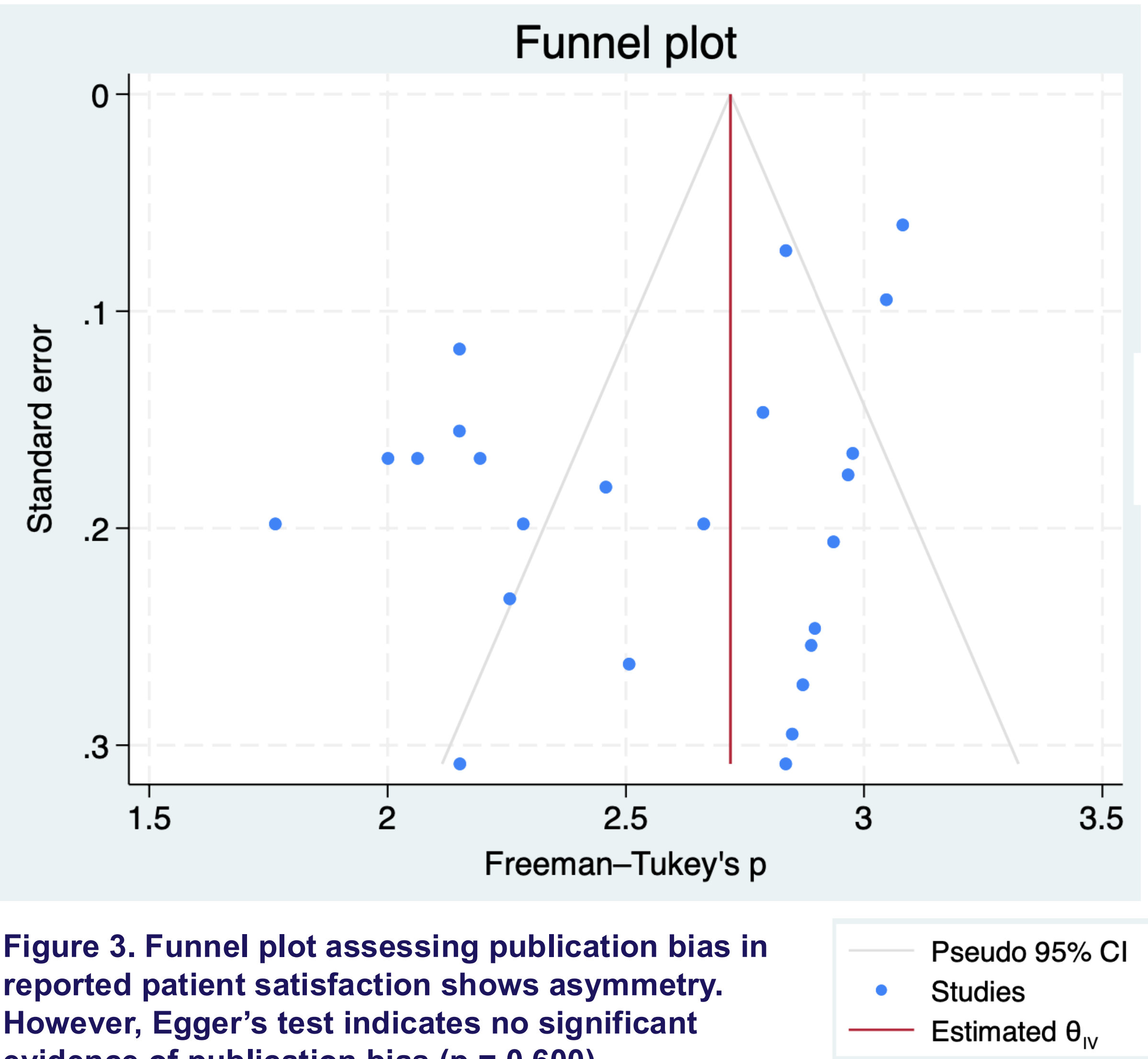


Figure 3. Funnel plot assessing publication bias in reported patient satisfaction shows asymmetry. However, Egger's test indicates no significant evidence of publication bias (p = 0.600).

CONCLUSION

- This systematic review highlights the increasing popularity and effectiveness of botulinum neurotoxin for off-label aesthetic applications, with a high overall patient satisfaction rate of 94% (95% CI 0.88, 0.98).
- Beyond its well-documented use for rhytid reduction, botulinum neurotoxin has proven to be an adaptable tool for both facial and body contouring, addressing a broad spectrum of aesthetic concerns.
- As the demand for aesthetic procedures grows, particularly among a more diverse patient population, these findings underscore the importance of expanding treatment protocols to meet evolving aesthetic needs.
- A comprehensive understanding of muscle targets and their effects post-injection will enhance clinical outcomes, improve decision-making, and facilitate patient expectation management. Moreover, these insights may inform future FDA approvals and broaden the scope of neurotoxin's clinical applications, benefiting both patients and practitioners.

ACKNOWLEDGMENTS

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Table 1. Summary of muscle targets and aesthetic outcomes

Author(s)/Year	Muscle Target	Off-Label Aesthetic Purpose(s) of Injection					
Face - Upper Third							
Dominguez-Duarte 2022 Wang 2023 (2)	Depressor supercillii			Eyebrow lift			
Farolch-Prats 2019	Procerus						
D'Emilio 2020 Farolch-Prats 2019	Orbicularis oculi	Eyelid lift or correction of lower eyelid hypertrophy					
Farolch-Prats 2019 Kang 2019	Frontalis	Forehead fat graft retention					
Farolch-Prats 2019 Kang 2019 Wang 2023 (2)	Corrugator supercillii						
Face - Middle Third							
Zhong 2022	levator labii superioris alaeque nasi		reduction of nasal flaring				
Helmy 2018 Zhong 2022	Dilator naris						
D'Emilio 2020 Helmy 2018	Depressor septi nasi		nasal tip definition and upward rotation				
Helmy 2018	Constrictor nasai						
Face - Lower Third							
Araujo 2018 D'Emilio 2020 Dureal 2019	zygomatic minor			Gummy smile correction			
Araujo 2018 D'Emilio 2020 Dureal 2019 Suber 2014 Zarone 2017	Levator labii superioris						
D'Emilio 2020 Dureal 2019 Suber 2014	levator labii superioris alaeque nasi						
Bae 2020 D'Emilio 2020 Moradi 2022 Qian 2016 Wu 2020 Zhou 2017	Depressor anguli oris	Correction of downturned mouth		Correction of chin retrusion Correction of mentalis strain			
Bae 2020 D'Emilio 2020 Guo 2023 Hsu 2017 Wu 2020 Zhou 2017	Mentalis						
D'Emilio 2020 Kantor 2017 Li 2022 Wu 2020 Zhou 2017 Zhou 2019	Platysma				Platysmal rejuvenation (treatment of lower face descent)		
Anand 2016 Bhattacharjee 2015 Bianco 2022 Chang 2016 D'Emilio 2020 Hong 2021 Jeong 2022 Klein 2014 Lee 2015 Quezada-Gaon 2016 Rho 2022 Scali 2015 Waniphakdeedecha 2017 Wu 2020 Zhou 2017	Masseter		Lower face slimming				
Body Contour							
Rho 2022 Wang 2023 (1) Zhou 2018	Trapezius				Neck contour		Shoulder contour
Rho 2022	Deltoid						
Rho 2022	Biceps	Arm contour					
Bogari 2017 Rho 2022	Gastrocnemius	Calf contour					
Ramelli 2020	Cremaster	Aesthetic lowering of testes					
Ramelli 2020	Dartos						