



Complications of Cosmetic Botulinum Toxin A Injections to the Upper Face: A Systematic Review and Meta-Analysis

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## background

- global increase in use of anti-aging products
- BoNT-A injections increasing due to relatively low price and perceived minimal downtime
- regulations are limited both nationally and internationally
- increasing concern in safety profile due to unregulated nature of administration

#### aim

 identify the overall complication rate of cosmetic BoNT-A across randomized controlled trials, thereby helping establish the safety profile of BoNT-A



# methods

#### systematic review

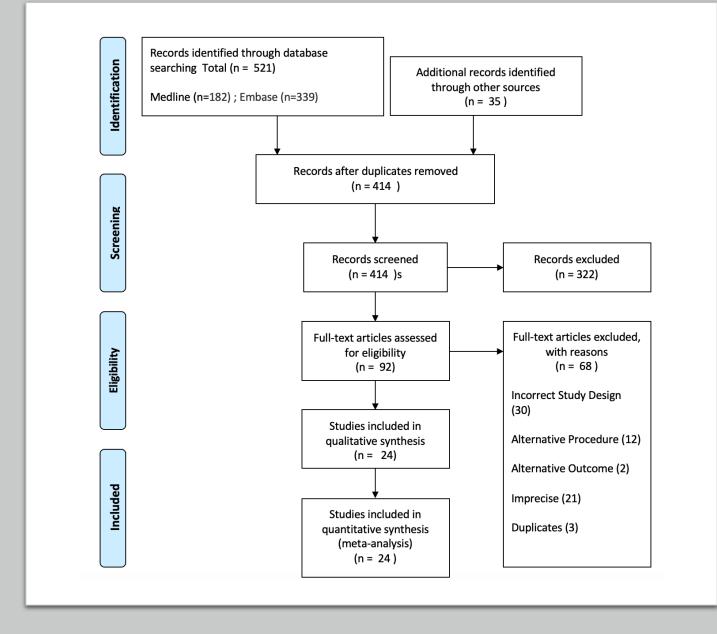






## inclusion criteria

- in-vivo studies
- english language
- adult humans over 18 years
- papers published prior to 1989 were excluded
- randomized placebo-controlled trials
- cosmetic facial BoNT-A injection in the glabellar or forehead region
- at least 1 complication reported



## complications

## confounders

#### subgroup analysis

- 1. localized skin reaction (erythema, eczema, hematoma, bruising, or contusion)
- 2. remote skin reactions (rash or edema)
- 3. wound infection
- 4. asymmetric or unsatisfying result;
- 5. facial neuromuscular symptoms (stiffness, weakness, pain, spasm, paresis, ptosis, dysesthesia)
- 6. headache
- 7. ocular symptoms and infections
- 8. pulmonary symptoms and infections
- 9. gastrointestinal symptoms
- 10. cardiovascular symptoms (hypertension, hypotension, tachycardia, myocardial infarction)
- 11. general symptoms (influenza-like symptoms, asthenia, chills, pyrexia, fatigue)
- 12. anaphylactic reaction
- 13. others

#### data extraction

**practitioners** were categorized as doctor, nurse, or non-medical professional

**BoNT-A formulations** were onabotulinum (ONA), abobotulinum (ABO), and incobotulinum (INCO)

**doses** were categorized as 0 to 10 U, 11 to 20 U, 21 to 30 U, 31 to 40 U, 41 to 50 U, and 50+ U.

**quality assessment tool**: Effective Public Healthcare Panacea Project

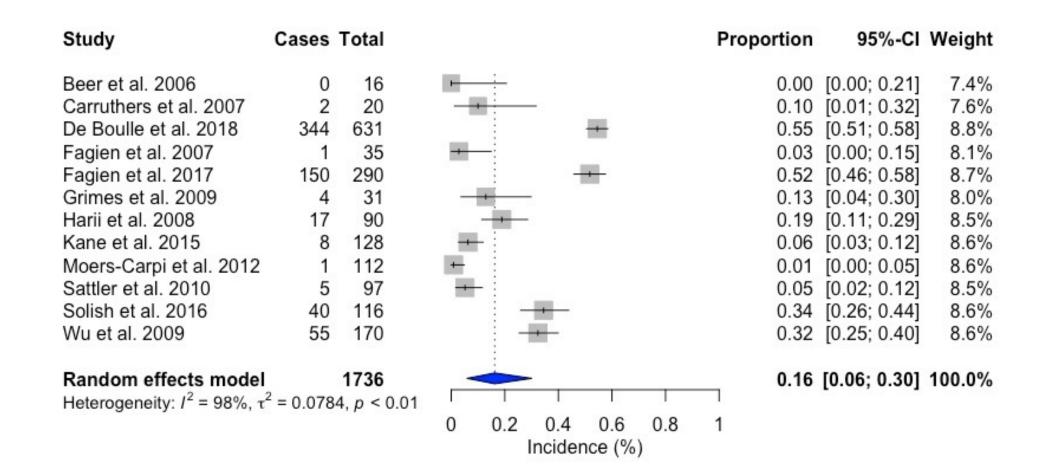
# results

Study	Cases	Total		Proportion	95%-CI	Weight
Ascher et al. 2004	7	102		0.07	[0.03; 0.14]	5.1%
Ascher et al. 2005	7	50		0.14	[0.06; 0.27]	4.9%
Beer et al. 2006	0	16		0.00	[0.00; 0.21]	4.3%
Brandt et al. 2009	24	105		0.23	[0.15; 0.32]	5.1%
Carruthers et al. 2002		203				0.0%
Carruthers et al. 2003		59				0.0%
Carruthers et al. 2005		80				0.0%
Carruthers et al. 2005		80				0.0%
Carruthers et al. 2007	2	20			[0.01; 0.32]	4.5%
Carruthers et al. 2013	13	184	+	0.07	[0.04; 0.12]	5.1%
De Boulle et al. 2018	344	631			[0.51; 0.58]	5.2%
Fagien et al. 2007	1	35	<b>—</b>		[0.00; 0.15]	4.8%
Fagien et al. 2017	150	290			[0.46; 0.58]	5.2%
Grimes et al. 2009	4	31			[0.04; 0.30]	4.7%
Hanke et al. 2013	22	182			[0.08; 0.18]	5.1%
Harii et al. 2008	17	90			[0.11; 0.29]	5.0%
Kane et al. 2009	51	544			[0.07; 0.12]	5.2%
Kane et al. 2015	16	250	-		[0.04; 0.10]	5.1%
Moers-Carpi et al. 2012	3	224	· · · · · · · · · · · · · · · · · · ·		[0.00; 0.04]	5.1%
Monheit et al. 2007	169	279			[0.55; 0.66]	5.2%
Rzany et al. 2006	11	146			[0.04; 0.13]	5.1%
Sattler et al. 2010	14	381			[0.02; 0.06]	5.2%
Solish et al. 2016	40	116			[0.26; 0.44]	5.1%
Wu et al. 2009	55	170		0.32	[0.25; 0.40]	5.1%
Random effects model		4268		0.16	[0.08; 0.26]	100.0%
Heterogeneity: $I^2 = 98\%$ , $\tau^2$	= 0.076	3, <i>p</i> < 0.01				
			0 0.2 0.4 0.6 0.8 Incidence (%)	1		

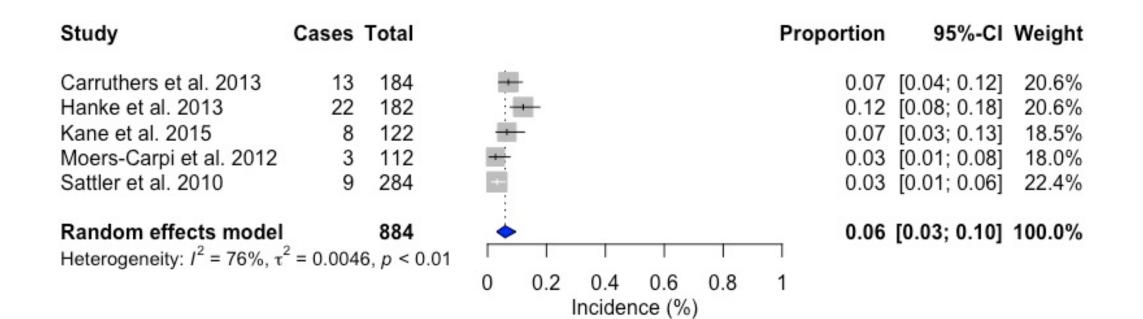
## breakdown of complications

headache and migraine	269 (6.3%)
local skin reactions (bruising or hematoma at the injection site)	163 (3.8%)
facial neuromuscular symptoms	141 (3.3%)
pulmonary symptoms	91 (2.1%)
ocular symptoms	39 (0.9%)
cardiovascular symptoms	22 (0.5%)
gastrointestinal symptoms	18 (0.4%)
remote skin reactions	11 (0.3%)
face asymmetry	6 (0.1%)
general symptoms such as fatigue	6 (0.1%)

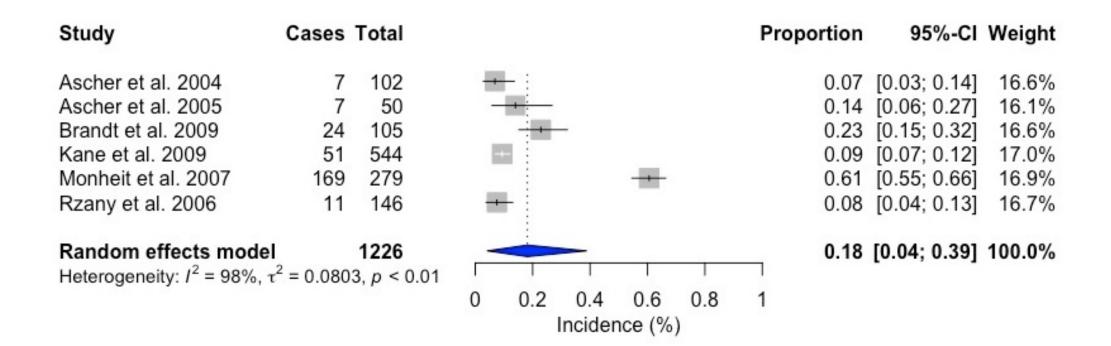
# onabotulinum



# incobotulinum



# abobotulinum



# practitioner

- 7 studies reported that the injections were administered by a doctor
- no further information was provided re specialty

# discussion

## discussion points



adverse events related to glabellar and forehead BoNT-A injection is approximately 16%



local skin reactions and headache were the most commonly reported complications in both BoNT-a and placebo, suggests these may be administration related



different definitions for complications



similar efficacy and safety profile across ona, inco and abo - botulinum toxin

#### lack of standardized reporting of complications

- MHRA database of complications found 188 complications over a 30-year period (1991 – 2020)
- underreporting of complications suspected given previous findings
- significant variations in reporting structures despite the use of the yellow card reporting scheme
- future work could look to create a framework around capturing cosmetic complications related to injectables

#### Botox leads to bad reactions for one in six users, says study

Doctors fear that the side-effects of the treatment are being hugely under-reported



■ An estimated 900,000 facial injections of Botox are carried out every year in the UK. Photograph: Alamy

One in six people who have Botox injected into their face suffer complications such as bruising, headache, nausea and "frozen" features, a study into the anti-ageing treatment has found.

The research shows that having facial Botox injections for cosmetic reasons can also produce side-effects including muscle stiffness, pain, dizziness and even a heart attack.

The findings - which the authors have shared with the *Observer* - have renewed calls for tighter regulation of deployment of the substance, which is administered in beauty clinics and temporarily removes signs of ageing such as frown lines and crow's feet.

An estimated 900,000 facial injections of Botox are carried out every year in Britain.

The finding of a 16% complication rate with the procedure has emerged in a review of global evidence undertaken by four doctors at the Royal Free and St Thomas' hospitals in London; three are plastic surgeons and all are academic researchers.

They found that, despite the high number of mishaps arising from facial

## limitations



search strategy focused on complications



some studies included patients who were not BoNT-A naïve



no consistent reporting of complications



treatment related or treatment emerged complications not distinguished

### thank you

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