

Supplementary File 2. Summary of cohort and cross-sectional studies reporting on the association between breast implants and risk of non-specific rheumatic symptoms

Study (Year) Location, study period	Category	No. with breast implants (% in silicone)	No. in comparator group	Measure of effect (95% CI)	Time since implant	Notes	NOS	\$
Brinton et al. (2004) United States, 1960-1996	All women	7,234 (50%)	2,138	RR, self-reported	12.1 years (mean)	- 18 plastic surgery practices - Comparator: other cosmetic surgeries	8	NR
	Other arthritis	724	201	1.3 (1.1-1.6)				
	Raynaud's	97	10	2.6 (1.3-5.1)				
Gabriel et al. (1994) United States, 1964-1991	All women	749 (85%)	1,498	A) Crude RR B) Adjusted HR	7.8 years (mean)	- Tertiary care centre and affiliated centers (visited by ~95% of local residents over three-year period) - Comparator: community, no BI - Matched +/- adjusted for age and calendar year; +/- matched on breast cancer - Unclear if included prevalent diagnoses	8	No
	Any arthritis	25	39	A) 1.35 (0.81-2.23) B) 1.38 (0.84-2.28)				
	Morning stiffness	30	35	A) 1.81 (1.11-2.95) B) 1.80 (1.10-2.93)				
	Symmetric muscle weakness	1	5	A) 0.43 (0.04-2.67)				
	Sicca (eyes/mouth)	33	50	A) 1.39 (0.89-2.16) B) 1.42 (0.92-2.21)				
	Salivary gland enlargement	2	3	A) 1.42 (0.22-7.98)				
	Photosensitivity	3	6	A) 1.04 (0.25-3.96) B) 1.12 (0.28-4.50)				
	Malar or discoid rash	1	5	A) 0.43 (0.04-2.67)				
	Oral ulcers	7	21	A) 0.71 (0.29-1.59) B) 0.69 (0.29-1.63)				
Serositis	18	21	A) 1.81 (0.96-3.39) B) 1.77 (0.94-3.32)					
Englert et al. (2004) Australia, 1979-1997	All women	458 (100%)	687	OR (95% CI)	15 years (mean)	- 16/28 plastic surgery practices in Sydney - Comparators: women with non-silicone plastic surgeries - Matched on age, sex, year of surgery, surgeon; excluded if cancer indication	8	Yes
	Dry mouth	12	27	0.66 (0.33-1.31)				
	Dry eyes	36	51	1.06 (0.68-1.66)				
	Joint swelling			NS				
	Morning stiffness	24	35	1.00 (0.78-1.30)				
	Muscle aches	79	90	1.15 (0.93-1.43)				
	Muscle weakness	12	16	1.01 (0.77-1.33)				
	Neck/back pain	196	28	1.03 (0.86-1.24)				
	Cluster: myalgia, stiffness, night sweats, low energy, dyspnea on exertion, orthopnea, numbness, breast pain, weight gain, dyspareunia	20	11	2.7 (1.3-5.6)				
Cluster: myalgia, night sweats, low energy, pins/needles, poor memory, reflux, hand weakness, burning hands/feet, breast pain	22	15	2.2 (1.2-4.2)					
Englert et al. (2001) Australia, 1979-1997	All women	458 (100%)	687	RR (95% CI)	15 years (mean)	Same as above	8	Yes
	Raynaud's	26	34	1.15 (0.70-1.89)				
	Abnormal capillaroscopy	7/329	11/377	0.60 (0.24-1.53)				
	Livedo reticularis	11/329	16/377	0.65 (0.31-1.37)				
Fryzek et al. (2001) Sweden, 1969-1996	All women	A) 884 (>60%) B) 396 (>50%)	2211	OR (95% CI NR); p<0.05 if bolded	13 years (mean)	- Swedish inpatient registry - A) Breast implants with no local complication - B) Breast implants with any local complication - Comparator: breast reduction surgery - Adjusted for age, parity, smoking, body mass index, university health care, alcohol, time since operation - Not adjusted for multiple comparisons - Self-reported symptoms	7	Yes
	Painful joint >3 months	-	-	A) 1.2; B) 1.5				
	Swollen joints >1 week	-	-	A) 1.1; B) 1.3				
	Muscle pain >3 months	-	-	A) 1.1; B) 1.5				
	Muscle weakness	-	-	A) 1.4; B) 1.5				
	Chronic neck ache	-	-	A) 1.5; B) 1.7				
	Chronic shoulder ache	-	-	A) 1.3; B) 1.6				
	Chronic backache	-	-	A) 1.3; B) 1.2				
	Abnormal fatigue	-	-	A) 1.3; B) 1.5				
	Regularly burning eyes	-	-	A) 1.1; B) 1.5				
	Persistent dry eyes	-	-	A) 1.1; B) 1.3				
	Sand/gravel in eyes	-	-	A) 2.1; B) 2.5				
	Dry mouth >3 months	-	-	A) 1.4; B) 1.7				
	Mouth ulcers >3 weeks	-	-	A) 0.7; B) 1.6				
	Difficulty swallowing	-	-	A) 2.3; B) 1.8				
	Redness of cheeks	-	-	A) 1.6; B) 1.8				
	Photosensitivity	-	-	A) 1.2; B) 1.1				
	Attacks of impaired circulation toes/fingers	-	-	A) 1.0; B) 1.6				
	Unexplained fever	-	-	A) 2.3; B) 3.1				
	Any of 28 symptoms	-	-	A) 1.3; B) 1.5				

Kjoller et al. (2004) Denmark, 1977-1997	All women	423 (84%)	A) 231; B) 183	OR (95% CI)	10 years (mean)	- 2 plastic surgery clinics - Comparators: A) Other cosmetic surgeries or consultation, matched on age and calendar year B) Women from general population, matched on age and postal area - Self-reported symptoms - Low response rate - Adjusted for age, history of connective tissue disease, depression, smoking, alcohol, body mass index, education, parity, age at first birth - Not adjusted for multiple comparisons	7	Yes
	Joint pain	–	–	A) 1.1 (0.7-1.8) B) 1.1 (0.7-1.9)				
	Joint swelling	–	–	A) 1.0 (0.5-2.2) B) 0.9 (0.4-2.2)				
	Finger swelling	–	–	A) 2.4 (1.1-5.5) B) 1.8 (0.7-4.5)				
	Joint stiffness	–	–	A) 2.3 (1.2-4.3) B) 2.3 (1.1-4.6)				
	Muscle pain	–	–	A) 1.5 (0.9-2.5) B) 1.0 (0.6-1.6)				
	Severe muscle weakness	–	–	A) 1.5 (0.7-3.2) B) 1.6 (0.7-3.8)				
	Eye dryness	–	–	A) 1.5 (0.7-3.2) B) 1.8 (0.7-4.1)				
	Eye gravel sensation	–	–	A) 1.0 (0.5-2.2) B) 1.6 (0.6-4.3)				
	Mouth dryness	–	–	A) 1.3 (0.6-3.1) B) 4.5 (1.0-20.7)				
	Oral ulcerations	–	–	A) 1.7 (0.1-30.8) B) –				
	Trouble swallowing with dry food	–	–	A) 0.7 (0.2-2.0) B) 3.7 (0.4-32.9)				
	Rash on both cheeks	–	–	A) 3.2 (0.6-16.0) B) 0.4 (0.2-1.0)				
	Abnormal skin tightness	–	–	A) 1.6 (0.2-11.3) B) 0.8 (0.1-6.0)				
	Photosensitivity	–	–	A) 0.7 (0.4-1.5) B) 0.4 (0.2-0.7)				
	Neck pain	–	–	A) 0.8 (0.5-1.2) B) 0.7 (0.5-1.1)				
	Shoulder pain	–	–	A) 0.8 (0.6-1.3) B) 0.9 (0.6-1.4)				
	White fingers with cold	–	–	A) 1.0 (0.5-1.9) B) 0.5 (0.3-1.0)				
	Chest pain on deep inspiration > 1 week	–	–	A) 1.3 (0.6-3.0) B) 1.8 (0.6-5.0)				
	Fever with no obvious cause for > 2 weeks	–	–	A) 1.4 (0.8-2.3) B) 1.4 (0.3-7.8)				
Abnormal fatigue	–	–	A) 1.6 (0.9-2.8) B) 1.0 (0.6-1.8)					
Mild (1-3) symptoms	154	A) 91 B) 79	A) 0.9 (0.6-1.3) B) 0.5 (0.3-0.7)					
Moderate (4-6) symptoms	52	A) 43 B) 42	A) 0.7 (0.4-1.2) B) 0.3 (0.2-0.5)					
Severe (>6) symptoms	58	A) 30 B) 20	A) 1.1 (0.6-2.1) B) 0.7 (0.3-1.3)					
Park et al. (1998) Scotland, 1982-1991	All women	C: 110 (100%) R: 207 (100%)	C: 128 R: 88	OR	5.9 years (mean)	- Plastic surgery and breast units in hospitals - Comparator: without BI - R: matched on age, cancer stage, time of operation - May have included prevalent symptoms - Inpatients only - Cross-sectional study	6	No
	Joint pain	C: 11 R: 21	C: 12 R: 13	C: 1.07 (0.42-2.74) R: 1.01 (0.45-2.28)				
	Muscle pain	C: 7 R: 12	C: 7 R: 3	C: 1.17 (0.36-3.88) R: 2.64 (0.67-12.15)				
	Fatigue	C: 13 R: 14	C: 8 R: 15	C: 2.01 (0.74-5.56) R: 0.54 (0.23-1.25)				
	Raynaud's	C: 1 R: 5	C: 3 R: 5	C: 0.38 (0.02-4.19) R: 0.61 (0.15-2.52)				
	Photosensitivity	C: 5 R: 5	C: 3 R: 5	C: 1.98 (0.40-10.75) R: 0.61 (0.15-2.52)				
	Rash	C: 3 R: 7	C: 3 R: 8	C: 1.17 (0.18-7.42) R: 0.52 (0.16-1.66)				
	Sclerodactyly	C: 0 R: 1	C: 0 R: 0	C: – R: ∞				
	Telangiectasia	C: 3 R: 2	C: 2 R: 1	C: 1.77 (0.24-15.41) R: 1.25 (0.09-35.41)				
Giltay (1994) Amsterdam; 1978-1992	All women	235 (100%)	210	OR	6.5 years (mean)	- University hospital plastic surgery department; 28% reconstructive surgery - Comparator: cosmetic surgery without silicone - Adjusted for age and calendar period - Self-reported symptoms	6	NR
	Painful joint >3 months	46	18	2.60 (1.45-4.64)				
	Swollen joints >1 week	14	10	1.27 (0.55-2.92)				
	Regularly burning eyes	37	15	2.43 (1.29-4.57)				
	Mouth ulcers >3 weeks	4	2	1.80 (0.33-9.93)				
	Raynaud's	12	7	1.56 (0.60-4.04)				
	Photosensitivity	20	4	5.05 (1.71-14.97)				
Pleuritis	4	5	0.71 (0.18-2.68)					

	Proteinuria/kidney dis.	8	4	1.81 (0.54-6.11)				
	Cytopenia	2	1	1.79 (0.16-19.93)				
	Any of the above	88	44	2.26 (1.48-3.45)				
Wells et al. (1994) United States, 1986-1991	All women	222 (100%)	80	OR	Up to 5 years	- Single plastic surgery practice - Comparator: other cosmetic surgeries - Self-reported symptoms	6	NR
	Raynaud's	1%	0%	0.49 (0.02-12.80)				
	Skin thickening	2%	7%	0.21 (0.04-0.99)				
	Skin tightness	12%	19%	0.58 (0.26-1.28)				
	Arthritis	5%	3%	1.16 (0.15-9.04)				
	Swollen joints	5%	3%	1.48 (0.26-8.29)				
	Painful joints	11%	5%	1.93 (0.52-7.14)				
	General stiffness	10%	10%	0.93 (0.38-2.27)				
	Muscle pain	15%	9%	1.40 (0.54-3.60)				
	Rashes	4%	4%	1.07 (0.27-4.17)				
Easily tired	15%	11%	1.38 (0.57-3.31)					
Jensen et al. (2002) Denmark, 1977-1992	All women with diagnostic code for muscular rheumatism	41 (100%)	A) 48; B) 50	P value	16 years (mean)	- National registry of patients (hospital and outpatient data) - Comparators: A) Breast reduction from same national registry of patients; B) Controls without BI or breast reduction from national population registry - Matched on date of breast surgery, date of muscular rheumatism diagnosis - Self-reported symptoms	6	NR
	Musculoskeletal symptoms	24	A) 26; B) 25	A) NS; B) NS				
	Pain score (median)	29	A) 52; B) 38	A) NS; B) NS				
	Stiffness score (median)	6	A) 38.5; B) 40	A) NS; B) NS				
	Fatigue score (median)	52	A) 68; B) 50	A) NS; B) NS				
	All women without diagnostic code for muscular rheumatism	26	A) 37; B) 114		15 years (mean)			
	Musculoskeletal symptoms	13	A) 22; B) 35	A) NS; B) NS				
	Pain score (median)	9	A) 15; B) 2	A) NS; B) NS				
	Stiffness score (median)	6.5	A) 4.5; B) 2	A) NS; B) NS				
	Fatigue score (median)	20.5	A) 15.5; B) 6	A) NS; B) p < 0.05				
Breiting et al. (2004) Denmark, 1973-1997	All women	190 (100%)	A) 186 B) 149	OR	19 years (mean)	- Plastic surgery practices (1 private clinic, 1 public hospital) - Comparators: A) Women with breast reductions from same plastic surgery practices B) Women from national population registry - Matched on age and surgery date - Adjusted for age - Self-reported symptoms	5	Yes
	Unspecified neck, shoulder or back pain	97	A) 100 B) 86	A) 0.9 (0.6-1.4) B) 0.8 (0.5-1.2)				
	Joint pain, swelling or stiffness >3 months	72	A) 66 B) 47	A) 1.1 (0.7-1.7) B) 1.3 (0.8-2.1)				
	Muscle pain or weakness > 3 months	60	A) 54 B) 39	A) 1.1 (0.7-1.7) B) 1.3 (0.8-2.1)				
	Mouth/eye symptoms	46	A) 52 B) 48	A) 0.8 (0.5-1.3) B) 0.7 (0.4-1.1)				
	White fingers/toes	28	A) 23 B) 10	A) 1.2 (0.8-2.2) B) 2.4 (1.1-5.1)				
	Abnormal hair loss	10	A) 9 B) 8	A) 1.1 (0.4-2.8) B) 1.0 (0.4-2.8)				
	Fatigue	38	A) 30 B) 13	A) 1.3 (0.8-2.2) B) 2.6 (1.3-5.1)				
	Mean number of groups of symptoms	3.2	A) 2.9 B) 2.6	A) P = 0.26 B) P = 0.11				
	Berner et al. (2002) Germany, 1984-1996	All women	32 (91%)	64				
Swelling of fingers		31.3%	12.5%	0.03				
Change in finger colour		31.3% (none had Raynaud's on oscillography)	1.6%	<0.0001				
Dry oropharynx		34.4%	14.1%	0.02				
Dry eyes		15.6%	17.5%	Non-significant				
Arthralgia		62.5%	60.9%	Non-significant				
Myalgia		50%	43.8%	Non-significant				
Photosensitivity		34.4%	34.4%	Non-significant				
Energy loss		40.6%	34.4%	Non-significant				
Fatigue		40.6%	25%	0.1				
Vermeulen and Scholte (2003) Netherlands, 1998	All women	319 (100%)	40		NR	- Readers of silicone implant support group with 2 nd BI surgery - Comparator: female co-workers - Cross-sectional study - Similar birth year, no other adjustments - Unclear if incident or prevalent disease - Self-reported symptoms	1	NR
	Debilitating chronic fatigue	71%	23%	-				
	Post-exertional malaise for over 24 hours	68%	28%	-				
	Muscle pain	76%	15%	-				
	Multi-joint pain	77%	18%	-				

BI: breast implant; C: cosmetic/augmentation; CI: confidence interval; HR: hazard ratio; N/A: not available; NOS: Newcastle-Ottawa scale (range 0 to 9); NR or -: not reported; NS: not statistically significant; OR: odds ratio; R: reconstruction; RR: relative risk; \$: potential financial or other conflict of interest