

**Supplementary File 7. Summary of studies reporting on risk of rheumatic disease according to type, indication and duration of breast implants**

**A) TYPE OF BREAST IMPLANTS**

Study (Year) Location, study period	Category	No. with silicone BI; measure of effect	No. with saline BI; measure of effect	Measure of effect or No. with no breast implants	Time since implant	Notes	NOS	\$
<b>Singh et al. (2017)</b> United States, 2007-2015	All women	40,396	14,883	RR (90% CI) Reference: saline BI	5 to 8 years (range)	- Prospective post-approval long-term study - Adjusted for implant indication, age, race, body mass index, occupation, smoking, marital status and/or other implant features - 61% follow-up at 5 years	7	Yes
	Systemic sclerosis	5	0	–				
	Sjögren’s syndrome	17	0	–				
	Lupus/lupus-like	12	6	0.64 (0.23-1.75)				
	Rheumatoid arthritis	27	4	1.24 (0.47-3.26)				
	Dermatomyositis/ polymyositis	1	0	–				
	Mixed CTD	4	1	1.50 (0.26-8.79)				
	CTD not otherwise specified	22	6	0.95 (0.39-2.31)				
	Polymyalgia rheumatica	5	0	–				
	Relapsing polychondritis	0	1	–				
	Behçet syndrome	1	0	–				
	Fibromyalgia	83	27	0.82 (0.55-1.22)				
Chronic fatigue syndrome	6	4	0.42 (0.09-1.86)					
<b>Lee et al. (2011)</b> United States, 2001-2005	All women	2,626; RR (90% CI)	1,384; RR (90% CI)	No breast implants (reference)	3.6 years (median)	- Health professionals (Women’s Health Study) - Matched on age; adjusted for age, body mass index, smoking, hormones, breast cancer	5	Yes
	Self-reported CTD	84; 1.68 (1.31-2.15)	20 1.48 (0.93-2.36)	377				
	CTD confirmed using validated questionnaire	62; 2.03 (1.50-2.73)	12; 1.45 (0.79-2.67)	226				
	CTD confirmed using medical records	18; 1.63 (0.93-2.86)	2; 0.79 (0.19-3.25)	74				

## B) INDICATION FOR BREAST IMPLANTS

Study (Year) Location, study period	Category	No. with cosmetic augmentation BI	No. with reconstructive BI or breast cancer	Measure of effect	Time since implant	Notes	NOS	\$
<b>Gabriel et al. (1994)</b> United States, 1964-1991	All women	534	90 (prophylaxis); 125 (cancer)	RR (95% CI) for C, prophylaxis, cancer Reference: no BI	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 CTD	2	1; 2	0.60 (0.12-2.36); 1.21 (0.12-6.64); 3.16 (0.60-12.24);				
	Any arthritis	13	6; 6	1.02 (0.53-1.86); 1.87 (0.74-4.15); 2.43 (0.97-5.40)				
	Sicca	20	6; 7	1.22 (0.72-2.02); 1.46 (0.59-3.19); 2.21 (0.95-4.62)				
	Malar or discoid rash	0	0; 1	0 (0-1.87); 0 (0-7.44); 3.20 (0.30-19.98)				
	Oral ulcers	4	1; 2	0.58 (0.18-1.55); 0.58 (0.06-2.92); 1.51 (0.3-5.30)				
	Photosensitivity	2	1; 0	1.00 (0.18-4.42); 2.00 (0.2-12.20); 0 (0-7.81)				
	Salivary gland enlargement	2	2; 0	2.04 (0.32-11.52); 0 (0-14.03); 0 (0-18.24)				
	Symmetric muscle weakness	0	1; 0	0 (0-1.87); 2.45 (0.23-15.36); 0 (0-9.67)				
	Morning stiffness	16	8; 6	1.40 (0.76-2.48); 2.78 (1.23-5.74); 2.71 (1.07-6.06)				
	Serositis	5	3; 10	0.72 (0.26-1.80); 1.74 (0.46-5.15); 7.53 (3.46-15.64)				
<b>Nyren et al. (1998)</b> Sweden, 1964-1993	All women	3,500	3,942 (R)	SHR (95% CI)	8.0 years (mean)	- Swedish national inpatient registry - National rates of first hospitalization standardized for age, sex and calendar year - Inpatients only - Included prevalent and misclassified diagnoses	7	Yes
	Systemic sclerosis	0	1 (prevalent)	C: 0 (0-4.6) R: 1.6 (0-9.0)				
	Sjögren's syndrome	3 (2 prevalent)	0	C: 5.0 (1.0-14.5) R: 0 (0-2.9)				
	SLE	5 (2 prevalent)	2 (1 prevalent, 1 misclassified)	C: 2.3 (0.7-5.3) R: 1.2 (0.1-4.2)				
	Rheumatoid arthritis	11 (4 prevalent)	8 (4 prevalent, 1 misclassified)	C: 1.3 (0.7-2.4) R: 0.7 (0.3-1.4)				
	Dermatomyositis	1	0	C: 7.3 (0.2-40.5) R: 0 (0-19.5)				
Any of above CTD	18 (6 prevalent)	11 (6 prevalent, 2 misclassified)	C: 1.6 (0.95-2.4) R: 0.8 (0.4-1.4)					
<b>Singh et al. (2017)</b> United States, 2007-2015	All women	29,148 primary; 5,901 revision	4,648 primary R; 699 revision R	SIR (95% CI: NR) for C-primary; C-revision; R-primary; R-revision	5 to 8 years	- Prospective post-approval long-term study - National rates standardized for female sex, age and race - 61% follow-up at 5 years	7	Yes
	Systemic sclerosis	0; 3	0; 1	0.0; 0.6; 0.0; 4.8				
	Sjögren's syndrome	10; 3	2; 2	1.1; 1.7; 1.3; 8.5				
	Lupus/lupus-like	9; 2	1; 0	0.1; 0.1; 0.1; 0.0				
	Dermatomyositis/ polymyositis	-; -	0; 1	-; -; 0.0; 30.4				
<b>Hennekens et al. (1996)</b> United States, 1962-1991	All women	Total 10,830	18%	P value for interaction	<4 to ≥10 years (range)	- Health professionals (Women's Health Study) - Self-reported diagnoses - Comparator: no BI	6	Yes
	Any CTD	-	-	0.93				
<b>Lee et al. (2011)</b> United States, 2001-2005	All women	-	56 (history of breast cancer)	RR (95% CI)	3.6 years (median)	- Health professionals (Women's Health Study) - Prospective cohort - Comparator: no BI - Matched on age; adjusted for age, body mass index, smoking, hormones, breast cancer	5	Yes
	Any CTD	-	34	1.66 (1.28-2.16) without cancer history; 1.30 (0.72-2.34) with cancer history				

### C) DURATION OF BREAST IMPLANTS

Study (Year) Location, study period	Category	Duration of breast implants	No. with rheumatic disease	Relative risk (95% CI)	Measures of interaction	Notes	NOS	\$
<b>Hennekens et al. (1996)</b> United States, 1962-1991	Any CTD	> 0 to 4 years	83	1.25 (1.10-1.55)	Trend P = 0.92; Ratio ≥10 years vs. 1-9 years: 0.99 (P = 0.94)	- Health professionals (Women's Health Study) - Self-reported diagnoses - Comparator: no BI	6	Yes
		5 to 9 years	70	1.23 (0.97-1.56)				
		≥ 10 years	78	1.23 (0.98-1.54)				
	Rheumatoid arthritis	> 0 to 4 years	36	1.09 (0.79-1.52)	Trend P = 0.42; Ratio ≥10 years vs. 1-9 years: 1.19 (P = 0.39)			
		5 to 9 years	31	1.12 (0.79-1.60)				
		≥ 10 years	40	1.32 (0.96-1.80)				
	SLE	> 0 to 4 years	14	1.36 (0.81-2.31)	Trend P = 0.34; Ratio ≥10 years vs. 1-9 years: 0.71 (P = 0.40)			
		5 to 9 years	10	1.15 (0.62-2.15)				
		≥ 10 years	8	0.90 (0.45-1.80)				
	Sjögren's syndrome	> 0 to 4 years	4	0.85 (0.32-2.28)	Trend P = 0.16; Ratio ≥10 years vs. 1-9 years: 1.62 (P = 0.26)			
		5 to 9 years	7	1.57 (0.75-3.31)				
		≥ 10 years	11	1.95 (1.07-3.55)				
	Dermatomyositis / polymyositis	> 0 to 4 years	8	1.86 (0.93-3.74)	Trend P = 0.29; Ratio ≥10 years vs. 1-9 years: 0.56 (P = 0.26)			
		5 to 9 years	7	1.76 (0.83-3.71)				
		≥ 10 years	5	1.01 (0.42-2.45)				
	Scleroderma	> 0 to 4 years	5	2.68 (1.11-6.51)	Trend P = 0.15; Ratio ≥10 years vs. 1-9 years: 1.22 (P = 0.76)			
		5 to 9 years	1	0.60 (0.08-4.30)				
		≥ 10 years	4	2.08 (0.77-5.61)				
	Other CTDs (including mixed)	> 0 to 4 years	29	1.33 (0.92-1.92)	Trend P = 0.99; Ratio ≥10 years vs. 1-9 years: 1.03 (P = 0.88)			
		5 to 9 years	24	1.24 (0.83-1.86)				
		≥ 10 years	30	1.33 (0.93-1.91)				
<b>Lee et al. (2011)</b> United States, 2001-2005	Self-reported CTD	< 10 years	10	1.34 (0.69-2.61)	P for trend = 0.80			
		10 to < 20 years	61	1.73 (0.29-2.30)				
		≥ 20 years	41	1.53 (1.10-2.13)				
	CTD confirmed using validated questionnaire	< 10 years	7	1.52 (0.67-3.44)	P for trend = 0.59			
		10 to < 20 years	43	2.00 (1.41-2.85)				
		≥ 20 years	26	1.64 (1.08-2.47)				
	CTD confirmed using medical record	< 10 years	3	1.54 (0.38-6.32)	P for trend = 0.42			
		10 to < 20 years	12	1.61 (0.83-3.14)				
		≥ 20 years	6	1.14 (0.49-2.64)				

BI: breast implant; C: cosmetic/augmentation; CI: confidence interval; CTD: connective tissue disease; MRI: magnetic resonance imaging; N/A: not applicable; NOS: Newcastle-Ottawa scale (range 0 to 9); NR or -: not reported; NS: not statistically significant; OR: odds ratio; R: reconstruction; RR: relative risk; SHR: standardized hospitalization ratio; SIR: standardized incidence ratio; SLE: systemic lupus erythematosus; \$: potential financial or other conflict of interest.