Supplementary Online Content

de Boer M, Van Leeuwen FE, Hauptmann M, et al. Breast implants and the risk of anaplastic large-cell lymphoma in the breast [published online January 4, 2017]. *JAMA Oncol*. doi:10.1001/jamaoncol.2017.4510

This supplementary material has been provided by the authors to give readers additional information about their work.

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1. eMethods:

1. Pathology review

All cytological preparations and histological biopsy and excision samples of potential breast-ALCL were reviewed by an experienced hematopathologist (DDJ). In all cases, CD30 and T-cell markers to support a T-cell immunofenotype were available. With sufficient material available to complete immunohistochemical evaluation, at least CD30, CD2, CD3, CD4, CD8, TIA1, granzyme B, ALK1, EBER and CD20 were included, and in selected cases molecular analysis (T-cell receptor rearrangement analysis according to standard BIOMED2 technology) was performed.[28,29] Local disease status was classified according to Clemens et al.[30]

2. Case-control selection

Via the nationwide network and registry of histo- and cytopathology in the Netherlands (PALGA) we identified 782 female patients diagnosed with a histologically or cytologically-proven non-Hodgkin lymphoma (NHL) of the breast in the Netherlands during 1990-2016.

For the period between 1990 and 2005, 398 eligible female patients, and for the period between 2006 and 2016, 384 eligible female patients were diagnosed. Of 782 subjects, only patients classified as anaplastic large cell lymphoma for the case group, and diffuse large B-cell lymphoma, Burkitt lymphoma, follicular lymphoma, nodal and mucosa-associated lymphoid tissue-type marginal zone lymphoma, and peripheral T-cell lymphoma not otherwise specified for the control group were included. 220 subjects were excluded based on other lymphoma types, including chronic lymphocytic leukemia and acute lymphoblastic leukemias as disseminated diseases per definition. Of the remaining 562 subjects, 325 were not confirmed as primary breast located lymphomas.

In the case group, 47 cases were selected; 4 were excluded since the breast was not confirmed as primary lymphoma location. In the control group, 190 controls were selected; 27 were excluded since the breast could not confirmed as primary lymphoma location, 15 controls were missing due to non-responding physicians, and 2 controls were lost to follow-up in medical follow-up records.

For the period between 1990 and 2005, eleven patients with breast-ALCL, among whom 5 with an implant, and 35 controls with non-Hodgkin lymphoma other than breast-ALCL, among whom 1 with an implant, were previously reported in our earlier study.[4] Subsequently, 32 breast-ALCL cases, among whom 27 with an implant, and 110 controls among whom 1 with a breast implant (contralateral, non-lymphoma-affected), were diagnosed between 2006-2016 (Table 1). Seventy-seven % of breast-ALCL cases was identified between 2006-2016, implying a substantially increased incidence (eFigure 4).[4]

3. Estimation of the prevalence of women with breast implants

We assessed the point prevalence of breast implants per 10-year age group in the general female population in 2015 based on evaluation of 3000 chest X-rays in two cohorts of female patients (20-70 years), and we used the differences in region-specific breast implant prevalence from the BCSP (Breast Cancer Screening Program) to derive a national breast implant prevalence (eFigure 2). The cohorts originated from two regional hospitals in the Netherlands (Maastricht University Medical Centre, Maastricht and Medical Spectrum Twente, Enschede). The validity (sensitivity and specificity) of this method was first examined in a separate validation study using a series of 180 X-rays, alternately positively (n=60) or negatively confirmed (n=120) for the presence of a breast implant by a simultaneously performed CT-scan. CT-scans demonstrating a breast implant were identified by a digital search of radiology reports of the Medical Spectrum Twente radiology database. Inter-observer reproducibility of eight blinded reviewers, including two specialized breast radiologists, two plastic surgeons, two plastic surgery residents, and two medical students, were assessed. Five out of eight reviewers completed the validation study satisfactorily with a median sensitivity of 72% (range 70-77%) and a median specificity of 94% (range 82-96%), of whom three were selected to participate in the prevalence study. To further improve specificity in the actual prevalence study, in case of discordance between two independent reviewers, consensus was reached during a specific reviewers' meeting.

Sales data from 2010-2015 were provided by all currently active breast implant vendors on the Dutch market, representing >95% of the total market share for this period. After exclusion of the component of tissue expanders (temporary implants used as a first-stage prior to definitive breast reconstruction with a permanent breast implant), market shares per vendor were determined. Data prior to 2010 was not considered sufficiently reliable to reflect the breast implant market, since sales data from various breast implant vendors, active prior to 2010, were unavailable, due to bankruptcy or retraction of companies and introduction of others, resulting in major variations in the market.

Subsequently, we determined the average annual percentage change (AAPC) of implant sales during the period with available data (2010-2015) by regressing the log-transformed number of sold implants per year on calendar year.[14] This estimated AAPC was used to extrapolate the number of sold implants in 2016. Corresponding numbers for the period 1965-2009 were extrapolated by applying an AAPC to the empirical 2010 data, which results in virtually no sold implants in 1965, the year the first implant was used in the Netherlands.

The change in implant prevalence by calendar year was determined by using the AAPCs for the period 1965-2016, and by using the age-specific size of the female Dutch population from Statistics Netherlands (CBS), resulting in the estimation of the prevalence of women with breast implants for the period 1965-2016.

4. Calculation of cumulative risk

The cumulative risk for breast-ALCL by age in the general female population, as well as in women with breast implants, was calculated using the number of breast-ALCL cases in the general female population, as well as breast-ALCL cases in women with breast implants from PALGA. The age-specific size of the general female Dutch population was obtained from Statistics Netherlands (CBS)[15], the age-specific size of the female population with breast implants was obtained as described in Supplementary methods 3. Cumulative risk to develop breast-ALCL up to age z was calculated as $P_{cri} = 1\text{-}\exp(\text{-}\Sigma_x l_x * c_x/n_x)$ where c_x and n_x are the numbers of cases and person-years in age-category x, respectively, l_x is the width of the age interval and z is the upper limit of the last age category.[16] For breast-ALCL risk in the general female population, cut-offs for age categories were 35, 45, 55, 65 and 75 years. For breast-ALCL risk among women with breast implants, cut-offs were 30, 40, 50, 60 and 70 years.

2. eResults

1. Lymphoma characteristics of breast-ALCL cases

Exposed breast-ALCL cases

Thirty-two breast-ALCL patients were diagnosed between 1997 and 2016 at a median age of 56 years (range 29-73). Primary breast lymphoma was defined as 1) the dominant primary or main symptomatic location in the breast OR 2) the breast lesion the dominant site of involvement on PET-PDG scanning. Twenty-one patients presented with stage I, 5 patients presented with stage II, 3 with stage III, and 3 with stage IV disease.

In 15 patients, large polymorphous lymphoid cells were restricted to the seroma space (T1, according to Clemens *et al.)*[30], in 5 patients additionally minor infiltrative foci were noted in the periprosthetic fibrous capsule (T2). Twelve patients presented with a tumorous mass with infiltration into the breast parenchyma (T3/T4) and histological features as in non-implant-associated patients. In all cases, expression of CD30 was uniform and ALK1 was negative. A T-cell phenotype based on expression of at least one T-cell marker (CD3, CD2, CD5, CD7, CD4, CD8, GB7, TIA1) in the absence of B-cell marker expression (CD20, CD79a, PAX5) was confirmed.

Non-exposed breast-ALCL cases

Eleven primary breast-ALCL patients without an implant were diagnosed between 1994 and 2010 at a median age of 61 years (range 24-87). Primary breast lymphoma was defined as above. In all patients, ALCL, ALK- was confirmed according to the criteria of the WHO classification using morphological and immunohistochemical markers as above and presented as a tumorous infiltrate in the breast parenchyma (T4).[7,30]

2. Contralateral breast surgery in exposed breast-ALCL cases

In all patients except one, the implant at the affected side was removed together with the surrounding fibrous capsule. In 18 of 26 patients with bilateral implants, removal of the contralateral implant was performed, for which all patients except one received a contralateral capsulectomy. Eleven patients received no further treatment; the remaining patients received various chemotherapy regimens.

3. References

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4. Supplementary legends to the eFigures

eFigure 1: Selection strategy of histologically or cytologically-proven primary non-Hodgkin lymphoma (NHL) of the breast in female patients diagnosed in the Netherlands between 1990-2016.

Initially, 782 patients for whom no previous lymphoma diagnosis was listed prior to breast lymphoma were identified. Of these 47 were diagnosed as ALCL and 190 as diffuse large B-cell lymphoma, Burkitt lymphoma, follicular lymphoma, nodal and mucosa-associated lymphoid tissue-type marginal zone lymphoma and peripheral T-cell lymphoma not otherwise specified and considered for this study. Of these, 59 patients were further excluded since primary breast localization could not be confirmed based on present clinical criteria and/or lack of sufficient clinical information thereof. Primary breast lymphoma was defined as 1) the dominant primary or main symptomatic location in the breast OR 2) the breast lesion the dominant site of involvement on PET-PDG scanning.

eFigure 2: Assessment of breast implant prevalence in the Netherlands in 2015, by A: Regional breast implant prevalence in 2015 in women between 20-70 as estimated from 3,000 chest X-rays in two large regional medical centers in the East and South of the Netherlands, B: Region-specific breast implant prevalence rates from the National Breast Cancer Screening Program (BCSP) and C: Derived estimation of breast implant prevalence in the Netherlands in 2015 in women between 20-70

Part A shows breast implant point prevalence derived from the chest X-ray study performed in two regional referral hospitals in the Eastern and Southern regions of the Netherlands in women between 20-70 years old. Part B shows region-specific breast implant prevalence rates from the National Breast Cancer Screening Program (BCSP). In part C, national breast implant prevalence in the Netherlands is shown, derived by combining differences in region-specific breast implant prevalence from the BCSP and regional point prevalences from the chest X-ray study (part A and part B).

eFigure 3: Estimated number of breast implants sold in the Netherlands by calendar year.

The average annual percentage change (AAPC) of sold breast implants between 2010-2015 (covering >95% of all sold breast implants) was used to extrapolate to the periods 1965-2009 (1965 as the year of the first implant used), and 2015-2016.

eFigure 4: Incidence of breast-ALCL in patients with breast implants and reasons for breast implantation

The incidence of breast-ALCL in patients with breast implants shows a strong increase between 1997 and 2016, most prominent after 2012. This increase may be caused by a higher frequency of breast-ALCL, or may in part be related to increased awareness of medical professionals and women with breast implants.

eFigure 5: Sales data of breast implants in the Netherlands between 2010 and 2015 by A: surface properties and B: filling properties.

Sales data were obtained from four manufactures (Allergan, Mentor, Polytech, Eurosilicone) active in the Dutch market between 2010 and 2015. This information covers approximately 95% of the market share in the Netherlands for the period of 2010-2015. Of one complying company, data were received for the period from 1995 to 2015, of one company for the period from 2009 to 2015, of one company for the period from 2007 to 2015 and of one company, who has only recently entered the Dutch market, from 2013-2015. Virtually no smooth and polyurethane implants or non-silicone filled implants were sold during this period, while macro- and micro-textured implants had largely similar market shares.

5. eTables and eFigures

eTable 1: Implant characteristics of 32 patients with breast-ALCL with breast implants.

		Breast-ALCL cases (N)	
Year of breast implant	1965-1975	1	
	1976-1985	4	
	1986-1995	6	
	1996-2005	14	
	2006-2015	7	
Age at breast implant (years)	21-30	10	
	31-40	7	
	41-50	8	
	51-60	6	
	>60	1	
Indications for implants	Cosmetic	22	
	Reconstruction after breast cancer surgery	7	
	Reconstruction after prophylactic mastectomy	3	
Type of implant	Macro-texture	Allergan/Inamed/ McGhan	22
		Nagor	1
	Microtexture	Eurosilicone	2
		Mentor	1
		PIP	1
		Sebbin	1

	Unknown		4
Side of implant	Unilateral	5	
	Bilateral	27	
Interval between first implant and ALCL diagnosis (years) (median interval 13 years, range (1-39 years)	1-5	6	
	6-10	5	
	11-20	14	
	21-30	5	
	31-40	2	
Number of implant revisions	None	21	
	Single	3	
	Multiple	8	
Indications for last revisional surgery	Capsular contraction		4
	Periprosthetic seroma	Inflammation-related	2
		Lymphoma-related	2
	Unknown		3

eTable 2: Clinical characteristics and treatment of 43 patients with breast-ALCL with and without breast implants.

		Primary breast ALCL with breast implants (N=32)	Primary breast ALCL without breast implants (N=11)
Lymphoma localisation	Unilateral	29	9
	Bilateral	3	2
Type of ALCL	Seroma-associated[11]	18	0
	Mass forming[11]	14	11
Stage	I	21	6
	II	5	2
	III	3	0
	IV	3	3
Treatment	First line surgical therapy only (excision or capsulectomy and explantation)	11	0
	First line surgical therapy and chemo-therapy and/or radiotherapy	12	10
	Second line high dose chemotherapy and hematopoietic stem cell transplant	9	1
Treatment results	Complete remission on first-line and or second-line treatment	29	8
	Partial remission on first line and/or second line treatment	1	0
	Progressive disease	2	3
	Local relapse	0	0
Outcome	Death due to lymphoma	2	3
	Death of other causes	1	0

	Alive without disease	23	8
	Alive under active treatment	6	0

eTable 3: Clinicopathological characteristics of 32 patients with breast-ALCL with breast implants, diagnosed between 1990 and 2016

Case	Age at diagnosis of breast-ALCL	Year of di-agno-sis breast-ALCL	Indication for breast implant	Breast implant side	Implant revision	Breast implant type present at lymphoma diagnosis	Interval between first breast implant and lymphoma diagnosis (years)	Interval between last implant revision and lymphoma diagnosis (years)	Involved lymphoma sites at diagnosis	Stage at diagnosis	ALCL type: seroma or tumor-forming	TNM	Treatment	Out-come	Follow-up (December 2016, in months)
1	38	1997	1984 Cosmetic augmentation	Bilat-lat-eral		Unknown	13		Left breast	II	mass	T2N0 M0	7x CAVmP/BV, explantation and capsulectomy after chemotherapy	CR	240
2	29	1999	1996 Cosmetic augmentation	Bilat-lat-eral		Nagor, macrotextured, silicone	3		Right breast, right axil-lary lymph node	II	mass	T2N1 M0	Explantation and capsulectomy bilateral, CHOP 6x, radiotherapy	CR, DOOC	72

3	49	2000	1977 Cosmetic augmentation	Bilat-lat-eral	1988, 1995: reason unknown, new implant unknown 1998: reason unknown, new implant McGhan, textured	McGhan, macrotextured, silicone	23	2	Bilateral breasts	II	mass	T2N0 M0	CHOP 3x, radiotherapy, -> PR followed by bilateral explantation and capsulectomy, IMVP 2x, BEAM/ASCT,	CR	204
4	53	2001	2000 Cosmetic augmentation	Bilat-lat-eral		Rofill PIP Hydrogel, micro-textured	1		Left breast	I	mass	T2N0 M0	Explantation and capsulectomy	CR	192
5	43	2005	1992 Cosmetic augmentation	Bilat-lat-eral		McGhan, macrotextured, silicone	13		Right breast, right axillary and infraclavicular lymph nodes, small bowel, right skull base	IV	mass	T2N2 M1	CHOP 8x, DHAP-VIM-DHAP/MTX, explantation and capsulectomyright	CR	144

6	47	2008	1988 Cosmetic augmentation	Bilat-lat-eral	1994: reason unknown, new implant unknown 2002: Seroma, new implant McGhan, textured	McGhan, macrotextured, silicone	20	6	Right breast, thoracic wall, right axillary lymph nodes	IIIE	com-bined sero-ma and mass	T3N2M1	Explantation and capsulectomy bilateral, CHOP 6x, DHAP+ ASCT	CR	108
7	70	2010	1971 Cosmetic augmentation	Bilat-lat-eral	1994: reason unknown, new implant unknown 2002: Seroma, new implant McGhan/Inamed CML 170, macrotextured	Inamed CML 170, macrotextured, silicone	39	8	Right breast, right axillary lymph node	IIE	sero-ma	T1N1M0	Explantation and capsulectomy	CR	84

8	54	2010	1981 Right-sided mastectomy for breast cancer (reconstruction in 1984)	Right	1984: Silastic 180 gel silicone filled 1995: reason unknown, McGhan 220 cc gell 2003: reason unknown, McGhan	McGhan, macro-textured, silicone	26	7	Right breast, right axillary and supra/infra-clavicular lymph nodes, sub pleural right	III	sero-ma	T1N2 M0	2010 ABVD, 2011 Explantation and capsulectomy, right, adjuvant chemotherapy (DHAP - VIM - DHAP and BEAM) ASCT	CR	84
9	45	2011	2000 Cosmetic augmentation	Bilat-lat-eral	2010: Capsular contracture, new implant Mentor Siltex round moderate plus profile	Mentor Siltex, micro-textured, silicone,	11		Right breast	I	sero-ma	T1N0 M0	Explantation and capsulectomy bilateral, CHOP 4, radiotherapy (45Gy)	CR	70

10	63	2011	1991 Cosmetic augmentation	Bilat-lat-eral		Unknown	20		Bilateral breasts, mediastinal and abdominal lymph nodes	III	mass	T4N2M0	Explantation and capsulectomy, 8 CHOP, DHAP-VIM-VIM, radiotherapy	DOD	11
11	64	2012	2001 left-sided mastectomy for breast cancer	Left		McGhan 410 MF 375cc, macro-textured, silicone	11		Left breast	I	sero-ma	T1N0M0	Explantation and capsulectomy left, explantation right, 6x CHOP	CR	55
12	42	2012	2004 Cosmetic augmentation	Bilat-lat-eral		Unknown	8		Left breast, upper abdominal lymph node	IV	mass	T4N1M1	CHOP 6, BEAM and ASCT	CR	54

13	48	2012	1998 Right-sided mastectomy for breast cancer, 2004 left-sided prophylactic mastectomy (BRCA2 mutation carrier)	1998 Right, 2004 bilat-lat-eral		McGhan, macro-textured, silicone	14		Left breast	I	sero-ma	T1N0M0	Explantation and capsulectomy left, CHOP 6x	CR	58
14	35	2013	2008 Cosmetic augmentation	Bilat-lat-eral		Eurosilicone type 81 micro-textured, silicone 260cc	5		Right breast	I	mass	T4N0M0	Explantation and capsulectomy bilateral, cisplatin	CR	37

15	67	2013	1987 Cosmetic augmentation	Bilat-lat-eral	2007: capsular contracture, new implant Inamed 110 330gr, macro-textured, silicone 2009: capsular contracture, new implant Inamed 110 330gr	Inamed 110 330gr, macro-textured, silicone	26	4	Right breast	I	sero-ma	T1N0 M0	Explantation and capsulectomy right, 6x CHOP	CR	40
16	55	2013	1987 Cosmetic augmentation	Bilat-lat-eral		McGhan matrix 210cc macro-textured, silicone	26		Left breast	IE	mass	T4N0 M0	Explantation and capsulectomy bilateral + 6 CHOP	CR	37
17	46	2014	2000 Cosmetic augmentation	Bilat-lat-eral		McGhan 410 245cc, macro-textured, silicone	14		Left breast	IB	sero-ma	T1N0 M0	Explantation right, Explantation and capsulectomy left	CR	33

18	40	2014	2002 Cosmetic augmentation	Bilat-lat-eral		McGhan 120cc, macro-texture, silicone,	12		Left breast, left axillary lymph nodes	IIA-E	mass	T4N2 M0	Explantation and capsulectomy bilateral, CHOP 5 DHAP 1	CR	5
19	72	2014	1977 Cosmetic augmentation using unknown type	Bilat-lat-eral	Multiple revisions: years and reasons unknown 2009: capsular contracture left, new implant McGhan Cohesive Gel Biocell	McGhan, macro-textured, silicone	37	5	Left breast	I	sero-ma	T1N0 M0	Explantation and capsulectomy left	CR	26
20	56	2014	2002 prophylactic mastectomy (BRCA1 mutation carrier)	Bilat-lat-eral		Alllergan, macro-textured silicone	12		Right breast	I	sero-ma	T1N0 M0	Explantation and capsulectomy bilateral	CR	25

21	57	2014	2005 Cosmetic augmentation	Bilat-lat-eral		Eurosilicone, micro-textured, silicone	9		Right breast	IE	sero-ma	T1N0 M0	Bilateral explantation and capsulectomy,radiotherapy	PR	33
22	57	2014	2008 Right-sided mastectomy for breast cancer, 2014 left-sided mastectomy for breast cancer	Bilat-lat-eral		Allergan type 410, macro-textured, silicone	6		Right breast	IE	mass	T3N0 M0	Explantation and capsulectomy, CHOP 3x, radiotherapy	CR	32

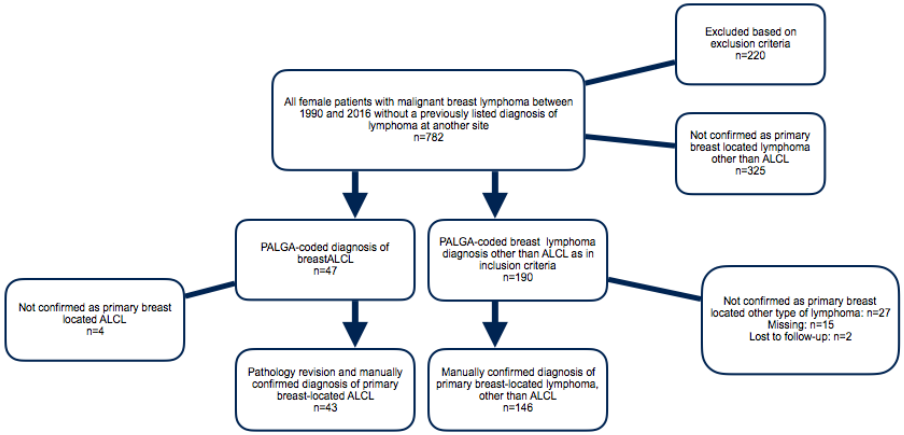
23	56	2015	2010 Right-sided mastectomy for breast cancer, left-sided prophylactic mastectomy (familial cancer, no proven mutation)	Bilat-lat-eral	2011: Infection, new implant McGhan Mx 550 2015: Seroma (cytological ALCL diagnosis), new implant McGhan Mx 620	Mc Ghan 620 Mx, macro-textured, silicone	5	1 month	Left breast	I	sero-ma	T1N0 M0	Explantation and capsulectomy bilateral, radiotherapy (30 Gy)	CR	16
24	43	2015	1993 Cosmetic augmentation	Bilat-lat-eral		Unknown	22		Right breast, right axil-lary lymph node	IA	mass	T4N1 M0	Explantation and capsulectomy bilateral, 6x CHOP, radiotherapy (40 Gy)	CR	22
25	73	2015	2003 Right-sided mastectomy for breast cancer	Right		McGhan 410, macro-textured, silicone	12		Right breast	I	sero-ma	T1N0 M0	Explantation and capsulectomy	CR	15

26	64	2016	2012 Left-sided mastectomy for breast cancer, right-sided prophylactic mastectomy (proven BRCA1 mutation carrier)	Bilat-lat-eral	2016: Periprosthetic seroma left, new implant Allergan Cohesive Gel BIocell	Allergan, macro-textured, silicone	4		Left breast	I	com-bined sero-ma and mass	T3N0 M0	Explantation and capsulectomy	CR	6
27	56	2016	2006 Cosmetic augmentation	Bilat-lat-eral		Allergan 495 cc 410, macro-textured, silicone	10		Left breast	I	sero-ma	T1N0 M0	Explantation and capsulectomy, CHOP 6x	CR	9
28	59	2016	2003 Left-sided mastectomy for breast cancer	Left		Inamed, macro-textured, silicone	13		Left breast	I	mass	T4N0 M0	Explantation and capsulectomy	CR	12

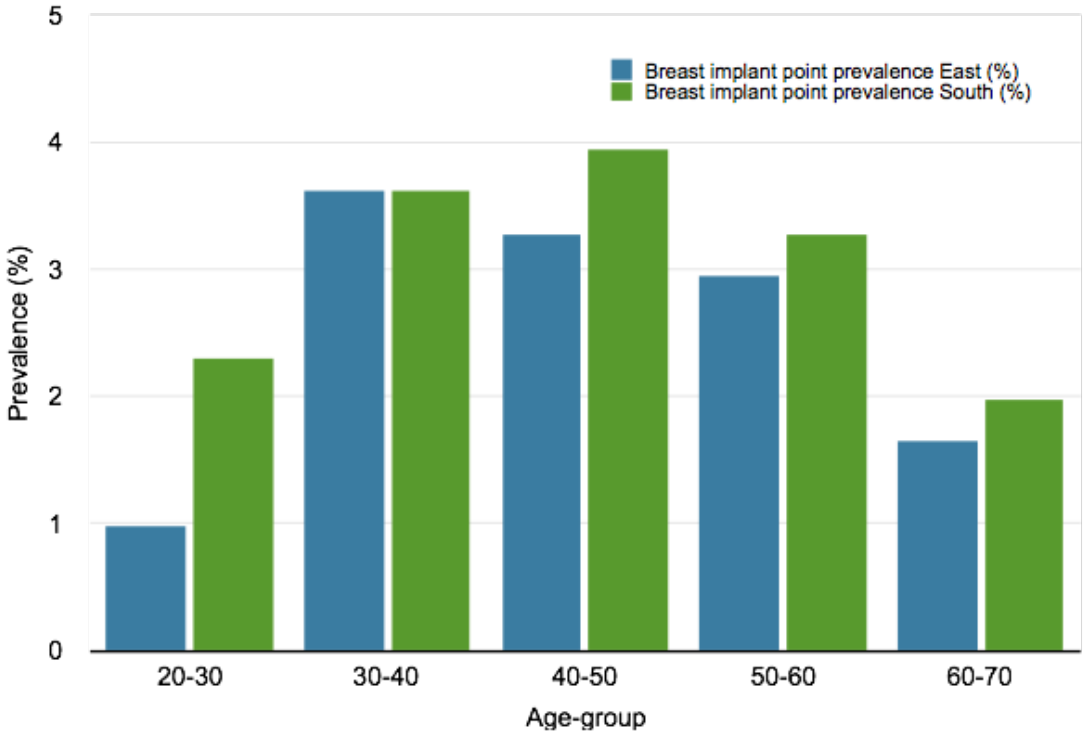
29	56	2016	1998 Cosmetic augmentation	Bilat-lat-eral	2000: pain (new implant Rofill high cohesive textured) 2012: rupture and capsular contracture (new implant Allergan Inspira)	Allergan Natrelle Inspira macro-textured, silicone	18	4	Left breast	I	sero-ma	T1N0M0	Explantation and capsulectomy	CR	5
30	60	2016	2009 Left-sided mastectomy for breast cancer	Left		McGhan, macro-textured, silicone	7		Left breast	I	mass	T4N1M0	Explantation and capsulectomy	CR	2

31	48	2016	2012 Cosmetic augmentation	Bilat-lat-eral	2015: Periprosthetic seroma left, new implant Sebbin LSC 72 330 (cytological diagnosis inconclusive)	Sebbin 330 gr, micro-textured, silicone	4		Left breast	I	mass	T1N0 M0	Explantation and capsulectomy	CR	5
32	56	2016	2001 Cosmetic augmentation	Bilat-lat-eral		McGhan, macro-textured, silicone	15		Left and right breast, abdominal lymphade-nopthy, bone	IV	mass	T3N2 M1	Explantation and capsulectomy, CHOEP 6x + ASCT	CR	2

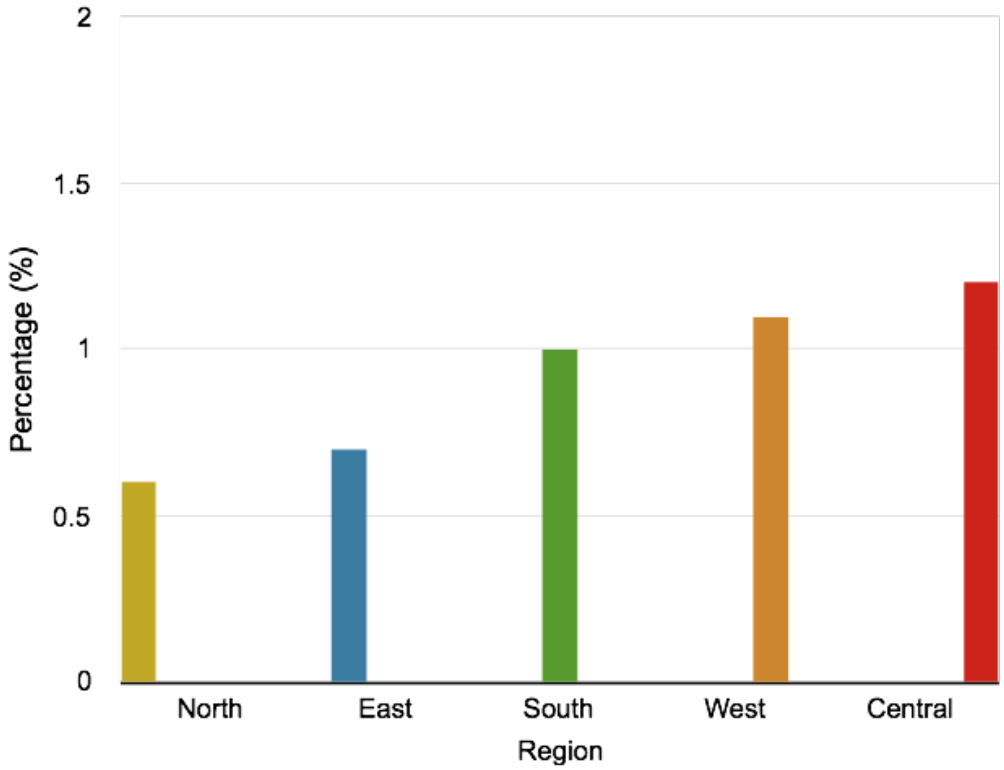
eFigure 1: Selection strategy of histologically or cytologically-proven primary non-Hodgkin lymphoma (NHL) of the breast in female patients diagnosed in the Netherlands between 1990-2016



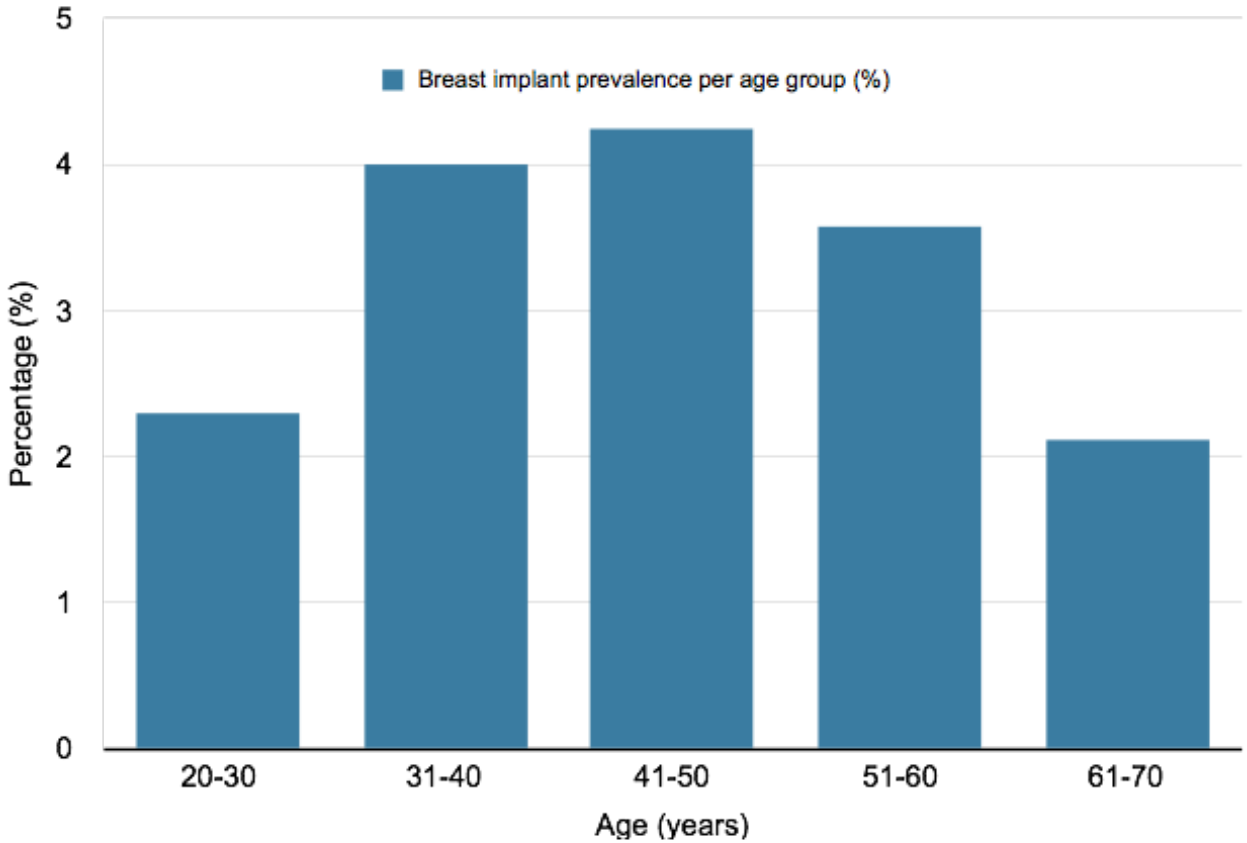
eFigure 2a: Regional breast implant prevalence in 2015 in women between 20-70 as estimated from 3,000 chest X-rays in two large regional medical centres in the East and South of the Netherlands



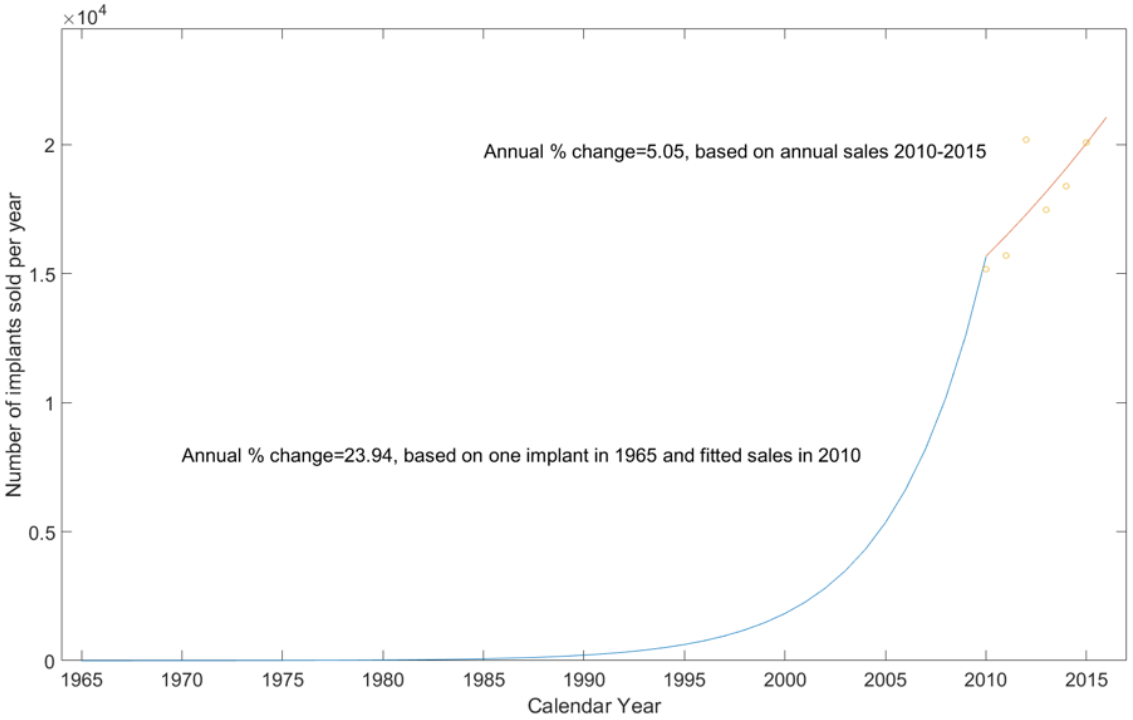
eFigure 2b: Region-specific breast implant prevalence rates from the National Breast Cancer Screening Program (BCSP)



eFigure 2c: Derived estimation of breast implant prevalence in the Netherlands in 2015 in women between 20-70 years of age



eFigure 3: Estimated number of breast implants sold in the Netherlands by calender year



eFigure 4: Incidence of breast-ALCL in patients with breast implants and reasons for breast implantation

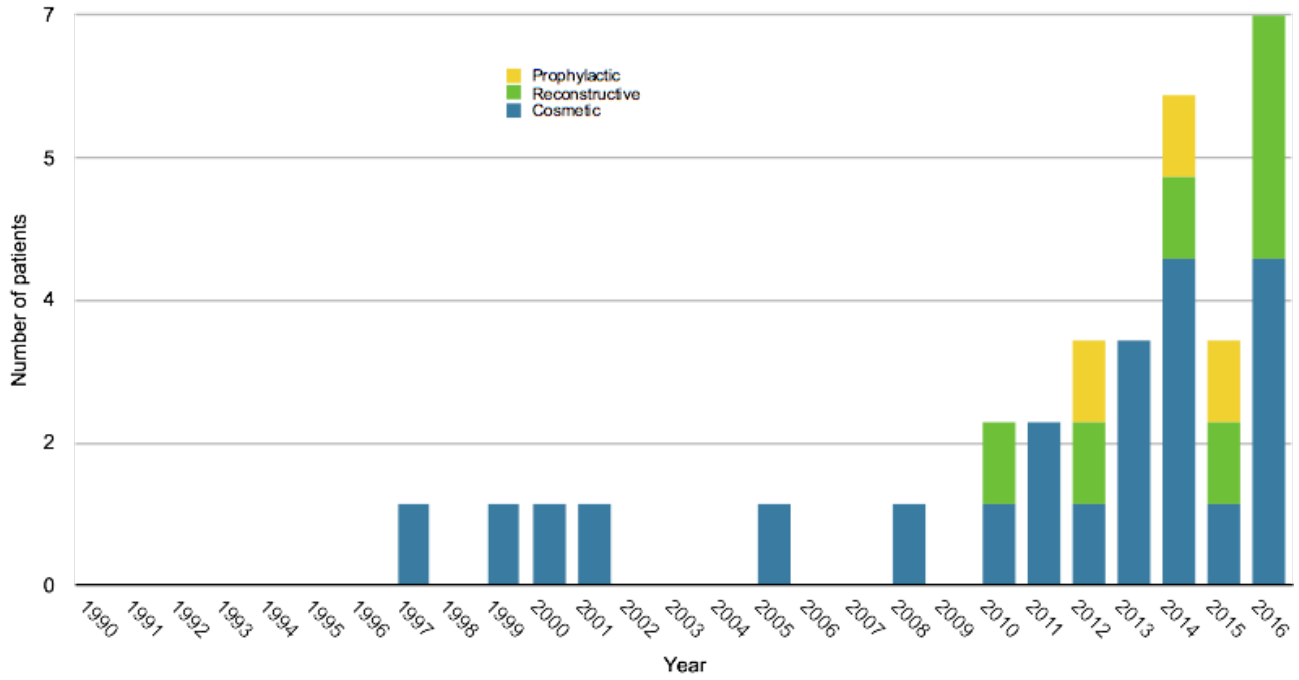
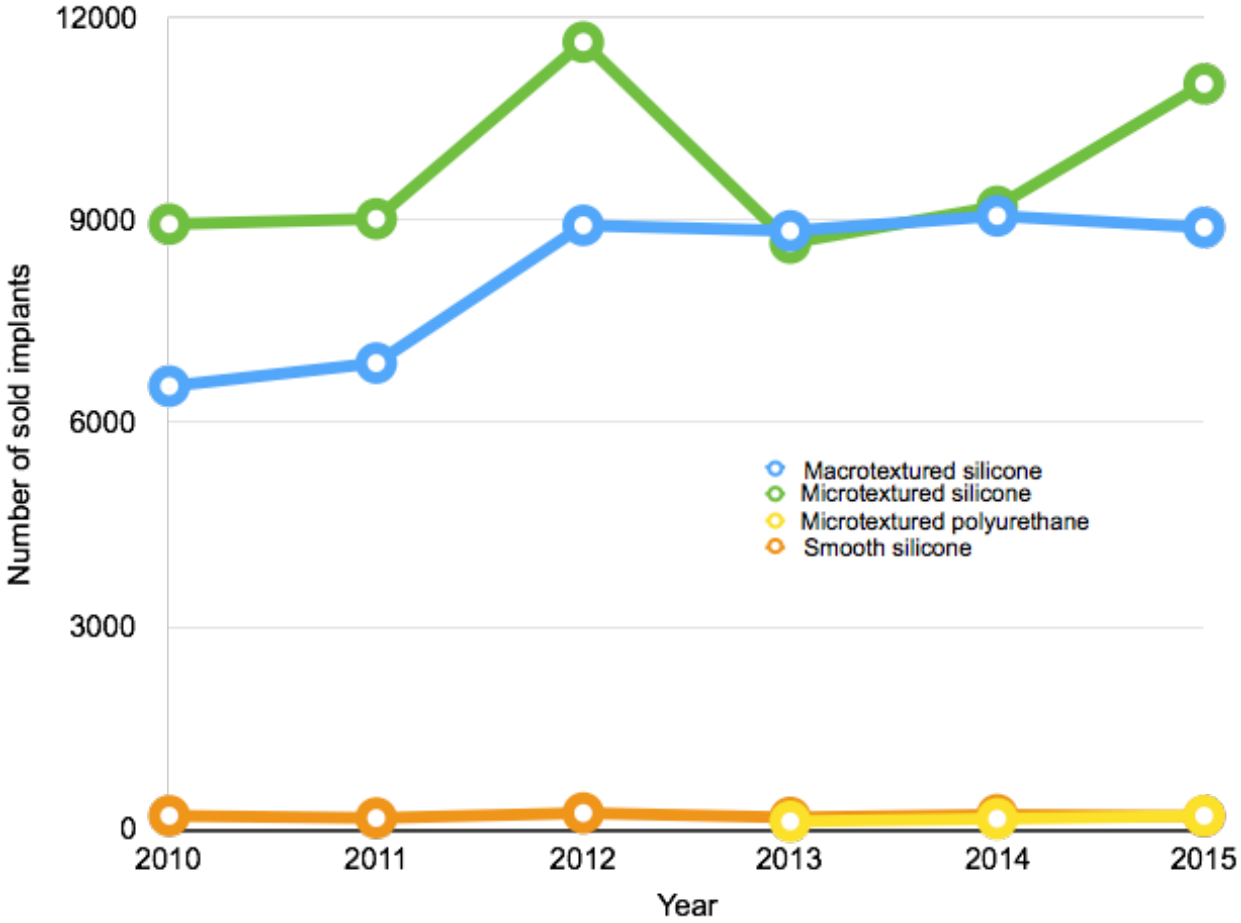


Figure 5a: Sales data of breast implants in the Netherlands between 2010 and 2015 by surface properties



eFigure 5b: Sales data of breast implants in the Netherlands between 2010 and 2015 by filling properties.