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1 A nation-wide analysis of incidence and outcome of breast cancer in the
2 country of Surinam 1994-2003

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Abstract

Introduction: In this study we describe the incidence, treatment and outcome of breast cancer (BC) in the period 1994-2003 in the South-American country of Surinam and compare this with BC in the Netherlands.

Materials and methods: Pathology reports and hospital charts from all BC cases diagnosed between 1994 and 2004 were retrieved from Surinam's single pathology laboratory and its 5 hospitals. Data on demographics, tumor characteristics, treatment and follow-up were gathered. We compared our data to BC statistics of first generation immigrants from Surinam to the Netherlands.

Results: 421 patients were diagnosed with BC during the study period. The age-adjusted incidence rate was 26 per 100,000 compared to 65/100,000 in first generation Surinamese women in the Netherlands. The majority had a fairly advanced stage at presentation, with 60% of tumors larger than 2 cm and 41.6% with lymph node involvement. Because of the absence of radiotherapy facilities, local treatment in most patients was radical mastectomy. Adjuvant hormonal therapy (51.6%) was administered more frequently than adjuvant chemotherapy (20.3%). A significant number of patients was lost to follow-up, resulting in a median follow-up duration of only 23 months. The five year overall survival was 79%.

Conclusions: BC incidence in Surinam is low compared to that in the western world, but the advanced stage at diagnosis, the low utilization of systemic adjuvant therapy and the inadequate follow-up may lead to poor outcomes. A number of steps are underway to improve the level of cancer care in Surinam.

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Introduction

BC is the most common malignancy among women worldwide. However, the incidence is highest in developed countries, and relatively low in the developing world[1].

The republic of Surinam is a former Dutch colony situated in South America, that gained independence in 1975. Its history of colonization, slave labor and contract laborers has led to great ethnic diversity in its population of almost 500,000[2]. The major ethnic groups are of Indian descent (the so called “Hindustani”, 27.4%), or mixed African descent (the so called “Creoles”, 17.7%), Marroons (descendants of runaway slaves,14.7%) and Javanese (descendants of Indonesian contract laborers,14.6%)[3]. In the 1970s and 1980s, after independence and during a period of civil unrest, mass emigration to the Netherlands took place, so that the Netherlands now has a population of almost 350,000 originally from Surinam[4].

In the year 2002 the Gross Domestic Product (GDP) per capita was US\$ 4, 447. The annual per capita health expenditure was US\$ 385, corresponding to an expenditure of 8.6% of the GDP[5]. The equivalent numbers for the USA in 2002 were US\$ 36, 056 for GDP, and US \$5,274 or 14.6% of the GDP for health[6].

There are five hospitals in Surinam, four of which are in the capital of Paramaribo. Medical specialists have all been trained, at least partly, in first world hospitals, mostly in the Netherlands. Surinam has one pathology laboratory in Paramaribo, where all biopsies and surgical specimens obtained anywhere in the country are sent.

Radiotherapy was not available in Surinam during the study period, so that patients who were eligible for radiotherapy had to go out of the country to receive it. A substantial part of the population has limited health care coverage and many patients have to contribute to the cost of health care out of private funds. There is at present no cancer registry.

1
2 Because of the paucity of data on BC in Surinam, the aim of this study was to
3 retrospectively investigate the epidemiology, treatment and outcome of BC over the last
4 decade in order to establish the baseline situation for future health care planning and
5 evaluation. We compared these data to BC statistics of first generation immigrants from
6 Surinam to the Netherlands.

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11 **Methods**

12 Between June 1, 2005, and September 30, 2005, data were collected for all patients
13 with a pathological diagnosis of invasive BC between January 1, 1994, and December
14 31, 2003.

15 After retrieval from the pathology laboratory archives, the patient charts in the different
16 hospitals were collected and hand-searched for the following data: patient
17 demographics; tumor characteristics (including TNM-stage, grade, and hormone
18 receptor status); treatment characteristics and follow-up data. The last date of follow-up
19 was the last recorded hospital contact, or death of patient. During the study period, there
20 were no national guidelines for treatment of breast cancer.

21 This study was approved by the Ministry of Health, the National Medical Ethics Board,
22 the boards of directors and the medical staffs of all hospitals in Surinam. The medical
23 ethics committee of Surinam granted a waiver for informed consent for this archival
24 study. Data on Surinamese women with breast cancer in the Netherlands were retrieved
25 from the Netherlands Cancer Registry. We used data for the provinces of North-Holland
26 and Flevoland, which host 35% of the Surinamese population in the Netherlands.

27

28 **Analysis**

29 A database was made in Access[®] to store all data. The interval between the different
30 therapies was calculated in this program. Kaplan-Meier curves and survival times were
31 calculated in SPSS[®]. The age standardized incidence rate was calculated using the

1 World Standard population.
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14 **Results**

15 **Incidence**

16 From January 1, 1994, until December 31, 2003, 421 patients were diagnosed with BC
17 in Suriname, two were male. The median incidence was 38,5 per year with a peak of 70
18 patients in the year 2000. The crude incidence rate in the study period was 15,7/100,000
19 per year. The age adjusted incidence rate was 28 per 100,000 per year (Table 1). The
20 age adjusted incidence rate for first generation Surinamese women in the Netherlands in
21 the same period of time was 65 per 100,000 per year (Table 1).
22

23 **Patient characteristics**

24 The median age at BC diagnosis was 55 years, with a range of 26 to 90. BC incidence is
25 higher in Surinamese women in the Netherlands than in Surinamese women in Surinam,
26 and this seems to be especially true for women over 55 (Figure 1). BC occurs more
27 often in Creoles (35,7/100,000/year), than in Hindustani (18,2/100,000/year) and
28 Javanese women (20,8/100,000/year).

29 Data on parity (n=173) and age at first pregnancy (n=61) were not available for the
30 majority of patients. Data on lactation and duration of lactation were so scarce that they

1 were left out of this report.

2

3 **Tumor characteristics**

4 In Surinam, ductal cancers were most common (94%), with a minority of lobular tumors
5 (1.7%) and tumors of unknown origin (4.3%). (Table 3)

6 More than 60% of all tumors were T2 (>20mm and <50mm) and larger, while less than a
7 quarter were T1 (<20mm). In almost 15% of cases, tumor size was not known, either
8 because the patients never came back after the diagnostic biopsy for further treatment,
9 or because they were not eligible for surgery due to tumor spread at presentation.

10 The lymph node status was known for 323 patients, with almost equal numbers with
11 tumor-positive (N+) and tumor-negative (N0) axillary nodes. The 96 patients with an
12 unknown axillary node status were either patients who only had a diagnostic biopsy and
13 did not return for further treatment or had an advanced stage at presentation and were
14 not eligible for surgery.

15 The hormone receptor status was known for 69 patients only (Table 3), 40% of whom
16 had a positive estrogen receptor (ER) and/or progesterone receptor (PgR). All but two of
17 these hormone receptor tests were done after 2000.

18 At time of presentation a small number of patients (5.7%) had distant metastases.

19 The majority of tumors for which the histological grade was known, was poorly
20 differentiated according to the Bloom-Richardson classification. The mitotic activity index
21 (MAI), which was determined in Surinam from the year 2000, was known for 95 tumors,
22 of which 53.7% had a MAI ≤ 10 mitotic figures/10 hpf and 46.3% had a MAI > 10 mitotic
23 figures/10 hpf.

24

25 **Treatment**

26 A large majority (79.7%) of patients underwent surgery. Modified radical mastectomy
27 was the procedure most often performed, with some form of breast conserving therapy
28 for a minority of patients (Table 4). The 20.3% of patients who did not receive surgery,
29 were diagnosed with BC, but either never came back for further treatment or had an
30 advanced stage of BC and were thus not eligible for surgery.

31

1 Hormone therapy was prescribed for 216 (51.6%) patients. The lymph node status was
2 known for 186 of these patients, and 62% of N+ patients and 52% of N0 patients
3 received hormone therapy.

4 In the 78 N0 patients who received hormone therapy, the indications for hormone
5 therapy were T1 tumor with BR 3 (n=4), T3 or T4 tumor (n=9), T2 with a BR2 or 3
6 (n=27). For 38 patients the indication for hormone therapy was not specified. 18 of 26
7 patients who had positive hormone receptors received hormone therapy. The 8 patients
8 with a positive hormone receptor who did not receive hormone therapy died or were lost
9 to follow-up soon after diagnosis.

10 A fifth of all patients received adjuvant chemotherapy. This was not appreciably
11 influenced by the size of the primary tumor. Chemotherapy was given to 35.1% of all
12 node positive (N+) patients. Fifty-one percent of N+ women <50 years and 20% of N+
13 women > 50 years received chemotherapy. Seventeen percent of N0 women <50 years
14 and 4% of N0 women >50 years received chemotherapy.

15 Thirty percent of all patients who were eligible for chemotherapy according to the 2005
16 Surinam guidelines. (obviously not available during the study period) actually received it
17 in our cohort.

18
19 Thirty-three patients (of 42 who had breast conserving surgery) were irradiated abroad
20 after lumpectomy. Twenty-six patients received radiotherapy after radical mastectomy.
21 The indication for adjuvant radiotherapy was irradiation in five patients, T3 tumor
22 (n=3), T4 tumor (n=3), age < 35 years (n=2), ER-/PgR- (n=2), and grossly positive lymph
23 nodes (>N2 in 7 patients). For 4 patients who were treated with adjuvant radiotherapy
24 after mastectomy, the indication could not be retrieved from the available records.

25

26 **Treatment duration**

27 The median time from the date of diagnosis until the date of surgery in Surinam was 17
28 days, with not much variation between the different hospitals in Paramaribo. The median
29 time between breast conserving surgery in Surinam and radiotherapy abroad was 11
30 weeks. For the 26 patients who received radiotherapy after mastectomy, the median
31 time between mastectomy and radiotherapy was 11.5 weeks.

1 The median time between surgery and second treatment modality, either chemotherapy
2 or radiotherapy was 9 weeks. The median time from the end of the first to the start of the
3 second adjuvant treatment modality was 12 weeks.

4 5 **Outcome**

6 Follow-up data of 384 (91.7%) patients were available, but median follow-up was only 23
7 months. Five-year follow-up was available for 73 patients. The five year overall survival
8 for these patients was 79%, with a median of 110 months (Figure 2).

9
10 During follow-up, 45 patients were diagnosed with distant metastases, 47 with a
11 locoregional relapse and 27 with both distant spread and locoregional relapse. Patients
12 who received breast conserving therapy developed locoregional relapse in 9.1% of
13 cases, while in patients who underwent mastectomy the locoregional relapse rate was
14 20.5%.

15 The mean disease free survival was 100 months (Figure 2), and highly correlated to T
16 stage, with 111 months for T1 tumors, 94 months for T2 tumors, 77 months for T3
17 tumors and for T4 tumors 44 months. For patients with negative lymph node status
18 mean survival was 116 months and for positive lymph node status 78 months (Figure 3).

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27 **Discussion**

28 In this retrospective population-based survey the incidence of BC in Surinam was
29 studied over a 10-year period. The strength of this study lies in the fact that all
30 pathology-confirmed diagnoses in the country were included in the analysis, and all
31 hospitals participated. The main weakness is the paucity of follow-up data with a median

1 follow-up of less than 2 years, which impedes discussion of outcome. Although all
2 pathologically confirmed BC diagnoses in Surinam during the study period were included
3 in the analyses, it is conceivable that additional women were diagnosed with advanced
4 BC during the study period without tumor biopsies or surgery. The absence of a national
5 cancer registry in the country makes it impossible to estimate or correct for this in any
6 way. However, this is the first population-based study to look at individual demographic,
7 tumor and treatment data.

8
9 The crude cancer incidence rate in Surinam increased from 9.5/100 000 in 1964-1976[7]
10 to 16.7/100 000 in 1980-2000[8], which is similar to our results. The rise in BC incidence
11 over the past decades is seen worldwide[9,10] and has been mostly correlated with
12 changes in reproductive factors. This may to a large degree account for the lower BC
13 incidence in developing countries vs. the western world[11;12]. Although increasing, the
14 mean age at first birth in Surinam is still low at 21 years[5], compared to over 28 years in
15 most western European countries[13]. In addition, mean parity in Surinam was 2.7
16 children per women in 2000[3], while in the Netherlands it was only 1.7 (2001-2003)[13].
17 Interestingly, the incidence of BC in Surinamese women in Surinam was considerably
18 lower than the incidence of first generation Surinamese women in the Netherlands
19 (Figure 1). The main possible explanation is thought to lie in demographic changes, with
20 Surinamese women in the Netherlands adapting to Dutch reproductive statistics with
21 less children at a higher age, although increased detection due to public awareness and
22 screening mammography programs may also play a part.

23
24 The median age at BC diagnosis was lower than the median age in the western world,
25 albeit fairly high compared to other low-income countries, underlining the in-between
26 state of development of Surinam society[11;12;14]. A confounding factor could be the
27 relatively low life expectancy of women in Surinam (69 years at birth[5], versus 80 in the
28 USA[6]), especially in view of the fact that 43% of new BC cases in the USA are
29 diagnosed in women older than 65 years. The most important competing risk for death in
30 Surinam is cardiovascular disease, which has a high mortality because (preventive) care
31 is not always optimized.

1 The fact that the proportion of Creole BC patients is higher than would be expected by
2 the distribution of ethnicities in the population, may both be explained by genetic factors
3 comparable to the incidence data for e.g. African-Americans in the USA, but also
4 because cardiovascular disease is much more prevalent in Hindustanis, the largest
5 ethnic group.

6

7 Women presented with late stage BC more often than in the western world, e.g. 41.6%
8 of patients had lymph node involvement at time of diagnosis, whereas during the same
9 time period this was only 30% in the USA and 31% in the Netherlands[15]. More
10 advanced stage at diagnosis is commonly found in developing countries[14], and is
11 thought to be related to lack of universal coverage, lack of screening programs, and fear
12 of cancer in general. Tumor size and stage decreased in the western world since the
13 introduction of mammography in the Netherlands in the last decades of the 20th
14 century[16-18], and this went hand in hand with increased public awareness and
15 reduced taboo status of the disease[19;20]. In Surinam, the vivid culture of traditional
16 medicine and taboo status of BC, almost certainly contribute to a more advanced stage
17 at diagnosis. However, the convergence of both incidence and stage of BC in first
18 generation immigrants from Surinam to the native Dutch population challenges the size
19 of the effect of different attitude and beliefs. It underscores both the relationship between
20 poor socioeconomic status and access to health care, and the positive effect of BC
21 campaigns to enhance BC awareness and possibly of screening[21].

22

23 Although data on tumor size and lymph node status were generally available from the
24 pathology lab, other prognostic and predictive factors were harder to interpret. We found
25 a discrepancy between the Mitotic Activity Index (MAI) and Bloom-Richardson grading.
26 The majority of tumors had low MAI (under 10 hpf) but this was paired with high tumor
27 grades according to Bloom-Richardson. Grading is generally considered more subjective
28 and less reproducible than MAI. According to several authors MAI is a strong, widely
29 available, easily assessable, inexpensive, well-reproducible prognosticator, if the
30 protocol is carefully followed. Fixation delay for as long as 24 hours after extirpation of
31 the tumor does not decrease the accuracy of the MAI, in contrast to BR evaluation[22].

1 In a country with limited resources, MAI could prove to be more reliable than grading,
2 but short of central pathology revision, there is no way of knowing what was most
3 accurate or consistent in Surinam.
4 Because of the absence of immunohistochemistry (IHC) technology in the pathology
5 laboratory in Surinam to determine hormone receptor status, paraffin-embedded archival
6 tissues were sent to the Netherlands to determine the receptor status of the tumor
7 whenever deemed necessary for treatment decisions. Unfortunately, only a minority of
8 patients had tissue sent to the Netherlands, and most of them had a negative receptor
9 status. Is this an accurate estimation? False negatives of hormone receptor are not
10 uncommon, especially with increasing time delay before tissue fixation, increased
11 duration of fixation and type of fixative, all of which may have been the case in our
12 patient cohort. False negatives increase especially in BC with a low receptor positivity
13 such as is typically seen in patients of African descent[23-26]. At present it is impossible
14 to say whether this played a part in our study population, but the lack of IHC to
15 determine predictive markers is bound to hamper treatment decision making, and
16 possibly outcome. Thus, since hormone receptor status was known for only 69 patients,
17 prescription of adjuvant hormone therapy was mostly blinded to ER-status. This seems
18 not unreasonable, in view of the uncertainty about the quality of the assessments, and
19 the mild cost and systemic effects of hormone therapy.

20
21 The indications for adjuvant systemic therapy for BC have broadened over the past
22 decades. Although regional differences exist, in general adjuvant systemic therapy is
23 prescribed for larger tumors, N+ tumors and small tumors that are poorly differentiated.
24 No guideline existed in Surinam during the study period, but in 2005 the National
25 Oncology Committee developed a BC treatment guideline based on both Dutch and
26 American (USA) guidelines[27;28], although in some cases the suggested drug
27 regimens differed to suit Surinam's economical situation[5]. Indications for adjuvant
28 systemic therapy according to this government-approved guideline were compared to
29 the proportion of patients receiving such therapy in the study cohort. It should be noted
30 that over the study time period, in western countries adjuvant chemotherapy practice
31 was also considerably more conservative than it is now. The aim of the comparison was

1 mainly to assist in future health care planning.

2 A minority of patients who would be eligible for adjuvant chemotherapy according to the
3 guideline actually received it (30%). Based on western experience after the introduction
4 of national guidelines[29], this number could go up to at least 70% for chemotherapy,
5 which means that the number of patients that will receive adjuvant chemotherapy may
6 double or even triple.

7
8 The treatment interval between the different treatment modalities is a predictor for
9 outcome, with a long treatment interval as an unfavorable factor. Compared to the
10 Netherlands, the median interval between diagnosis and surgery was shorter (17 days
11 vs. around 28 days), which points to the absence of long waiting lists for surgery so
12 common in the Netherlands. However, treatment intervals between surgery and
13 chemotherapy compared unfavorably to the Netherlands (9 vs. 4 weeks). We speculate
14 that the lack of availability of cytotoxic drugs in Surinam may in some case account for
15 the delay, but lack of a sense of urgency in both doctors and patients may also play a
16 part.

17 The time between surgery and radiotherapy was approximately 11 weeks. In the
18 Netherlands an 8 week interval is considered the upper limit of what is acceptable, with
19 a preference for 4-6 weeks. Because of the absence of radiotherapy facilities within the
20 country, a longer interval may have been unavoidable in this group. In view of this, it
21 may be worth considering advising radical mastectomy instead of breast conserving
22 therapy for all patients, until radiotherapy will be available in the country.

23
24 For a relatively large part of our cohort (20-25%), no data on lymph node status or local
25 treatment were available. Some of these patients may not have received local treatment
26 because of advanced stage of disease at time of diagnosis, but we speculate that others
27 never returned for further treatment. This is consistent with the relatively short length of
28 follow-up, in spite of our concerted efforts to track down the disease course of all
29 patients. We were unable to determine whether patients in general did not return for
30 follow-up because disease was uncontrolled, or because they were asymptomatic. In
31 either case, this may have biased the survival data, which raises doubt about their

1 validity, even though obvious trends such as worse outcome for higher stages could be
2 confirmed.

3

4 **Conclusion**

5 In this study we have shown the feasibility of conducting a nationwide epidemiologic
6 survey in Surinam. Most of our findings could be related to the demographics of Surinam
7 and the low-resource status of the economy. The introduction of the Surinam BC
8 treatment guideline, the planned introduction of immunohistochemistry, and the
9 anticipated introduction of radiotherapy in late 2010 are expected to ameliorate
10 diagnosis and treatment of BC patients in Surinam. The projected start of a national
11 cancer registry, combined with a recently improved continued medical education
12 program will further enhance these goals. Improvement in BC awareness and possible
13 implementation of BC screening programs will take much longer.

14

15

16

17

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15

16 **Conflict of interest statement**

17 No conflict of interest

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22 **Figure legends**

23 Figure 1: Age specific breast cancer incidence in Surinam and in Surinamese women in
 24 the Netherlands

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 26 Figure 2: Overall & disease free survival of breast cancer patients in Surinam

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 28 Figure 3: Overall cumulative survival of breast cancer patients with N0/N+ in Surinam

29 **Table 1: Characteristics of breast cancer patients in Surinam and**

30 **Surinamese women in the provinces North-Holland and Flevoland in the**

31 **Netherlands, 1994-2003**

	Surinam		The Netherlands	
	Number of patients (ASR*)	%	Number of patients (ASR*)	%
Total	419 (28)		196 (65)	

1994-1998	167 (25)		88 (62)	
1999-2003	252 (31)		108 (68)	
Age				
<30	3	0.7	2	1.0
30-39	43	10.3	29	14.8
40-49	108	25.8	42	21.4
50-59	94	22.4	53	27.0
60-69	94	22.4	44	22.4
>70	75	17.9	26	13.3
Unknown	2	0.5	-	

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2 *ASR= age standardized rate per 100,000 women per year

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14 Table 2 Characteristics of breast cancer patients in Surinam 1994-2003

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Strata	Number of patients	%	Incidence rate per 100.000/year
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Ethnicity

Creole	156	37.2	35.7
Marroons	8	1.9	2.2
Hindustani	123	29.4	18.2
Javanese	75	17.9	20.8
Chinese	8	1.9	
Mixed	31	7.4	10.1
Dutch	6	1.4	
Others	12	2.9	

Parity

0	15	3.6	
1-3	92	22.0	
>3	66	15.8	
unknown	246	58.7	

Age of first pregnancy

<20	22	5.3	
20-30	34	8.1	
30-40	5	1.2	
Unknown	358	85.4	

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Table 3: Tumor characteristics of breast cancer patients in Surinam

Strata	Number of patients	Percentage
Total	419	100%
Type of tumor		
Ductal	394	94
Lobular	7	1.7
Unknown	18	4.3
T-size		
T1 (≤ 20 mm)	98	23.4
T2 ($> 20, \leq 50$ mm)	157	37.5
$> T3$ (> 50 mm)	96	22.9
Unknown	68	16.2
Number of involved axillary lymph nodes		
No	149	35.6
N1(1-3)	93	22.2
N2(4-9)	51	12.2
N3(≥ 10)	30	7.2
Unknown	96	23.2

Metastases	24	5.7
ER/PgR		
ER+/PgR+	26	6.2
ER-/PgR-	39	9.3
ER+/PgR-	2	0.5
ER-/PgR+	2	0.5
Unknown	350	83.5
Bloom-Richardson differentiation		
Well =grade 1	7	1.7
Moderately=grade 2	52	12.4
Poor=grade 3	181	43.2
Unknown	179	42.7
Mitotic Activity Index		
≤10	51	12.2
>10	44	10.5
Unknown	324	77.3

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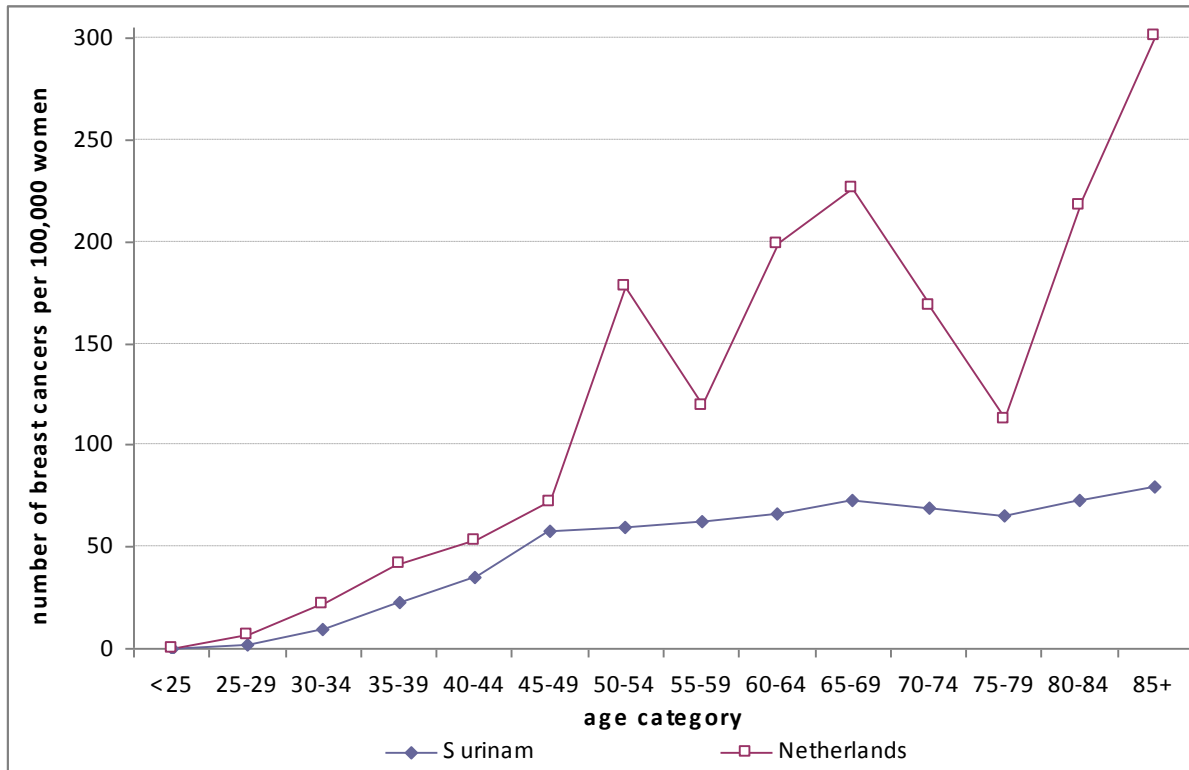
10 **Table 4: Therapy characteristics of breast cancer patients in Surinam**

	n	%	Lymph node positive	Lymph node negative	
Total	419	100			12
Surgery	334	79,7			13
- Mastectomy	292	69,7	150	127	14
- Lumpectomy	42	10,0	14	20	15
Radiotherapy	59	13,8	33	24	16
- after lumpectomy	33	7,9	20	16	17
- after mastectomy	26	5,9	13	8	18
Chemotherapy	86	20,5			19
- CMF	45	10,5	35	4	20
- Anthracycline-containing	31	7,9	21	7	21
- Unknown	10	1,9			22
Hormone therapy (Tamoxifen)	216	51,6	107	76	23
					24

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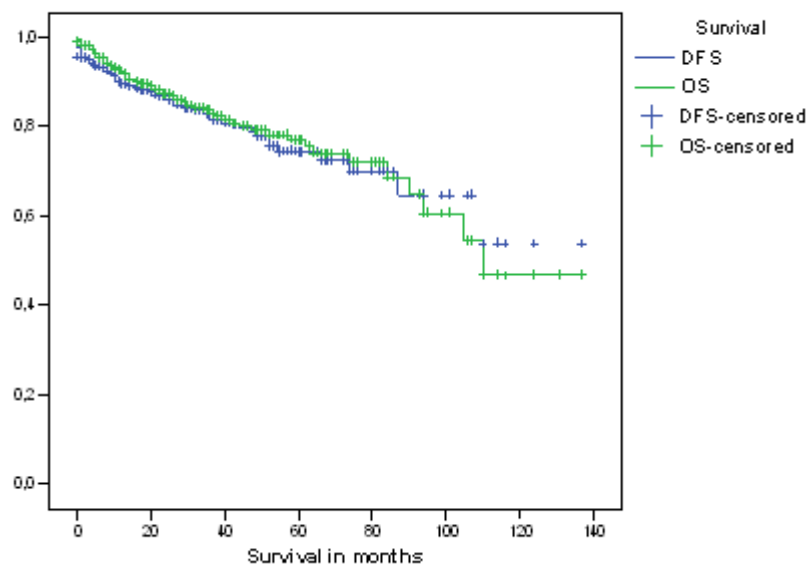
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Figure 1: Age specific breast cancer incidence in Surinam and in Surinamese women in the Netherlands



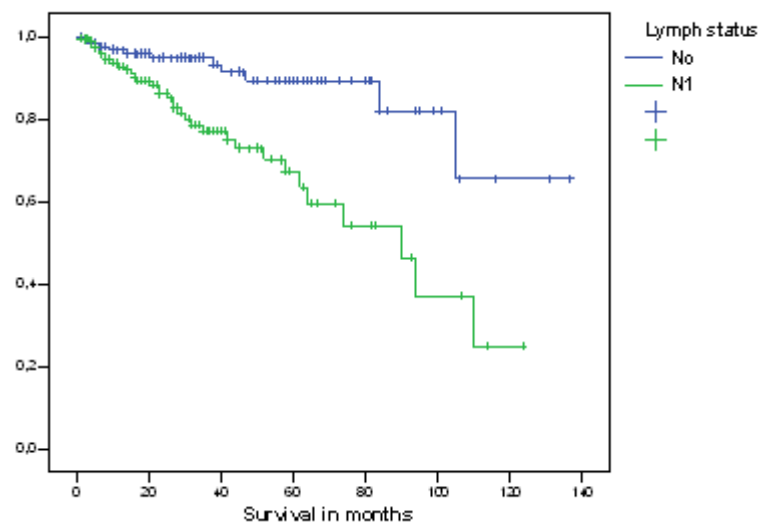
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Figure 2: Overall & disease free survival of all patients



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Figure 3: Overall cumulative survival of patients with N0/N+



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