

A nationwide analysis of incidence and outcome of breast cancer in the country of Surinam, during 1994-2003

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1	A nation-wide analysis of incidence and outcome of breast cancer in the
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6 Abstract

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

10 Materials and methods: Pathology reports and hospital charts from all BC cases

11 diagnosed between 1994 and 2004 were retrieved from Surinam's single pathology

12 laboratory and its 5 hospitals. Data on demographics, tumor characteristics, treatment

13 and follow-up were gathered. We compared our data to BC statistics of first generation

- 14 immigrants from Surinam to the Netherlands.
- 15 Results: 421 patients were diagnosed with BC during the study period. The age-

16 adjusted incidence rate was 26 per 100,000 compared to 65/100,000 in first generation

17 Surinamese women in the Netherlands. The majority had a fairly advanced stage at

18 presentation, with 60% of tumors larger than 2 cm and 41.6% with lymph node

19 involvement. Because of the absence of radiotherapy facilities, local treatment in most

20 patients was radical mastectomy. Adjuvant hormonal therapy (51.6%) was administered

21 more frequently than adjuvant chemotherapy (20.3%). A significant number of patients

22 was lost to follow-up, resulting in a median follow-up duration of only 23 months. The

23 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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8 Introduction

9 BC is the most common malignancy among women worldwide. However, the incidence

10 is highest in developed countries, and relatively low in the developing world[1].

11 The republic of Surinam is a former Dutch colony situated in South America, that gained

12 independence in 1975. Its history of colonization, slave labor and contract laborers has

13 led to great ethnic diversity in its population of almost 500,000[2]. The major ethnic

14 groups are of Indian descent (the so called "Hindustani", 27.4%), or mixed African

15 descent (the so called "Creoles", 17.7%), Marroons (descendants of runaway

16 slaves,14.7%) and Javanese (descendants of Indonesian contract laborers,14.6%)[3]. In

17 the 1970s and 1980s, after independence and during a period of civil unrest, mass

18 emigration to the Netherlands took place, so that the Netherlands now has a population

- 19 of almost 350,000 originally from Surinam[4].
- 20 In the year 2002 the Gross Domestic Product (GDP) per capita was US\$ 4, 447. The

21 annual per capita health expenditure was US\$ 385, corresponding to an expenditure of

22 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].

24 There are five hospitals in Surinam, four of which are in the capital of Paramaribo.

25 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

27 biopsies and surgical specimens obtained anywhere in the country are sent.

28 Radiotherapy was not available in Surinam during the study period, so that patients who

29 were eligible for radiotherapy had to go out of the country to receive it. A substantial part

30 of the population has limited health care coverage and many patients have to contribute

31 to the cost of health care out of private funds. There is at present no cancer registry.

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

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11 Methods

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

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

and Flevoland, which host 35% of the Surinamese population in the Netherlands.

27

28 Analysis

A database was made in Access[©] to store all data. The interval between the different

30 therapies was calculated in this program. Kaplan-Meyer curves and survival times were

31 calculated in SPSS[©]. The age standardized incidence rate was calculated using the

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14 **Results**

15 Incidence

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

22

23 Patient characteristics

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
- 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 progestagen 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,
- 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

- 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
- 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 irradical resection 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**

- 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
- 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). 19 20 21 22 23 24 25 26 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

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

The fact that the proportion of Creole BC patients is higher than would be expected by
 the distribution of ethnicities in the population, may both be explained by genetic factors
 comparable to the incidence data for e.g. African-Americans in the USA, but also
 because cardiovascular disease is much more prevalent in Hindustanis, the largest
 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 introduction of mammography in the Netherlands in the last decades of the 20th 13 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 guality 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

For a relatively large part of our cohort (20-25%), no data on lymph node status or local treatment were available. Some of these patients may not have received local treatment because of advanced stage of disease at time of diagnosis, but we speculate that others never returned for further treatment. This is consistent with the relatively short length of follow-up, in spite of our concerted efforts to track down the disease course of all patients. We were unable to determine whether patients in general did not return for 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

validity, even though obvious trends such as worse outcome for higher stages could beconfirmed.

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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22 Figure legends

- Figure 1: Age specific breast cancer incidence in Surinam and in Surinamese women inthe Netherlands
- 25
- 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	Number of patients % %	
	(ASR*)	(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	-	
Table 2 Characte	eristics of breast ca	ncer patients	s in Surinam 19	94-2003

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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5 Table 3: Tumor characteristics of breast cancer patients in Surinam

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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, ≤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		
- CMF	45	10,5	35	19 4
- Anthracycline-containing	31	7,9	21	20 7
- Unknown	10	1,9		21
Hormone therapy				22
(Tamoxifen)	216	51,6	107	⁷⁶ 23
				24

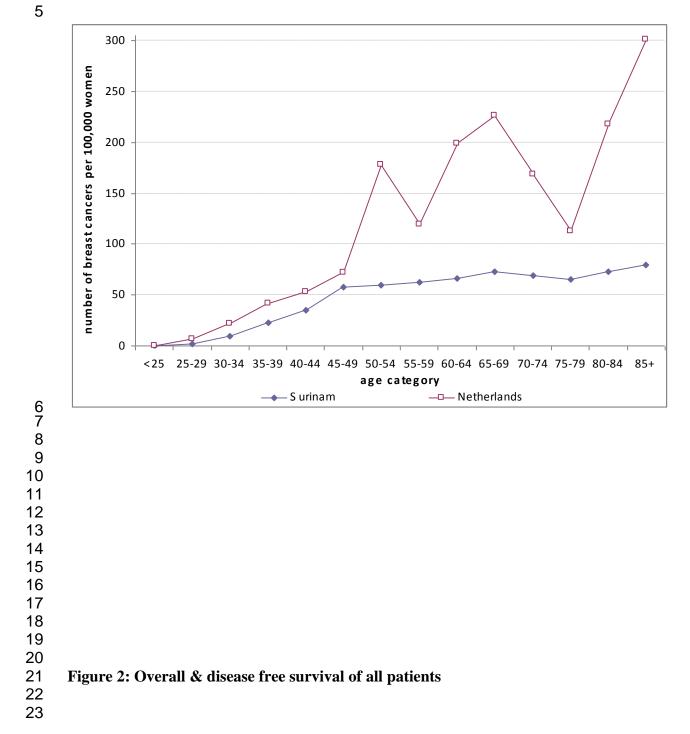


Figure 1: Age specific breast cancer incidence in Surinam and in Surinamese women in the Netherlands

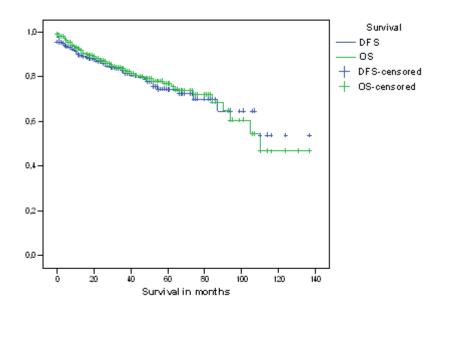




Figure 3: Overall cumulative survival of patients with N0/N+

