SCIENTIFIC REPORT

PATTERNS OF CARE OF BREAST CANCER PATIENTS IN SWITZERLAND: A POPULATION BASED STUDY

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SUMMARY

Purpose: The aim of this study was to investigate how breast cancer patients are cared for in Switzerland and to determine whether regional disparities in the patterns of care can account for regional and cantonal differences in outcomes that had been previously reported [1].

Methods: We analyzed patient and tumor characteristics as well as therapeutic approaches among 4749 women diagnosed with invasive breast cancer in the years 2003-2005 and residing at the time of diagnosis in one of the 7 regions covered by one of the participating cancer registries in Switzerland. Information on mode of detection, tumor characteristics and treatments was abstracted from medical records and obtained from practitioners in outpatient settings. Patterns of care were compared to published guidelines and recommendations [2-14]. Differences among regions were tested for statistical significance using chi-square tests. We used logistic regression to investigate the effect of the geographical region on the patterns of care while controlling for potential confounders (e.g. age, tumor extension).

Results: Patients resident in Valais and Geneva were more frequently diagnosed in stage I (44% and 42% respectively) than residents of St. Gallen-Appenzell (28%) (P<0.01). Further tumor characteristics associated with favorable prognosis (low histological and nuclear grade, positive estrogen (ER) receptor, tumor size<=10mm) were more frequently reported in Geneva and Valais, regions where mammography screening programs are running. Accordingly 42% of patients were detected in Valais through a screening procedure while in St. Gallen-Appenzell only 16% of breast cancers were detected in this way (P<0.01).

Malignancy was confirmed pre-operatively in 76% of patients treated with breast surgery in curative intention. Proportions varied considerably from 96% in Geneva to 62% in Grison-Glarus (P<0.01). From 2003 to 2005 a steady increase of pre-operative diagnoses was observed in all regions as well as a shift in the technique used for this purpose (increased use of core needle biopsy, reduced number of fine needle aspirations (FNA)).

Only 39% of cases were reported as having been discussed in a multidisciplinary conference as recommended [15], mostly post-operatively. The highest proportion of patients discussed multidisciplinary was reported in Grisons-Glarus (57%) and the lowest in St. Gallen-Appenzell (35%) (P<0.01).

The most frequent type of breast surgery was breast conserving surgery (BCS) used in 67% of patients who underwent breast surgery. The highest mastectomy rate was observed in St. Gallen-Appenzell (38%) and the lowest in Geneva (24%). Differences persisted after adjusting for age and stage (P<0.01). The rate of reconstruction after mastectomy was almost 30% in Geneva but less than 10% in Basel, Ticino and Grisons-Glarus (P<0.01). About 15% of patients with surgical treatment had more than one breast operation. Patients without pre-operative diagnosis were three times more likely to be re-operated.

Sentinel lymph node biopsy as only axillary procedure in patients with node-negative disease was more frequently performed in Geneva (71% of patients with pN0) and less frequently in St Gallen-Appenzell (26% of patients with pN0) (P<0.01). The use of this technique increased in all regions from 2003 to 2005.

After breast conserving surgery 92% of patients <80 years with stage I-III disease received radiotherapy in the remaining breast [4, 16]. Omission of radiotherapy after BCS was reported more frequently in Ticino (9%) Basel and Grisons-Glarus (both 8%) (P<0.01). A boost in the tumor bed was delivered to 95% of patients <50 years in all regions. However, considerable variation was observed among patients 50 or older: In Geneva only 50% of patients in this age group received a boost whereas 98% of patients residing in Ticino did (P=0.03). Radiotherapy of the chest wall after mastectomy in patients with locally advanced disease (T3-T4 or N2-N3, M0) and aged <80 was delivered to 68% of patients (range 55% in Ticino to 84% in Valais, P<0.01).

90% of patients with endocrine responsive disease and average or increased risk of recurrence [3] were prescribed adjuvant endocrine therapy. Lower rates were reported in Grisons-Glarus (79%), Ticino (83%) and Basel (87%) the highest in Valais (98%) (P<0.01). Endocrine therapy prescription in postmenopausal women in the minimal risk group of recurrence [3] varied according to region, extending from 94% in Geneva and Valais to 74% in Grison-Glarus (P<0.01).

Regional variations were also observed in the prescription of pre-operative (neo-adjuvant) treatment (either chemotherapy or endocrine therapy). Neo-adjuvant treatment was prescribed to 8% of patients (range 4% in Zurich to 13% in Geneva, P<0.01)

The highest rates of chemotherapy in patients with endocrine non-responsive disease (stages I-III) and age<70 were reported in St. Gallen-Appenzell (88%) and Ticino (84%), the lowest in Basel (71%) (P<0.01). Chemotherapy was prescribed in 75% of patients with nodal positive, endocrine responsive disease and age<70 (range 54% (in Basel) to 89% (in Grisons-Glarus), P<0.01). Similar variations were observed when considering patients with similar characteristics but locally advanced disease.

Conclusions: Important regional variations in the whole chain of care for breast cancer patients (early diagnosis, malignancy confirmation, therapeutic approach and therapies) were found across regions in Switzerland. It seems therefore possible that differences in the implementation of state of the art management as well as differences in tumor's characteristics have contributed to the disparities in survival reported previously [1]. Additionally, we have seen significant differences in the proportion of patients having benefited from modern trends in surgery that have been associated with improved quality of life [17].

INTRODUCTION

Breast cancer is the most frequent malignancy among women in Switzerland accounting for almost a third (32.3%) of all newly diagnosed cancer cases in women. Breast cancer mortality is decreasing in Switzerland since 1990 [18] reflecting increased awareness, earlier detection and better treatment.

A study published in 2005 by the Swiss association of cancer registries [1] has shown marked differences in the 5 year relative survival rate after diagnosis of breast cancer in women according to their area of residence. The disparities subsisted after controlling for age, tumor size and nodal involvement, suggesting that other factors may be at the origin of these disparities. Five year survival rates of breast cancer patients have been compared to other European countries and the USA in the Concord Study [19] as well as in the EUROCARE IV study [20]. Within Switzerland, survival in urban regions was reported better than in rural areas.

Evidence from the scientific literature suggests, that all elements in the continuum of care such as early diagnosis and loco-regional and systemic therapy can affect survival and quality of life [21] [22]. In recent years there has been increasing attention paid to the variations in the process of care for cancer patients. Improved survival has been related to clinicians' workload and the availability of multidisciplinary care and treatment options [23]. In particular breast cancer patients treated in centers with on-site radiotherapy, research activity, or teaching status had significantly better outcomes [24].

Geographical variations in the care process have been shown to contribute to disparities in morbidity and mortality in the United States [25]. Regional differences included rates of breast conserving surgery and the proportion of women receiving radiotherapy after breast conserving surgery. Also in Australia rural-urban differences have been described both in survival as in treatment patterns such as the type of breast surgery and in the use of adjuvant radiotherapy and systemic therapies. [26] Socio-economic features and health insurance type have been associated with differences in outcomes in breast cancer patients [27]. Also the method of detection has been discussed as influencing the type of therapies [28].

The U. S. National Cancer Institute started in 1987, together with the Survival Epidemiology and End Results (SEER) registries, a series of patterns of care studies in order to learn more about how oncological care was delivered in the community. This initiative has been continued up to now. Findings have been used to identify potential areas for educational programs in collaboration with professional societies. In the United Kingdom the National Health Service (NHS) cancer screening program collects data from all screening units on new detected breast cancer patients [29]. Regularly audits on diagnostic accuracy and subsequent treatment patterns are performed to analyze surgical techniques, waiting times and adjuvant therapies and to compare them to the outcomes. Health management dysfunctions or sub-optimal treatments can be detected in this way. The case reviews and recommendations issued from these reports are used to improve breast cancer care.

In the context of patterns of care (PoC) studies, study design is crucial in order to avoid selection bias [30]. PoC studies aim to assess the use of management approaches in defined patient populations. The way however the patient population is defined, has important implications regarding the external validity of the study. In order to provide a valid picture of how cancer patients are cared for in current medical practice, it is necessary to study all cases occurring in the population or representative samples of it.

Cancer registries collect data to determine incidence and the completeness of their data is very high [31]. Identification of cases using data from population based cancer registries is admitted to be the best method to avoid selection bias and is the method being used by Center for Disease Control (CDC) in the USA in the latest PoC studies [32].

Little is known about the way care is delivered to breast cancer patients in Switzerland and how the multidisciplinary team approach is implemented. The aim of this study was therefore to investigate the

therapeutic approach, to assess whether variations in the process of care exist and to estimate the magnitude of possible variations as well as to ascertain the proportion of breast cancer patients receiving appropriate treatment according to national and international recommendations and state-of-the-art knowledge. This first report is focused on the description of patterns of care and their geographical variations. Further analyses will deal with other underlying causes for variation and provide more detailed analysis of each of the elements of care.

PATIENTS AND METHODS

DESIGN AND STUDY POPULATION

To analyze and assess patterns of breast cancer care in the community setting in Switzerland, a retrospective analysis of patient, tumor and treatment characteristics of 4749 unselected female patients diagnosed with invasive breast cancer in the years 2003-2005 was performed. Detailed information was collected by trained staff of the seven population-based cancer registries that participated in the study: Geneva, Valais, Ticino, Basel, Zurich, St. Gallen-Appenzell and Grison–Glarus. These registries collect information on all cancers diagnosed within their geographic regions. All cases included in the study had been previously registered.

Inclusion criteria included women diagnosed with invasive breast cancer (morphology codes M8000 to M9589 according to the WHO International Classification of Diseases for Oncology, 3rd Edition[33]), first diagnosis between January 1st, 2003 and December 31st, 2005 and resident in the area of one of the participating cancer registries at the time of diagnosis. According to international guidelines [34] the date of the first histological or cytological confirmation of the malignancy was taken as reference date for the diagnosis. When the diagnosis had not been confirmed histologically, the date of admission to the hospital or the date of the first consultation (for patients never admitted to the hospital), was used as date of diagnosis.

Exclusion criteria included local recurrence of previous breast cancer, lymphomas of the breast, diagnosis made at the autopsy and cases for which all the information the registry possesses is restricted to the death certificate (DCO cases).

Each observation represents a different patient, even in the presence of bilateral breast cancer. When bilateral invasive breast cancer was diagnosed within 30 days, it was defined as synchronic breast cancer. Only the first of two non synchronic breast cancer tumors diagnosed in the study period was included. For synchronic tumors the one with highest stage (according to the TNM classification[35]) was used as index case.

The seven participating registries cover seven cantons and four half-cantons of Switzerland or 47 % of the Swiss population. The percentage of urban population is very high in Geneva (99%) but also Basel, Zurich (95%) and Ticino (87%) are above the Swiss mean value of 73%. The regions of St. Gallen-Appenzell (59%), Valais (57%) and Grisons-Glarus (40.7%) on the other hand, are below the national mean [36].

The project was submitted to and accepted by the Ethics Committee in Canton St. Gallen, where the study center is located. Other registries informed their respective cantonal Ethics Committee.

SAMPLING

To determine the total number of cancer patients necessary for the patterns of care study a confidence interval strategy was used [37]. Based on the literature as well as on routinely collected data, we estimated that approximately 60% of patients were receiving treatment according to guidelines.[32] Based on this assumption we calculated that a sample size of at least 470 cases per registry would be necessary to detect relevant differences. This number corresponded to the totality of cases diagnosed in the cancer registry with the lowest catchment

population, i.e. the cancer registry Grison-Glarus. The cancer registries of Geneva, St. Gallen-Appenzell and Ticino accepted to enlarge the study to all incident breast cancer cases in their area of registration in order to increase the power of the study. In consequence all cases diagnosed in the catchment area of 4 registries (St. Gallen-Appenzell, Geneva, Ticino and Grison-Glarus) are included. For the remaining registries (Basel, Valais and Zurich) the coordinating center of the Swiss Association of Cancer Registries selected from all cases meeting the required inclusion criteria a random sample of 500 cases using the STATA 9.2 software package (STATA Corp, College Station, Texas, USA), which was the number of cases used in the CONCORD Study [19] to compare countries among them. The sample size represented 83% of cases diagnosed in Valais, 62% of those from Basel and 18% of cases registered in Zurich. Tests for representativeness of these samples with regard to age distribution, breast cancer laterality and morphology showed similar values for these samples as for the data of those registries collecting the totality of cases.

TRAINING, DATA COLLECTION AND QUALITY CONTROLS

Based on the items required by the European Society of Mastology (EUSOMA) database for the quality audit system [38] a modified database was designed (see annex for the list of items). Required data items were abstracted from pathology reports, medical records and questionnaires sent to treating in order to secure missing information.

To ensure that data was entered and supplied in a constant format and in order to minimize errors during data input, a software package with drop-down menus was developed and distributed to all participating registries. Three workshops were held. The first two were used to instruct data collectors, to explain variable definitions and minimize differences between registries in the interpretation of medical records and questionnaires. At the end of the data collection a third workshop was held to discuss difficulties met during the period of data collection and to validate interpretation queries.

The study coordinating office in St. Gallen carried out extensive validation checks after receipt of the data and before the incorporation in the common dataset. These quality-control routines included search for invalid codes, impossible sequence of dates, unlikely or conflicting combinations of values or outliers. When inconsistencies were observed, queries were returned to registries for checking.

DATA ITEMS

A total of 150 variables on demographic characteristics, clinical presentation, co-morbidity, investigation techniques leading to diagnosis, morphology and biological characteristics of the tumor, stage at diagnosis, as well as planned and effectively delivered local-regional (surgery and radiotherapy) and systemic therapies of all patients included in the study were collected (Annex).

Items on patient's characteristics, as date and place of birth, nationality, profession and place of residence were checked at the population office of the respective canton or municipality. Occupation was recorded in 4 categories reflecting the degree of education necessary to practice it (university, college, apprenticeship, basic education) plus housewife and retired/unknown.

Under "screen detected tumors" cases detected by: a) screening mammography performed in the asymptomatic patient without palpable findings and no personal or familiar history of breast cancer (opportunistic screening mammography), b) tumors detected by routine clinical breast examination by the gynecologist in the asymptomatic patient, c) tumors detected in the frame of the follow up after breast cancer and d) screening performed because of a familiar history of breast cancer have been grouped.

The multidisciplinary conference (MDC) was defined as a meeting in which all members of the caring team (but at least the surgeon in charge of the patient as well as the pathologist, radiotherapist and medical oncologist) were present for the case review and planning of the therapy, according to international recommendations[2]. A record of attendance as well as the written conclusions of the conference had to be available.

One operation was defined as one visit to the theater with one general anesthesia. Different surgical procedures (e.g. re-excision, mastectomy after lumpectomy, axillary surgery) occurring during the same session were considered as one operation.

Only the first course of treatment was considered. Treatments decided because of relapse or disease progression were not recorded. Treatments delivered at the hospital and those provided at outpatient facilities have been taken into account.

For systemic therapies, state of the art knowledge at the time patients were diagnosed, was best reflected from the 2003 Expert Consensus Meeting in St. Gallen[3]. Accordingly, the risk categories proposed at this meeting were used, since these were the same of those of the 7th International Expert Consensus Meeting from 2001 [9]. Because of the difficulty in retrieving reliable data concerning hormonal menopausal status of patients between 46 and 55, the age of 50 was taken as proxy for menopausal status and patients 50 or older considered postmenopausal.

Certain variables, such as risk category according to the St. Gallen Consensus conference [3] or stage of disease at diagnosis were computed combining information of different variables. Stage according to the TNM classification [35] was computed using the best information available from the fields extent of the primary tumor (pT), involvement of regional lymph nodes (pN), distant metastasis (M), size of the tumor (in mm) and number of examined and positive lymph nodes found by the pathologist. When pathological information was not available (no surgery) or when neoadjuvant therapy was delivered the clinical assessment was used (cT and cN). For computing risk category according to the St. Gallen Consensus Conference Meeting [3] information on extent of primary tumor, nodal status, hormonal receptors, histological grading and age was combined.

MISSING DATA

Some observations were missing in that for a number of cases the relevant information for one or several variables could not be obtained. Incompleteness of the data varied among the regions but cases with incomplete information were observed in all of them. The reasons for missing data were various, including unanswered queries from practitioners or inaccessible information because the patient was treated outside the catchment area or lost contact with the treating physician after surgery or because the registry lacked of time to collect the information required. In the canton Zurich two big institutions specialized in the treatment of breast cancer patients (one private and one public) did not provide data. In Grison-Glarus one private cabinet did not provide data as well. Missing information therefore cannot be considered at random [39]. Percentages of missing information are shown in the corresponding tables.

ANALYSIS OF THE CARE PROVIDED

In order to evaluate geographical differences we compared the care delivered to what was recommended in the national [4-8] and international guidelines [2, 3, 9-14] published at the time.

STATISTICAL ANALYSIS

All descriptive information is presented as observed counts and percentages. Comparisons of regions were performed using chi-square tests. Logistic regression techniques were used to test the relationship between care

patterns and geographical regions after controlling for potential confounders (e.g. age, tumor extension). All statistical analysis were performed using STATA 9.2 software (STATA Corp, College Station, Texas, USA)

RESULTS

PATIENT AND TUMOR CHARACTERISTICS

Median age at diagnosis was 62 years (range 20-101 years). The 25th percentile was found at age 52 and the 75th percentile at age 72. Thus 50% of women newly diagnosed with breast cancer were aged 52 to 72 years. Age by region is shown in Figure 1 and Table 1. Mean and median age at diagnosis in Geneva and Valais were lower than in other regions (P<0.05).

The proportion of patients younger than 65 years old with a profession requiring a university degree was higher in Geneva and Zurich (9%) than in Grisons-Glarus (2 %) where housewives represented 48%. In patients aged 65 or older information on former profession was difficult to retrieve and has been coded housewife when unknown. No information was available on this item neither from Basel nor from Ticino.

High levels of private health insurance were prevalent in Geneva (48%) and to a lesser extent in Zurich (41%) while in Valais only 8% of patients were reported as having a special type of health insurance. In Basel, Zurich and St.Gallen-Appenzell the proportion of unknown values for this variable were between 10 and 20%, in Grisons-Glarus 22%. Ticino did not collect this variable.

The proportion of Swiss nationals was 84% among all study patients. The proportion of foreign nationals was highest In Geneva (25%) and lowest in Grison-Glarus (6%).

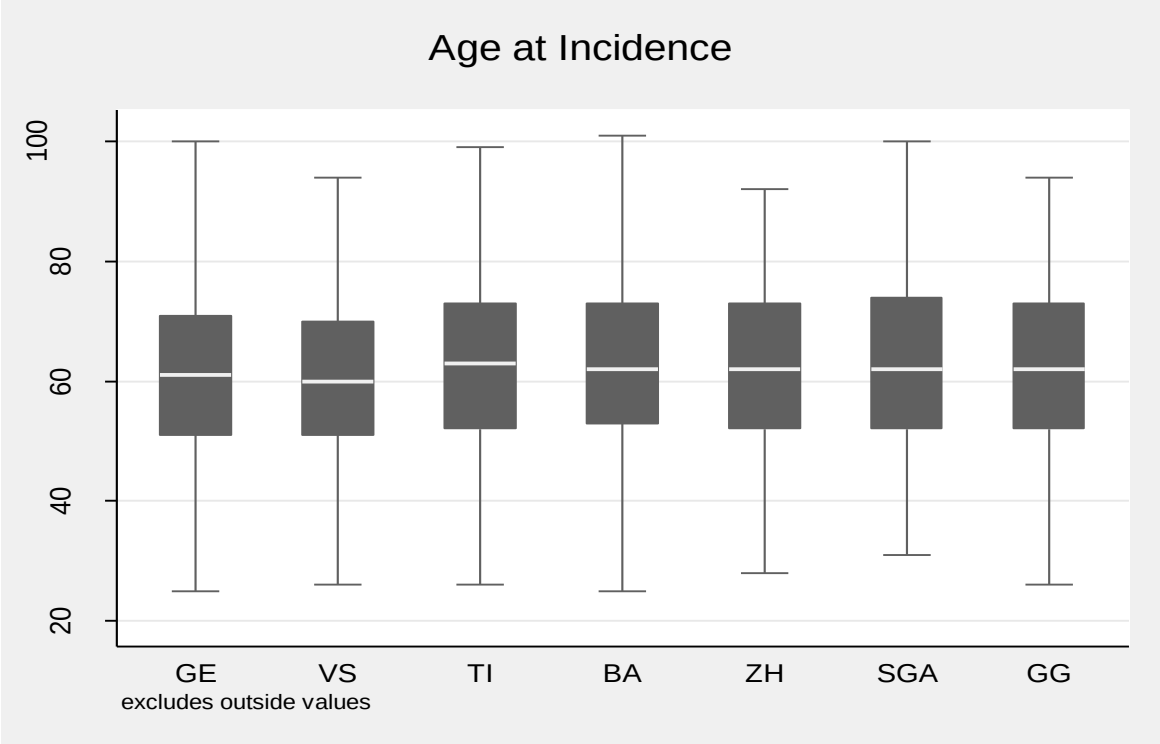

Figure 1- Box plots showing median age and 25th and 75th percentage of age at diagnosis according to region.

Table 1	Age groups per region							
Age group	**GE**	**VS**	**TI**	**BA**	**ZH**	**SGA**	**GG**	**Total**
<35	27	12	7	11	11	13	7	88
	2%	2%	1%	2%	2%	1%	1%	2%
35 to 49	228	99	159	92	106	180	90	1000
	21%	20%	20%	18%	21%	21%	19%	21%
50 to 69	552	260	364	254	238	390	232	2290
	50%	52%	46%	50%	47%	45%	49%	48%
70 to 79	185	74	145	93	100	166	87	850
	17%	15%	19%	18%	20%	19%	19%	18%
80 or >	118	58	108	67	63	135	60	609
	11%	12%	14%	13%	12%	16%	13%	13%
Total	1110	503	783	506	507	871	469	4749
	100%	100%	100%	100%	100%	100%	100%	100%

P=0.02

TUMOR CHARACTERISTICS

Stage at diagnosis in the different regions is shown in Table 2. Proportions varied significantly among regions. The highest proportion of patients diagnosed with stage I disease was reported in Valais (44%) followed by Geneva (42%) while the lowest proportions of patients with stage I breast cancer were reported in St.Gallen-Appenzell (28%) and Basel (29%).

Table 2		Distribution of Stage at diagnosis according to region of residence of the patient (n=4749)							
Stage		**GE**	**VS**	**TI**	**BA**	**ZH**	**SGA**	**GG**	**Total**
I	n	465	221	283	148	171	240	149	1677
		42%	44%	36%	29%	34%	28%	32%	35%
IIA	n	280	126	208	151	142	264	109	1280
		25%	25%	27%	30%	28%	30%	23%	27%
IIB	n	132	55	83	69	60	129	40	568
		12%	11%	11%	14%	12%	15%	9%	12%
IIIA	n	82	29	78	33	56	89	50	417
		7%	6%	10%	7%	11%	10%	11%	9%
IIIB	n	37	21	27	19	15	35	14	168
		3%	4%	3%	4%	3%	4%	3%	4%
IIIC	n	23	15	28	26	26	33	22	173
		2%	3%	4%	5%	5%	4%	5%	4%
IV	n	59	22	38	26	21	75	50	291
		5%	4%	5%	5%	4%	9%	11%	6%
unknown	n	32	14	38	34	16	6	35	175
		3%	3%	4%	5%	3%	1%	7%	3%
Total	n	1110	503	783	506	507	871	469	4749

P<0.001

The highest proportion of patients diagnosed with stage IV disease (distant metastasis) was 11% in Grisons-Glarus followed by St.Gallen-Appenzell (9%) while in other regions the percentage of cases diagnosed in stage IV reached only 4 to 5% (P<0.01).

Tumor characteristics associated with favorable prognosis (cytological low grade (grade 1), high proportion of cells with positive receptors) were also more frequently reported in Geneva and Valais (Table 3)

The presence or absence of vascular invasion was not mentioned in one third of cases in the pathology reports. The proportion differed among regions from 75% in St. Gallen-Appenzell to less than 5% in Ticino and Basel. Similarly, the proportion of the *in situ* component of the tumor was more frequently expressed in categories (extensive, not extensive) than in percentages. Reporting of the distance, orientation and type of tumor (invasive or DCIS) in relation to the closest margin was not found in the definitive report in over 30% of cases. This was frequently observed with re-excision specimens, for which information concerning orientation was not always available, with the consequent difficulties in the interpretation of margin status.

Multiple foci of disease (multifocal and multicentric disease combined) were found in 22% of cases. Multifocal disease was more frequently (15%) described than multicentric (7%) disease. No distinction between multifocal and multicentric disease was reported by the Ticino registry. Highest rates of multiple foci of disease were reported in Grisons-Glarus and Geneva (31%, 28% respectively) and lowest in Ticino (16%).

Table 3 **Tumor characteristics associated with good prognosis (in number of cases and proportion of all patients per region in the study population)**

		GE	VS	TI	BA	ZH	SGA	GG	Total
T<=10mm	n	252	101	102	67	58	91	68	739
		23%	20%	13%	13%	11%	10%	15%	16%
ER receptor>50%	n	851	316	563	347	353	585	311	3326
		77%	63%	72%	69%	70%	67%	66%	70%
G1	n	285	147	141	74	72	120	79	918
		26%	39%	18%	15%	14%	14%	17%	19%

DIAGNOSIS AND THERAPEUTIC APPROACH

MODE OF DETECTION

Most women (58%) included in this study sought medical advice because of signs or symptoms detected by the patient herself (Table 4). The percentage of breast cancer detected by screening in asymptomatic patients varied significantly among the participating registries from 42 % in Valais (including 27% of women being detected through the mammography screening program) to 16% in St. Gallen-Appenzell. All cases detected through mammography (independently of the setting) were small in size (mean diameter 14 mm, SD 7.5 mm).

Table 4	Method of Detection							
		GE	VS	TI	BA	ZH	SGA	GG	Total
Mammography Screening Program	n	69	134	0	0	0	0	0	203
		6%	27%	0%	0%	0%	0%	0%	4%
Other screening methods	n	353	76	41	139	117	141	80	948
		32%	15%	5%	27%	23%	16%	17%	20%
Signs & symptoms	n	546	244	345	360	306	632	328	2761
		49%	48%	43%	71%	60%	73%	70%	58%
Follow up after breast cancer	n	34	15	19	4	13	28	12	125
		3%	3%	2%	1%	3%	3%	3%	3%
Other / unknown	n	108	34	378	3	71	70	49	715
		9%	7%	48%	1%	14%	8%	10%	15%

P<0.001

PRE-OPERATIVE PATHOLOGICAL CONFIRMATION OF MALIGNANCY

In the study population 76% of the cases with breast surgery had a pre-operative confirmation of malignancy. Only in Geneva was the EUSOMA target of 90% met [13] with 96% of patients diagnosed pre-operatively, while in the other regions the percentage of pre-operative diagnosis was much lower (59% in Ticino, 62% in Grisons-Glarus)

Table 5 Method of definitive confirmation of diagnosis of breast cancer according to region in patients treated with breast surgery in curative intention* (n=4221)

	GE	VS	TI	BA	ZH	SGA	GG	Total
Pre-operative diagnosis confirmation	934	388	414	298	347	586	242	3209
	96%	83%	59%	65%	75%	77%	62%	76%
Surgical confirmation	37	79	11	161	115	165	93	661
	4%	17%	2%	35%	25%	22%	24%	16%
Unknown	3	1	279	0	3	7	58	351
	0%	0%	40%	0%	1%	1%	15%	8%

*Excluded are patients with stage IV disease or severe comorbidities and life expectancy under one year. P<0.001

(Table5). Patients detected within the screening program in Geneva and Valais had significantly higher rates of pre-operative diagnosis than patients detected in other settings.

Core needle biopsy (CNB) was more frequently used than FNA in all regions except in St.Gallen-Appenzell. Minimal invasive breast biopsy (MIBB) was not frequently used in the study period, mostly in Geneva (8% of all pre-operative diagnosis performed).

DECISION MAKING PROCESS AND THERAPEUTIC APPROACH

39 % of cases had been discussed in a multidisciplinary conference (MDC) either before or after surgery (Table 6) with important variations among the regions. Pre-operative MDC in the study period took place in Geneva and St.Gallen-Appenzell, pre- and postoperative MDC only in St.Gallen-Appenzell.

Table 6 Multidisciplinary conference*

		GE	VS	TI	BA	ZH	SGA	GG	Total
Multidisciplinary conference	n	532	257	0	270	231	307	268	1865
	%	48%	51%	0%	53%	46%	35%	57%	39%
No multidisciplinary conference	n	572	214	0	232	187	545	116	1866
	%	52%	43%	0%	46%	37%	63%	25%	39%
Unknown	n	6	32	783	4	89	19	85	1018
	%	1%	6	100%	1%	18%	2%	18%	21%

*Pre- or post-operative MDC. Definition of multidisciplinary conference in the methodology section.

TREATMENT DECISION AFTER WORK-UP

The treatment decision after work-up was primary surgery for over 90% of patients in stage I-III with significant regional variations. A total of 528 patients (11%) presented at the time of diagnosis either metastasis, severe co-morbidities or life expectancy less than one year. Treatment in this group of patients was assumed palliative.

The highest rates for decision of surgery as the first treatment were observed in Basel (98%) the lowest in Geneva (89%) where almost 11% received preoperative systemic therapy (P<0.001). Less than 25% of patients with large clinical stage IIA and IIB tumors (>=40 mm) and T3 N1 M0 tumors received preoperative chemotherapy or endocrine therapy, more frequently in Geneva (33%).

LOCAL-REGIONAL THERAPIES

BREAST SURGERY

Over 90% of women in the study (n=4375) were treated with breast surgery including 134 patients with metastatic disease and 20 more in the palliative setting. No information on surgery was available for 24 patients (0.5%) in the study. Within the group of patients treated in curative intention (n=4221) the final type of surgery was breast conserving surgery in 2838 (67%) patients and mastectomy in 1380 patients (32%). Breast reconstruction following mastectomy (either immediate or delayed breast reconstruction) was reported for 188 patients (14% of those having experienced a mastectomy). The highest rate was reported in Geneva (30%) the lowest in Basel (2%).

Mastectomy rate in patients treated in curative intention varied significantly among regions (Table 7). The highest rate of mastectomy was observed in St.Gallen-Appenzell (38%) and the lowest in Geneva (24%). Unadjusted

analysis showed that mastectomy was associated with tumor size (size >30mm vs. size <=30 mm OR: 6.35; CI 4.80-6.83), presence of multicentric disease (OR: 24.81; CI 16.10-38.25), extensive DCIS (OR: 1.79; CI 1.47-2.17) and more than one breast surgery (OR: 1.84; CI 1.58-2.13). Mastectomy was also associated with age (70 years old or older) (OR: 1.68; CI 1.46-1.93) in all regions except in Geneva. Logistic regression analysis showed that the differences in mastectomy rates between Geneva and the other regions persisted after controlling for tumor size (size>30mm), age (age>=70), multicentric disease and presence of extensive DCIS .

Table 7 **Type of definitive breast cancer surgery in patients treated in curative intention *(n=4221)**

	GE	VS	TI	BA	ZH	SGA	GG	Total
BCS	743	297	464	311	307	470	246	2838
	76%	63%	66%	68%	66%	62%	62%	67%
Mastectomy	164	144	222	145	131	254	132	1192
	17%	31%	32%	32%	28%	34%	33%	28%
Mastectomy w. reconstr	67	27	17	3	26	34	14	188
	7%	6%	2%	1%	6%	4%	4%	4%
Unknown	2	0	1	0	2	0	8	13
	0%	0%	0%	0%	0%	0%	2%	0%

*Excluded are patients with stage IV disease or severe comorbidities and life expectancy under one year- P<0.001

Non-disease-free margins (defined as margins of less than 1mm tissue free from invasive tumor or *in situ* carcinoma after the final surgical intervention) were reported in almost 10% of patients . Geographical differences were statistically significant. The ratio varied from 2% in Grison-Glarus to 15% in Valais.

Less than 2% of patients experienced 3 or more breast surgeries, but 15% were operated twice. The number of surgeries was significantly related to pre-operative diagnosis of disease. Patients with pre-operative confirmation had a 3-fold reduced risk of having more than one surgery than those without preoperative confirmation (OR: 0.32; CI 0.27-0.37). Patients with 2 or more surgeries had an increased risk of mastectomy (OR: 3.20 CI: 2.70-3.79). The rate or re-intervention was lower in Geneva (under 10%) and highest in Zurich (over 20%). The risk of a being re-operated was significantly higher (30 to 100% higher) in all regions (except Basel) when compared to Geneva (taken as reference region).

AXILLARY LYMPH NODE SURGERY

Surgical axillary staging was performed in 93% of stage I, IIA and IIB patients (n=3525). The most frequent type of definitive axillary staging procedure was the axillary dissection level I and II. Only in Geneva sentinel node biopsy (SNB) was more frequently performed as traditional axillary dissection. Median number of lymph nodes examined

Table 8 **Type of definitive axillary procedure in patients with pathological nodal negative disease (n=2355)**

	GE	VS	TI	BA	ZH	SGA	GG	Total
Traditional axillary dissection	142	208	101	141	107	283	138	1120
	24%	70%	28%	57%	44%	71%	65%	48%
Sentinel node biopsy	423	84	223	103	131	104	57	1125
	71%	28%	62%	42%	54%	26%	27%	48%
Unknown[§]	33	6	36	3	4	10	18	110
	6%	2%	10%	1%	2%	3%	8%	5%

§ unknown whether sentinel node biopsy or non-selective axillary dissection. P<0.001

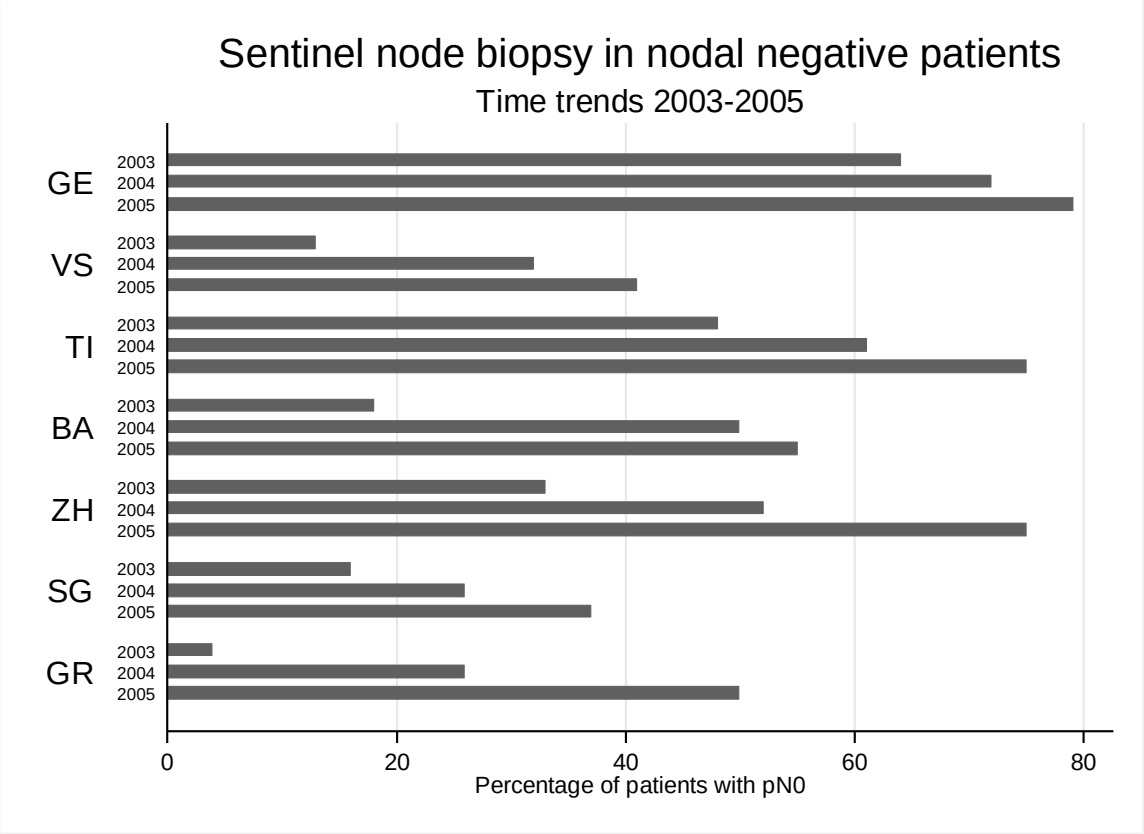

Figure 2- Time trends in sentinel node biopsy in nodal negative patients according to regions

in traditional axillary lymph node dissection was 13 (range 1 - 67), in 20% of cases a non-selective lymph node sampling of less than 10 lymph nodes (range 1-9) was performed. Among 583 patients with 4 or more positive lymph nodes, 12% had less than 10 lymph nodes examined.

48% of patients classified as pN0 had only SNB as definitive axillary procedure with important regional differences. The proportion was highest in Geneva (71%) followed by Ticino (62%) and Zurich (54%) and lowest in St.Gallen-Appenzell (26%) (P<0.001). The use of the sentinel technique increased in all regions during the study period (Figure 2).

RADIATION THERAPY

Adjuvant radiation therapy after breast conservation surgery

Overall the rate of radiation therapy after conservation surgery attained 88% for all age groups combined. When only patients younger than 80 were considered, the percentage increased to 92% and to 95% for patients younger than 70 years. Regional differences concerned especially the age group 70 to 79 years. The highest rate of radiation therapy after BCS among women aged 70-79 was found in Geneva (90%) and the lowest in Grisons-Glarus (64%) (P=0.03).

Almost all patients received external radiotherapy; brachytherapy was reported for only 5 patients (0.03%). The most common dose delivered to the conserved remaining breast was 50 Gy, about 70% of the patients received this dose. Other frequent used total doses were 45 Gy (with single doses of 2.25 to 2.5 Gy) and 54.6 Gy (with fraction doses of 1.8 Gy).

95% of patients younger than 50 years received a boost to the tumor bed after conservation surgery followed by radiotherapy, but considerable significant regional variations were observed among patients 50 or older. In Ticino almost all patients received a boost to the tumor bed, but less than a half in this age group in Geneva.

Table 9 **Radiotherapy in the remaining breast in patients with breast conserving surgery, stage I-III and age ≤ 80 (n=2618)**

	GE	VS	TI	BA	ZH	SGA	GG	Total
Radiation therapy delivered	651	269	383	259	255	407	190	2414
	94%	95%	91%	91%	89%	94%	88%	92%
No radiation therapy delivered	27	13	40	22	13	25	18	158
	4%	5%	9%	8%	5%	6%	8%	6%
Unknown	14	1	0	3	17	3	8	46
	2%	0%	0%	1%	6%	1%	4%	2%

P<0.01

ADJUVANT RADIATION THERAPY FOLLOWING MASTECTOMY SURGERY

507 patients in the study population presented no metastatic disease and four or more positive axillary nodes, large primary tumors (T3-T4) or very close or positive deep margins of resection of the primary tumor, all conditions requiring radiotherapy of the chest wall after mastectomy. From these 403 were aged <75 years. In this group only 68% received adjuvant radiation therapy of the chest wall. The lowest rate was reported in Ticino (59%) the highest in Valais (84%) (P<0.01). Less than 5% of patients refused radiotherapy.

Table 10	Radiotherapy to the chest wall in patients with no metastatic disease, mastectomy and T3- T4 or N2-N3 or involved surgical margins and aged < 75 years (n=403)							
	GE	VS	TI	BA	ZH	SGA	GG	Total
Radiation therapy delivered	57	33	41	20	35	69	21	276
	74%	89%	59%	71%	60%	68%	70%	68%
No radiation therapy delivered	20	4	29	8	20	33	3	117
	26%	11%	41%	29%	35%	32%	10%	29%
Unknown	0	0	0	0	3	1	6	10
	0%	0%	0%	0%	5%	1%	20%	3%

P<0.001

ADJUVANT RADIATION OF OTHER REGIONAL ANATOMICAL REGIONS

Axillary radiotherapy after mastectomy in high risk patients was reported in 39% of patients in Ticino but in less than 5% of cases in St.Gallen-Appenzell. Radiotherapy of the supra/infraclavicular areas was on the other hand more often delivered in Geneva (13%), St.Gallen-Appenzell (14%) and Zurich (13%) than in Basel (7%) and Ticino (1%) (P<0.001).

SYSTEMIC ADJUVANT THERAPIES

ENDOCRINE THERAPY

Estrogen receptor (ER) was known in 96% of cases almost always with additional determination of progesterone receptor (PR) status. As described in the methodology section, in order to judge the appropriateness of use of endocrine therapy in the light of the knowledge and guidelines at the time, the risk categories issued by the 8th Consensus Meeting in St. Gallen in 2003[3] (Table 11) were used.

MINIMAL RISK GROUP

Significant regional variations could be observed both concerning the proportion of women that met the criteria for minimal risk as well as in the prescription of endocrine therapy for this group. In Geneva and in Valais the highest prescription rates of endocrine therapy were reported (Geneva 93%, Valais 95%). In those regions higher use of endocrine therapy was observed both for pre- and postmenopausal ER positive breast cancer.

AVERAGE AND HIGH RISK GROUP

Endocrine therapy was prescribed in 90% of patients <80 years with endocrine responsive disease in the group of average or high risk of recurrence. The analysis of the regional data revealed significant differences. The rate of

Table 11	Definition of Risk Categories for Patients with Early Breast Cancer according to the St Gallen Consensus Guidelines 2003 [3]		
		Endocrine-Responsive Disease [§]	**Endocrine-Non responsive Disease**
Minimal Risk	Node-Negative	ER and / or PR expressed, and all of the following: pT ≤ 2cm grade 1 age ≥ 35	Not applicable
Average Risk	Node-Negative	ER and / or PR expressed, and at least one of the following features: pT> 2cm, or grade 2 - 3 age <35 years	Estrogen receptor and progesterone receptors absent
High risk	Node-Positive	ER and / or PR expressed	Estrogen receptor and progesterone receptors absent

[§] Threshold for endocrine responsiveness: 10% positive staining of cells for either receptor

non-prescription of endocrine therapy in group varied significantly from 17% in Ticino and 12% in Basel to 1% in Valais and 4% in St.Gallen-Appenzell (P<0.001) (Table 12). No information on endocrine therapy was available for 10% of patients in Zurich and 15% in Grisons-Glarus.

Overall less than 2% of patients refused endocrine therapy when proposed.

Table 12		Endocrine therapy prescription in patients with endocrine responsive disease average or high risk of relapse and aged <80 years (n=2525)							
		GE	VS	TI	BA	ZH	SGA	GG	Total
Endocrine therapy prescribed		553	241	346	225	270	444	188	2267
		93%	98%	83%	87%	88%	95%	79%	90%
No prescription		37	2	71	31	6	17	14	178
		6%	1%	17%	12%	2%	4%	6%	7%
Unknown		2	3	0	4	32	4	35	80
		0%	1%	0%	2%	10%	1%	15%	3%

P<0.001

ADJUVANT CYTOTOXIC CHEMOTHERAPY

ENDOCRINE NON-RESPONSIVE DISEASE

Overall 842 patients presented with endocrine non-responsive disease. From these 779 (92%) were aged <80 and 670 (80%) were younger than 70 years. Age distribution of patients with endocrine non-responsive disease was similar in all regions.

Rates of metastatic disease in endocrine unresponsive breast cancer were 8% (range: 1% in Zurich to 20% in Grisons-Glarus) (P<0.01).

We analyzed the patterns of chemotherapy prescription in 651 patients with stage I to III breast cancer, age <80 years and endocrine non-responsive disease. Overall chemotherapy was prescribed in 523 patients (80%). The highest rates of chemotherapy prescription were observed in St.Gallen-Appenzell (88%) and the lowest in Basel (71%). Differences among regions were not statistically significant (P==0.22). Patient refusal was reported in less than 5%.

The principal factors related to no prescription of chemotherapy in endocrine non-responsive disease were age and stage. Age 70 or older was, when compared to age <70, significantly associated with no chemotherapy (OR: 11.07, CI: 5.67-24.24), after adjusting for stage (4 categories) and canton of residence.

36 patients in this category were aged <35 years. 35 (97%) received chemotherapy

Table 13 **Chemotherapy prescription in patients with endocrine unresponsive disease stage I-III and younger as 80 (n=651)**

	GE	VS	TI	BA	ZH	SGA	GG	Total
Chemotherapy prescribed	111	57	82	58	48	126	41	523
	80%	80%	84%	71%	73%	88%	79%	80%
Chemotherapy not prescribed	27	14	16	19	10	16	9	111
	19%	20%	16%	23%	15%	11%	17%	17%
Unknown	1	0	0	5	8	1	2	17
	1%	0%	0%	6%	12%	1%	4%	3%

P<0.001

ENDOCRINE RESPONSIVE DISEASE

Overall chemotherapy was prescribed in the adjuvant setting to 35% of patients with endocrine responsive disease (n=1173) most of which (72%) presented nodal involvement.

Chemotherapy in nodal negative, endocrine responsive disease was prescribed to 16% of patients in the study, more frequently in Grisons-Glarus (30%) than in other regions (P<0.01). Grade III (OR: 4.13 95% CI: 3.03-5.64), tumor extension more than 20 mm (OR: 2.97; 95%CI 2.29-3.85) and region Grisons-Glarus (OR: 2.28 95%CI: 1.50-3.49) were significantly associated with prescription of chemotherapy in the adjusted analysis.

512 patients aged<80 years presented with locally advanced endocrine responsive breast cancer (T3/4 or N2/3 and M0). The rate of chemotherapy prescription in this group of patients showed significant regional variations from 89% in Grisons-Glarus to 60% in Basel (P=0.001).

50 patients in this group were aged <35 years. 44 (88%) received chemotherapy and 6 (12%) did not. Regional differences were not observed.

SCHEDULES USED

More than 15 different approved chemotherapy regimens and schedules were used.

Four courses of doxorubicin and cyclophosphamid (ACx4) or epirubicin cyclophosphamid (ECx4) were the most frequently used chemotherapy regimen in 34% of cases (n= 534 cases) followed by FEC100x6 in 21% of cases. Longer EC/AC based regimens (followed by paclitaxel x4 or CMFx3) were used in 8% (n= 109), CMF alone was used in 9% of cases (n=135).

Antracycline-taxane combinations were infrequently used (2%). A small minority of cases received low dose metronomic cyclophosphamide-methotrexate after an approved standard chemotherapy as part of a clinical study in the framework of an IBCSG protocol.

In 9% of patients (n=143) adjuvant chemotherapy contained drugs which were not registered or not investigated for adjuvant use or proved to be inferior when tested against standard regimens. The list of these drugs include navelbine, gemcitabine, capecitabine, liposomal doxorubicin, mitoxantrone, carboplatin, cisplatin, bevacizumab, pemetrexed, low-dose 5FU 24h cont. iv infusion, mitomycin C,5FU-leucovorin, ifosphamide.

Chemotherapy was reported to have been completed as planned in over 80% of cases. Frequent reasons for chemotherapy not completed as planned were dose reduction and stop of therapy because of toxicity. Even if reported “completed as planned” the number of cycles given or the duration of the chemotherapy was not always consistent with the original regimen. In some cases the chemotherapy was stopped for radiation therapy and continued afterwards.

PARTICIPATION IN CLINICAL TRIALS

Only 6% of patients are reported as having participated in a clinical trial. Patients residing in St.Gallen-Appenzell or Geneva were enrolled significantly more frequently in clinical trials than in other regions (P<0.01).

DISCUSSION

This study shows important variations in the way breast cancer care is delivered in Switzerland and that this variation affects all elements in the chain of care.

Most women in our study have detected the cancer herself, especially in the German speaking regions. In two of the regions providing data to our study, Geneva and Valais, mammography screening programs are running. In these regions the proportion of women diagnosed in stage I was higher as in other regions. In Valais, where over 65% of invited women have participated in the screening program in 2004-2005[40], 27% of newly diagnosed invasive breast cancers were detected through the program and breast cancer cases from Valais showed the highest proportion of stage I breast cancer. In Geneva, where the attendance to the mammography screening program reached only 25% in 2005[40], only 6% of new cases were diagnosed through the program. In this canton most women undergo opportunistic screening. Data on the performance of opportunistic screening are limited. While quality controls are possible within an organized screening program, this is not possible for opportunistic screening. As surrogate indicators stage at diagnosis (e.g. the percentage of breast cancer diagnosed in stage I; described in table 2) and percentage of tumors with pathologic size <=10mm (Table 3) have been proposed [41]. In two regions participating in our study (Basel and Ticino) no organized screening program is running but a high percentage of women using mammography as screening tool have been reported [42]. However only in regions with programs (Geneva and Valais) the surrogate indicators show a better profile. The need for improvement in the field of early detection has to be stressed.

It is widely accepted that multidisciplinary teams form the basis for best practice in the management of breast cancer [2, 43, 44]. Our data show that the implementation of this strategy needs to be improved in most regions. The sequential consultation of the surgeon, the radio oncologist and the medical oncologist was the most frequent form of delivery of breast cancer care in most regions in Switzerland. Neo-adjuvant chemotherapy and endocrine therapy was significantly higher in regions where cases were discussed in a pre-operative multidisciplinary conference.

Although breast conservation surgery (BCS) followed by radiotherapy and mastectomy have equivalent outcomes in terms of survival [45], BCS is preferred whenever possible in order to reduce morbidity. As already described by other authors [46-48], mastectomy rates in our study population showed significant regional differences after adjusting for differences related to tumor size, multicentricity, presence of extensive DCIS and positive margins. Similar geographical differences have been reported in other countries [46, 47]

Important are also the differences in the rate of breast reconstruction after mastectomy and in the use of sentinel node biopsy in nodal negative patients. Although these techniques do not affect survival several studies have shown that they improve quality of life [49, 50] and in the case of SNB reduce morbidity associated with breast cancer surgery [17]. The regional variations are also clinically and statistical significant concerning the time trends in the adoption of new surgical techniques.

Less important in magnitude (although partly statistically significant) were the regional differences in the use of radiation therapy after BCS and systemic therapies. The rate of adherence to guidelines [3, 16]for these items was very high.

Participation in clinical trials has been acknowledged to improve the delivery of care because of the expertise accumulated by researchers and trainees [43]. However, only 6% of patients in our study have been included in a trial.

Variations in the process of care have been associated to patient-related factors (e.g. urbanity, affluence, education, knowledge, awareness and compliance) to provider-related factors (e.g. expertise, team approach) to health system-related factors (e.g. provision of systematic mammography screening within a quality controlled

program) [51]. The role of some patient related factors like urbanity and affluence that has been put forward in previous analysis [1] do not seem to be confirmed in the present study. The differences between two geographical regions with almost the same level of urbanity and affluence as Geneva and Basel let think, that other factors may play a more substantial role.

Both strengths and limitations of the study are related to the retrospective perspective of data collection. On the positive side the time gap between diagnosis and the start of the study provided the opportunity to obtain information about therapies delivered many months after diagnosis, although corresponding to the initial therapy concept. Moreover, the time gap assured a more complete registration of patients not treated in centers or not treated at all, reducing a possible selection bias [52]. Through the external approach we were able to avoid biases related to self selection of care givers, self report and poor documentation.

On the negative side, the data obtained was partially incomplete, especially in some regions where the number of cases with missing information was substantial. Another limitation of this study is that in a field of rapid transformation, the patterns of care described correspond to the state-of-the-art-knowledge in the past. However, even if guidelines may evolve and there may be circumstantial reasons for not adhering to them, many features of good care remain the same. As with most observational studies, unobservable as well as unobserved differences between those receiving standard, guideline congruent therapies versus nonstandard therapies are very likely to play a role in the patterns of care we observed.

The strengths of this study are the following a) we were able to study patients in the community setting, in all type of practices, b) we could assess a great number of elements that are taken in consideration in the therapeutic decision making process and c) the fact that parameters, their exact definition and categorization had been defined prospectively.

Only population-based cancer registries collect data on all cancer cases in the community and can thus show the dissemination of good practice at the community level and thus avoid selection bias. Less clear is the question whether or not these studies are to be conducted as “ad hoc” studies with a well defined study question and the set of variables necessary to answer them, or whether information regarding oncological care has to be collected in routine. For the “ad hoc” studies speaks the fact that it is not intuitively obvious how much additional data should be collected or how allowance should be made for the rapid changes occurring within cancer therapy. Indicators of quality of care may involve the employment of different modalities of treatment in a general way (e.g. surgery, radiation therapy), or may include more detailed indicators as the use of specific diagnostic tools, delays incurred before receipt of treatment, the degree of specialization of the doctor or hospital responsible for management, specific drugs used and any of a potentially large number of markers of cancer care. To collect all this markers in routine may severely increase the costs of data collection in cancer registries.

CONCLUSIONS

In this study we found important variations in the way care is provided for breast cancer patients in Switzerland. Differences regard not only early detection but the therapeutic approach and the delivery of care in all their different multidisciplinary aspects. It remains unclear whether previously reported survival differences [1] reflect a) only differences in early detection strategies with a higher proportion of patients presenting tumor characteristics associated with better prognosis b) consistent use of state-of-the-art management and the more frequent multidisciplinary team approach c) other, in this study not measured differences (e.g. the more frequent use of state of the art care without directly measurable effect on survival as mentioned above might also be an indicator of improved care in general and for parameters relevant for survival but not investigated in this study) or d) a combination of all.

This first report focuses on geographical variation in the delivery of care. The wealth of data collected during this study has however not been fully exploited. We will therefore continue to analyze the collected data in order to search for factors that promote high quality care and those that may prevent it.

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List of collected items

Data on the person
Patient ID
TumorID
Municipalty of residence
Date of Birth
Nationality
Country of Birth
Profession
Profession of the partner
health insurance type
Heigth in cm
Weight in kg
Family history of breast cancer
Previous breast cancer
Previous breast cancer laterality
if previous breast cancer which: invasive, DCIS, LCIS
Date of diagnosis of previous breast Ca
Stage at diagnosis of previous breast cancer
Actual status of previous breast cancer
Surgical Treatment of previous breast cancer
Homonal Treatment of previous breast cancer
Radiotherapy of previous breast cancer
Chemotherapy of previous breast cancer
MULTIDISCIPLINARY TEAM DISCUSSION
Institutional tumor board (multidisciplinary team discussion) of the present case with written statement of conclussions
DIAGNOSIS
Tumor detected due to
Preoperative Confirmation of malignancy through
Date of preoperative biopsy
Tumour size by imaging or clinical examination in mm
Method employed in determining size
Side location of the lesion
Predominant area of the tumour
Simultanously contralateral breast cancer

Primary Tumour (clinical)
Regional nodes affected (clinical)
Distant metastases (clinical)
localisation of metastases detected
Treatment decision after work-up
if no treatment why?
Date of the first visit with the general practitioner
Date of first request for clinic / hospital appointment
Date of first clinic/ hospital appointment
Date of definitive Diagnosis
HISTOPATHOLOGY
adequate Specimen orientation
maximal pathological diameter of inv. cancer in mm
M-code ICD-O-3 of invasive histological type at final pathology rapport
Grade of invasive cancer (Nottingham or BRE-combined grades)
Lymphatic vessel invasion
Venous invasion
Peritumoral DCIS component
% of DCIS of total tumor
Grade of in situ (DCIS) lesions
Minimum distance of the invasive tumour from the margins (mm)
Minimum distance of the in situ component from the margins (mm)
Pathological classification of primary tumour
Pathological classification of regional nodes
Number of lymph nodes examined by the pathologist
Number of axillary lymph nodes containing tumour
Disease extent
Oestrogen receptor status: % of positive cells
Progesteron receptor status: % of positive cells
HER2 Receptor status
Method used for the determination of HER2 Receptor status
Pathology department type
Code of the pathology department
BREAST SURGERY
Date of admission for 1st intervention
Date of a discharge after 1st intervention

Type of conclusive operation performed during surgical session (1st breast operation)
Date of 1st breast operation
Result of frozen section of the lesion (specimen margins) (1st breast operation)
Pathological evaluation of margins for invasive cancer after first surgery
Pathological evaluation of margins for in Situ component after first surgery
Type of Hospital
Code of the hospital where surg 1 was performed
Number of primary surgeries per year in the institution
Date of 2nd breast surgery
Type of conclusive operation performed during surgical session (2nd breast operation)
Pathological evaluation of margins for invasive cancer after 2nd surgery
Pathological evaluation of margins for in Situ component after first surgery
2nd surgery performed in
if another institution: type
Code of the hospital where surg 2 was performed
Number of primary surgeries per year in the institution
final type of surgery (after 3 or more interventions)
Pathological evaluation of final margins for invasive cancer
Pathological evaluation of final margins for in Situ component
final margins obteined after x number of surgeries
Indications for Mastectomy
If other explain why
AXILLARY DISSECTION
Execution of axillary operation
Sentinel lymph node procedure
Date of sentinel procedure
Result of intraoperative analysis of sentinel node
Definitive histologic result of sent. node
Type of axillary operation (level)
Date of axillary dissection if at a separate session
Time relationship between axillary operation and breast surgery
axilla dissection performed in same hospital?
if another institution: type
Code of the hospital where ax.surg was performed
Number of primary surgeries per year in the institution
RADIOTHERAPY
Radiotherapy (RT) performed
whole breast irradiated

Chest wall radiation after mastectomy
Boost in tumour bed
Boost dose administered (Gy)
dose per fraction (Gy)
Total dose (Gy): total administered dose
Supra/infra clavicular nodes radiation
dose per fraction (Gy)
Total dose (Gy): total administered dose
Radiation of internal mammary nodes
dose per fraction (Gy)
Total dose (Gy): total administered dose
Radiation of the axilla
dose per fraction (Gy)
Total dose (Gy): total administered dose
Interruption to therapy for technical reasons
Start Date Rxth
End Date of Rxth
if another institution type of hospital
Radiotherapy department code
Number of patients treated per year
SYSTEMIC THERAPY Hormone therapy
Hormone therapy planned
Endocrine therapy started
Ovarian ablation for premenopausal pat
Drug prescribed
Treatment start date
Planned duration of treatment in months
Early stop of hormontherapy
Reasons for early stop of hormonal therapy
Chemotherapy / Herceptin therapy
Chemotherapy planned
Chemotherapy started
Chemotherapy completed as planned
Reasons for chemotherapy not completed as planned
Date of first cycle
Treatment end date
Combination of drugs (Regimen)

if other chemotherapy: specify
Number of cycles performed
Herceptin (Trastuzumab) therapy planned
Herceptin therapy started
Herceptin therapy completed as planned
Reasons for Herceptin therapy not completed as planned
Date of therapy start
Date of treatment end
Setting in which the systemic therapy was done
Setting code for Hormon/Chemotherapy
Number of patients treated per year
Entry in clinical trials
Trial name