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Influence of department volume on cancer survival for gynaecological cancers—A population-based study in Tyrol, Austria

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Abstract

Objective. The objective of this study was to assess the effect of department volume on survival of patients with gynaecological cancer.

Methods. We conducted an observational population-based study in Tyrol, Austria. The analysis includes all patient data on incident gynaecological cancer collected by the Cancer Registry of Tyrol. Data were collected since 1988 on a population-based perspective; publication of incidence data since 1988 in Cancer Incidence in Five Continents gives evidence for good completeness and validity of the database. Patient survival status is assessed in a passive way by probabilistic record linkage between incidence data and official mortality data. We applied a multivariate Cox regression with variables age, sex, stage, year of diagnosis, histological verification of diagnosis, transfer to other hospital and department volume. Department volume was categorised in ≤11/12–23/24–35/≥36 patients per year reflecting one/two/three/more than three patients per month; categories were computed separately for every site we analysed. Departments with up to 11 patients per year were called small departments.

Results. For 4191 breast cancer patients, we found a negative effect for small departments; hazard ratio (HR) 1.39, 95% confidence interval (CI) 1.22, 1.58. For ovarian cancer patients, we also found a negative effect for small departments (HR 1.27, 95% CI 1.05, 1.54). For cervical cancer patients, we found a positive effect for small departments (HR 0.67, 95% CI 0.51, 0.88). No effect was shown for corpus cancer (HR 0.80, 95% CI 0.63, 1.01).

Conclusion. The results indicate that, in our country, rules on minimum department case-load can further improve survival for breast and ovarian cancer patients.
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Keywords: Gynaecological cancer; Survival rate; Department volume; Minimum caseload; Cancer epidemiology

Introduction

The question whether for cancer patients department volume has an influence on overall survival and other outcome parameters has been investigated for more than a decade. Answers are of great relevance for health planning and policy in the respective countries. An overview published in 2000 [1] concludes that there is an association between centre size and survival for all solid cancer sites for which therapy is complex. One group of publications concentrates on specific cancer sites and/or specific therapy modalities, while another group analyses this question primarily on a population basis. In addition, some authors discuss interesting methodological questions like publication bias or self-interest bias.

In our country, about 25% of patients with gynaecological cancer are treated in small departments (with less than 11 patients per year), ranging from 16% to 52% of patients depending on specific cancer site. Hence, studying the association between department volume and survival was of special public health interest. We consequently analysed the question on a population basis taking into the study all cancer patients diagnosed in the population of Tyrol, not only patients qualifying, for example, for clinical trials. Also, we analysed all major gynaecological cancer sites. In this way, we tried to avoid both biases mentioned above

Abbreviations: CI, confidence interval; HR, hazard ratio; pat/year, patients per year; DCO, death certificate only.

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by reporting results for all investigated cancer sites, irrespective of the kind of results.

Material and methods

The Cancer Registry of Tyrol was established in 1986. Cancer data for the population of Tyrol have been registered on a population basis since 1988. Also, since 1988, data have been published in Cancer Incidence in Five Continents [2], thus giving evidence of good completeness for the incidence data.

Registration is performed from a standardised questionnaire including sex, age, cancer site and histology, date of diagnosis, stage and basic information on primary treatment. Information on co-morbidity is not collected routinely. There are strict rules for collecting these variables in accordance with international guidelines (see for example [3]). The questionnaire is either completed by a physician, or a Cancer Registry clerk collects data directly from clinical records in the treating hospital. Two independent data bases are built up, one incidence database and one we call search database including all information on possible cancer diagnoses (mainly pathology reports, but also information from radiotherapy units and various other data sources) allowing the registry to check completeness. Cancer cases are attributed to treating departments according to place of initial treatment.

Patient life status is assessed in a passive way. We do a probabilistic record linkage between incidence data and the official mortality data set for Tyrol collected by Statistics Austria [4]. In Austria, there is no general use of unique person identifiers as, for example, in Scandinavian countries. Therefore, the Cancer Registry of Tyrol developed a method for probabilistic record linkage based on probabilistic record linkage theory. Using the components last name, birth surname, first name, date of birth, sex and municipality code or zip code, a probability of identity is computed for every pair of persons (denoted p-val), also taking into account phonetic translations and documentation and typing errors. If p-val is greater than 0.95, we assume without further checks that the components describe the same person; for a p-val smaller than 0.75, we assume, again without further checks, that the components describe different persons. A p-val between 0.75 and 0.95 calls for a decision on a case-by-case basis. In general, this means that further information is needed to describe the persons more precisely.

Closure of this study was end of 2003. For a few cases, we received information on out-migration, but only by chance. We cannot systematically check for out-migrant status due to data privacy constraints. However, aggregated data on out-migrants in the population of Tyrol show that, in the age classes above 50, which are the relevant age classes for cancer survival, the out-migrant rate is less than one percent of the population.

We analysed the main gynaecological cancer sites: breast, ovary, cervix and corpus. From 1988 to 2000, 4366 breast cancer cases, 976 ovarian cancer cases, 819 cervical cancer cases and 923 corpus cancer cases were registered in the Cancer Registry. Of these, 169 breast cancer cases, 64 ovarian cancer cases, 15 cervical cancer cases and 16 corpus cancer cases were excluded from analysis because of death certificate only (DCO) status and six breast cancer cases and one ovarian cancer case because of other reasons, mainly due to loss of follow-up. Thus, the final study included 4191 breast cancer cases, 911 ovarian cancer cases, 804 cervical cancer cases and 907 corpus cancer cases.

Care is provided by gynaecologists, medical oncologists and radiation oncologists for ovarian, cervix and corpus cancer and, in addition, by general surgeons for breast cancer. There is no training available in gynaecologic oncology in Austria. Radiotherapy is offered by one Department of Radiotherapy of Innsbruck Medical University and by a radiotherapy unit within the Department of Gynaecology of Innsbruck Medical University. Transfer to another hospital was defined as transfer during primary treatment.

A multivariate Cox model was applied using the variables age at diagnosis, year of diagnosis, histological confirmation, stage according to UICC, transfer to another hospital and residence. Age was categorised in groups 0≤54/55–64/65–74/≥75 and year of diagnosis in groups 1988–1992/1993–1996/1997–2000. Follow-up time is shorter for more recent periods. From a theoretic point of view, this should not bias the results under the assumption that events are evenly distributed over time for all three period groups. The study area is served by one university hospital treating about half of the patients and nine regional hospitals. Department size was defined as average number of incident patients per year (pat/year) and categorised in groups ≤11/12–23/24–35/≥36 pat/year; department size was computed for every site separately. We defined categories a priori according to the rationale one, two, three or more than three patients per month. Departments with ≥36 pat/year are called large departments and departments with 1–11 pat/year are called small departments. In Cox analysis, reference group is defined by large departments except for ovarian cancer and corpus cancer, for which the largest departments had no more than 24–35 pat/year.

Residence was grouped in the capital city Innsbruck and surroundings (Ibk), the western part of Tyrol (OL), the eastern past of Tyrol (UL) and East Tyrol (LZ), which is a county geographically separate from the main part of the state.

Statistical analysis was done with Stata Version 8.0 [5]. After univariate analysis, we fitted a multivariate Cox model separately for every cancer site by initially entering all variables into the model and then removing variables without significant influence (backward elimination). To check the influence of variables, the likelihood ratio test was applied. After the model was set up, we checked proportional hazard ratio assumption first graphically and then by procedure stphtest of Stata.

Significance was tested at the alpha level of 5%. We present hazard ratios (HR) together with 95% confidence intervals (95% CI).

The population of Tyrol was 612,309 in the year 1988, of which 316,057 were females (51.6%). The female population increased to 342,728 in the year 2000.

Results

Fig. 1 and Table 1 show an overview of all cancer sites investigated. For following cancer sites, we found a significant negative effect for small departments as compared to large departments: breast cancer with HR 1.39 (95% CI 1.22, 1.58) and ovarian cancer with HR 1.27 (95% CI 1.05, 1.54). For cervical cancer, we found a positive effect with HR 0.67 (95% CI 0.51, 0.88). A nonsignificant effect was found for corpus cancer at HR 0.80 (95% CI 0.63, 1.01), although the effect was near significance.

The following section describes results for individual cancer sites in more detail.

Of 4191 breast cancer patients, 1/3 were age 54 or younger and 22% were age 75 or older; see Table 2. Multivariate analysis was adjusted for age, histological confirmation, stage, year of diagnosis and department volume; see Table 1.

Of all cases, 3% had no histological verification (HR 2.68, 95% CI 2.17, 3.30), while 33% were stage I (reference category),

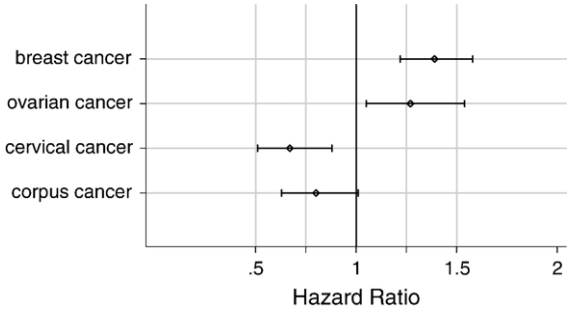

Fig. 1. Hazard ratio for small departments, by cancer site (HR: Hazard ratio adjusted for age, stage, histological confirmation and year of diagnosis. Reference category is large departments ≥36 pat/year for breast cancer and cervical cancer and 24–35 pat/year for ovarian and corpus cancer).

Table 1
Multivariate hazard ratios with 95% confidence interval[a]

	Breast cancer	Ovarian cancer	Cervical cancer	Corpus cancer
Age group	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
≤54	1.00	1.00	1.00	1.00
55–64	1.19 (1.02, 1.39)	2.07 (1.55, 2.78)	1.35 (0.98, 1.86)	2.64 (1.35, 5.14)
65–74	1.37 (1.19, 1.58)	2.93 (2.23, 3.85)	1.96 (1.44, 2.66)	5.97 (3.18, 11.21)
≥75	2.51 (2.20, 2.87)	4.34 (3.29, 5.72)	3.08 (2.28, 4.16)	16.34 (8.75, 30.51)
No histological verification	2.68 (2.17, 3.30)	2.77 (2.01, 3.80)	10.14 (6.38, 16.10)	4.08 (2.27, 7.34)
UICC Stage				
I	1.00	1.00	1.00	1.00
II	2.11 (1.83, 2.44)	2.61 (1.68, 4.04)	1.98 (1.34, 2.94)	1.91 (1.30, 2.81)
III	4.16 (3.51, 4.93)	4.02 (2.99, 5.42)	4.19 (3.02, 5.82)	3.16 (2.10, 4.76)
IV	9.89 (8.26, 11.83)	7.64 (5.60, 10.42)	9.45 (6.04, 14.76)	6.62 (4.40, 9.97)
X	4.51 (3.69, 5.53)	3.27 (2.32, 4.63)	3.77 (2.66, 5.34)	2.62 (1.95, 3.51)
Year of diagnosis			[b]	[e]
1988–1992	1.00	1.00		1.00
1993–1996	0.85 (0.76, 0.95)	0.89 (0.73, 1.09)		0.83 (0.63, 1.09)
1997–2000	0.78 (0.68, 0.90)	0.76 (0.61, 0.95)		0.66 (0.48, 0.91)
Department volume				
≥36 pat/year	1.00	[c]	1.00	[d]
24–35 pat/year	1.07 (0.93, 1.23)	1.00	[d]	1.00
12–23 pat/year	1.10 (0.96, 1.27)	[c]	[d]	[d]
≤11 pat/year	1.39 (1.22, 1.58)	1.27 (1.05, 1.54)	0.67 (0.51, 0.88)	0.80 (0.63, 1.01)

[a] Transfer to other department and Study Region make no significant contribution to multivariate model for any cancer site.
[b] Year of diagnosis makes no significant contribution to multivariate model for cervical cancer.
[c] There are no departments with ≥36 or 12–23 pat/year for ovarian cancer or corpus cancer.
[d] There are no departments with 12–35 pat/year for cervical cancer.
[e] The global effect of year of diagnosis is significant and so remains in the multivariate model, $P = 0.0492$ (Likelihood Ratio Test) and $P = 0.0498$ (Wald Test).

43% were stage II (HR 2.11, 95% CI 1.83, 2.44), 11% were stage III (HR 4.16, 95% CI 3.51, 4.93), 7% were stage IV (HR 9.89, 95% CI 8.26, 11.83) and 7% were stage X (HR 4.51, 95% CI 3.69, 5.53). Of all breast cancer patients, 34% were diagnosed in the years 1988–1992 (reference category), 32% in 1993–1996 (HR 0.85, 95% CI 0.76, 0.95) and 34% in 1997–2000 (HR 0.78, 95% CI 0.68, 0.90). Of these patients, 51% were treated in large departments, 17% in departments with 24–35 pat/year (HR 1.07, 95% CI 0.93, 1.23), 16% in departments with 12–23 pat/year (HR 1.10, 95% CI 0.96, 1.27) and 16% in small departments (HR 1.39, 95% CI 1.22, 1.58).

We analysed a total of 911 ovarian cancer patients, of whom 29% were age 54 or younger and 24% were age 75 or older, see Table 3. Multivariate analysis was adjusted for age, histological confirmation, stage, year of diagnosis and department volume; see Table 1.

Of all ovarian cancer patients, 7% had no histological verification (HR 2.77, 95% CI 2.01, 3.80), while 26% were stage I (reference category), 6% were stage II (HR 2.61, 95% CI 1.68, 4.04), 34% were stage III (HR 4.02, 95% CI 2.99, 5.42), 20% were stage IV (HR 7.64, 95% CI 5.60, 10.42) and 14% were stage X (HR 3.27, 95% CI 2.32, 4.63). Of these patients, 36% were diagnosed in the years 1988–1992 (reference category), 31% in 1993–1996 (HR 0.89, 95% CI 0.73, 1.09) and 32% in 1997–2000 (HR 0.76, 95% CI 0.61, 0.95); 50% of patients were treated in departments with 24–35 pat/year (reference category), 50% in small departments (HR 1.27, 95% CI 1.05, 1.54). We observed no patients in other size categories.

Of 804 cervical cancer patients, 58% were age 54 or younger and 13% were age 75 or older; see Table 4. Multivariate analysis was adjusted for age, histological confirmation, stage and department volume; see Table 1.

Of all cervical cancer patients, 4% had no histological verification (HR 10.14, 95% CI 6.38, 16.10), while 47% were stage I (reference category), 13% were stage II (HR 1.98, 95% CI 1.34, 2.94), 18% were stage III (HR 4.19, 95% CI 3.02, 5.82), 4% were stage IV (HR 9.45, 95% CI 6.04, 14.76) and 17% were stage X (HR 3.77, 95% CI 2.66, 5.34). Of these patients, 44% were diagnosed in the years 1988–1992, 29% in 1993–1996 and 27% in 1997–2000 (year of diagnosis had no significant influence in the multivariate model); 64% of patients were treated in large departments and 36% in small departments (HR 0.67, 95% CI 0.51, 0.88).

We analysed 907 corpus cancer patients, of whom 15% were age 54 or younger and 27% were age 75 or older; see Table 5. Multivariate analysis was adjusted for age, histological confirmation, stage, year of diagnosis and department volume; see Table 1.

Of all corpus cancer patients, 2% had no histological verification (HR 4.08, 95% CI 2.27, 7.34), while 64% were stage I (reference category), 7% were stage II (HR 1.91, 95% CI 1.30, 2.81), 7% were stage III (HR 3.16, 95% CI 2.10, 4.76), 4% were stage IV (HR 6.62, 95% CI 4.40, 9.97) and 18% were stage X (HR 2.62, 95% CI 1.95, 3.51). Of these patients, 34% were diagnosed in the years 1988–1992 (reference category), 32% in 1993–1996 (HR 0.83, 95% CI 0.63, 1.09) and 35% in 1997–2000 (HR 0.66, 95% CI 0.48,

Table 2
Patient characteristics and univariate HR for breast cancer by department size (N=4191)

	Department size				Totals	Univariate HR (95% CI)
	≥36 pat/year	24–35 pat/year	12–23 pat/year	≤11 pat/year		
Age group						
≤54	791 (37.0%)	224 (31.5%)	202 (29.6%)	177 (26.9%)	1394 (33.3%)	1.00
55–64	460 (21.5%)	142 (20.0%)	157 (23.0%)	132 (20.0%)	891 (21.3%)	1.18 (1.01, 1.38)
65–74	474 (22.2%)	164 (23.1%)	187 (27.4%)	145 (22.0%)	970 (23.1%)	1.52 (1.32, 1.75)
≥75	413 (19.3%)	137 (20.1%)	137 (20.1%)	205 (31.1%)	936 (22.3%)	3.35 (2.94, 3.81)
No histological verification	20 (0.9%)	5 (0.7%)	17 (2.5%)	101 (15.3%)	143 (3.4%)	8.13 (6.78, 9.74)
UICC stage						
I	752 (35.2%)	240 (33.8%)	222 (32.5%)	180 (27.3%)	1394 (33.3%)	1.00
II	968 (45.3%)	317 (44.6%)	311 (45.5%)	200 (30.3%)	1796 (42.9%)	2.14 (1.86, 2.48)
III	208 (9.7%)	93 (13.1%)	82 (12.0%)	55 (8.3%)	438 (10.5%)	4.77 (4.03, 5.65)
IV	122 (5.7%)	40 (5.6%)	31 (4.5%)	92 (14.0%)	285 (6.8%)	12.47 (10.47, 14.86)
X	88 (4.1%)	21 (3.0%)	37 (5.4%)	132 (20.0%)	278 (6.6%)	6.83 (5.66 8.24)
Year of diagnosis						
1988–1992	706 (33.0%)	251 (35.3%)	211 (30.9%)	269 (40.8%)	1437 (34.3%)	1.00
1993–1996	670 (31.3%)	251 (35.3%)	227 (33.2%)	192 (29.1%)	1340 (32.0%)	0.74 (0.66, 0.83)
1997–2000	762 (35.6%)	209 (29.4%)	245 (35.9%)	198 (30.0%)	1414 (33.7%)	0.62 (0.54, 0.71)
Transfer to other department	28 (1.3%)	11 (1.6%)	8 (1.2%)	21 (3.2%)	68 (1.6%)	1.78 (1.28, 2.49)
Study region						
Ibk	1653 (77.3%)	3 (0.4%)	10 (1.5%)	318 (48.3%)	1984 (47.3%)	1.00
UL	257 (12.0%)	353 (49.6%)	438 (64.1%)	154 (23.4%)	1202 (28.7%	1.00 (0.95, 1.10)
OL	203 (9.5%)	355 (49.9%)		145 (22.0%)	703 (16.8%)	1.02 (0.89, 1.16)
Lz	25 (1.2%)		235 (34.4%)	42 (6.4%)	302 (7.2%)	1.10 (0.90, 1.33)
Department volume						
≥36					2138 (51.0%)	1.00
24–35					711 (17.0%)	1.14 (0.99, 1.31)
12–23					683 (16.3%)	1.13 (0.98, 1.31)
≤11					659 (15.7%)	1.94 (1.71, 2.20)

0.91); 48% of patients were treated in departments with 24–35 pat/year (reference category) and 52% in small departments (HR 0.80, 95% CI 0.63, 1.01). We observed no patients with other department size categories.

Discussion

Departments

The main conclusion of the analysis is highly influenced by how we define which department is responsible for initial treatment. For cancer patients treated by only one department, this definition was clear. But for some of the patients, more than one department was involved in initial treatment. Our country has no strict rules governing prime responsibility for cancer treatment. So we assigned the chronologically first treating department, and this rule seems to be rather straightforward and make sense. The percentage of patients treated by more than one department is rather small. In addition, when subsetting the analysis of patients treated by only one department, the effects were of similar size. We thus conclude that errors made in defining who holds prime responsibility for cancer treatment did not disturb our results.

The variable for transfer is defined as transfer during primary treatment. Our cancer register is an incidence register that does not collect information on the whole period from diagnosis to death. Therefore, we are not able to present more in-depth information on transfer and we especially do not have data on co-morbidities.

We attempted to estimate the percentage of patients treated by more than one department. Since full data are lacking, we can present only a rough estimate for primary treatment, namely 6% of breast cancer patients, 17% of cervical cancer, 18% of corpus cancer and 9% of ovarian cancer patients.

Staging and other confounders

Every survival analysis depends on how well we can adjust for inter-departmental differences in patient characteristics. In Cox regression, we can adjust for patient characteristics if the information is available. Our Cancer Registry contains information on sex, age at diagnosis, staging, year of diagnosis, histological verification of cancer, transfer to other departments, and residence. We set up a model specific for every cancer site by starting with all parameters in the model and then eliminating parameters with no significant influence on the effects (backward elimination). This is a standard procedure described in many textbooks; see for example [6].

Staging is collected as either TNM stage or FIGO for ovarian cancer sites. Because there were too many combinations of TNM values, we transformed TNM stage to stages I to IV according to UICC rules [7]. For example, the Finnish

Table 3
Patient characteristics and univariate HR for ovarian cancer by department size ($N = 911$)

	Department size		Totals	Univariate HR (95% CI)
	24–35 pat/year	≤11 pat/year		
Age group				
≤54	155 (34.2%)	108 (23.6%)	263 (28.9%)	1.00
55–64	100 (22.1%)	96 (21.0%)	196 (21.5%)	2.27 (1.70, 3.03)
65–74	123 (27.2%)	112 (24.5%)	235 (25.8%)	3.46 (2.64, 4.54)
≥75	75 (16.6%)	142 (31.0%)	217 (23.8%)	5.69 (4.36, 7.43)
No histological verification	3 (0.7%)	62 (13.5%)	65 (7.1%)	4.43 (3.36, 5.85)
UICC stage				
I	128 (28.3%)	108 (23.6%)	236 (25.9%)	1.00
II	26 (5.7%)	30 (6.6%)	56 (6.2%)	2.73 (1.76, 4.22)
III	215 (47.5%)	93 (20.3%)	308 (33.8%)	3.72 (2.78, 4.99)
IV	43 (9.5%)	141 (30.8%)	184 (20.2%)	9.24 (6.81, 12.52)
X	41 (9.1%)	86 (18.8%)	127 (13.9%)	5.04 (3.63, 7.00)
Year of diagnosis				
1988–1992	163 (36.0%)	168 (36.7%)	331 (36.3%)	1.00
1993–1996	137 (30.2%)	149 (32.5%)	286 (31.4%)	0.87 (0.71, 1.06)
1997–2000	153 (33.8%)	141 (30.8%)	294 (32.3%)	0.75 (0.60, 0.94)
Transfer to other department	6 (1.3%)	27 (5.9%)	33 (3.6%)	1.61 (1.07, 2.42)
Study region				
Ibk	225 (49.7%)	197 (43.0%)	422 (46.3%)	1.00
UL	154 (34.0%)	117 (25.5%)	271 (29.8%)	0.88 (0.72, 1.08)
OL	70 (15.5%)	81 (17.7%)	151 (16.6%)	1.11 (0.88, 1.41)
Lz	4 (0.9%)	63 (13.8%)	67 (7.4%)	1.16 (0.84, 1.60)
Department volume				
24–35			453 (49.7%)	1.00
≤11			458 (50.3%)	1.78 (1.50, 2.12)

nationwide cancer registry categorises staging information as localised/nonlocalised/unknown, and the European Network of Cancer Registries recommends collecting not detailed TNM stage but only what they call condensed TNM. If one of the TNM components is missing, this transformation results in stage X, thus counting unknown as well as imprecise stages. Percentage of stage X depends heavily on cancer site but also on department, because we have indications that some departments have a higher percentage of imprecise staging information (at least imprecise staging information documented in the Cancer Registry). Thus, some problems are encountered when comparing stage X between departments. The percentage of stage X is in line with other publications when we consider that our data set contains all cancer patients of a population, and not only histologically verified cases or cases treated in the framework of clinical trials [8,9].

What remains is the question whether our adjustment for staging effects was precise enough. Following international studies and well-established registries, adjusting for UICC stage seems to be precise enough. For certain cancer sites and for clinical aspects, our analysis may be too imprecise, but on a population basis, this was the best we could achieve. We also tried to find a surrogate measure for terminal cases (meaning cases with very poor prognosis), which were also part of our population-based analysis. We believe that the combination of histological verification, age and stage IV should allow adjustment for terminal patients.

Age at diagnosis was modelled in categories also allowing adjustment for nonlinear effects in age. Age categories were defined a priori. For all cancer sites, the reference category "≤54" was large enough to provide stable estimates. We observed poorer survival in older patients, also in multivariate analysis. In general, our cancer register contains only limited information that can help to explain this fact, especially since we do not collect data on co-morbidities. Information about primary treatment for patients aged 75 and older as compared to patients up to age 74, reveals less radiotherapy and chemotherapy for breast cancer, less surgery and chemotherapy for cervical cancer, less radiotherapy for corpus cancer and less chemotherapy for ovarian cancer. Our results are in line with, for example, those of the EUROCARE working group, who found survival rates to decrease with increasing age for almost all cancer sites [10].

Period effects were modelled to adjust for time effects, for example departments changing their treatment guidelines over the years. Reference category was defined as years of diagnosis 1988–1992. Thus, HR can be interpreted as change in treatment as compared to years 1988–1992. Multivariate analysis shows improved survival over time for breast cancer and ovarian

Table 4
Patient characteristics and univariate HR for cervical cancer by department size ($N = 804$)

	Department size		Totals	Univariate HR (95% CI)
	≥36 pat/year	≤11 pat/year		
Age group				
≤54	291 (56.7%)	175 (60.1%)	466 (58.0%)	1.00
55–64	89 (17.3%)	41 (14.1%)	130 (16.2%)	1.93 (1.41, 2.64)
65–74	67 (13.1%)	39 (13.4%)	106 (13.2%)	3.41 (2.54, 4.58)
≥75	66 (12.9%)	36 (12.4%)	102 (12.7%)	6.02 (4.53, 7.99)
No histological verification		31 (10.7%)	31 (3.9%)	17.62 (11.73, 26.47)
UICC Stage				
I	233 (45.4%)	148 (50.9%)	381 (47.4%)	1.00
II	85 (16.6%)	22 (7.6%)	107 (13.3%)	2.70 (1.85, 3.95)
III	124 (24.2%)	18 (6.2%)	142 (17.7%)	5.83 (4.28, 7.94)
IV	17 (3.3%)	18 (6.2%)	35 (4.4%)	14.12 (9.22, 21.64)
X	54 (10.5%)	85 (29.2%)	139 (17.3%)	5.55 (4.05, 7.61)
Year of diagnosis				
1988–1992	233 (45.4%)	123 (42.3%)	356 (44.3%)	1.00
1993–1996	144 (28.1%)	90 (30.9%)	234 (29.1%)	0.88 (0.68, 1.13)
1997–2000	136 (26.5%)	78 (26.8%)	214 (26.6%)	0.68 (0.50, 0.92)
Transfer to other department	10 (1.9%)	41 (14.1%)	51 (6.3%)	1.15 (0.75, 1.77)
Study region				
Ibk	274 (53.4%)	80 (27.5%)	354 (44.0%)	1.00
UL	158 (30.8%)	112 (38.5%)	270 (33.6%)	0.82 (0.64, 1.05)
OL	75 (14.6%)	57 (19.6%)	132 (16.4%)	1.03 (0.77, 1.39)
Lz	6 (1.2%)	42 (14.4%)	48 (6.0%)	0.49 (0.27, 0.88)
Department volume				
≥36			513 (63.8%)	1.00
≤11			291 (36.2%)	0.87 (0.69, 1.09)

Table 5
Patient characteristics and univariate HR for corpus cancer by department size ($N = 907$)

	Department size		Totals	Univariate HR (95% CI)
	24–35 pat/year	≤11 pat/year		
Age group				
≤54	70 (15.9%)	62 (13.2%)	132 (14.6%)	1.00
55–64	116 (26.4%)	126 (26.9%)	242 (26.7%)	2.35 (1.21, 4.55)
65–74	140 (31.9%)	153 (32.7%)	293 (32.3%)	4.80 (2.57, 8.95)
≥75	113 (25.7%)	127 (27.1%)	240 (26.5%)	014.18 (7.66, 26.24)
No histological verification	1 (0.2%)	17 (3.6%)	18 (2.0%)	3.78 (2.16, 6.59)
UICC Stage				
I	297 (67.7%)	281 (60.0%)	578 (63.7%)	1.00
II	27 (6.2%)	38 (8.1%)	65 (7.2%)	2.23 (1.52, 3.27)
III	31 (7.1%)	31 (6.6%)	62 (6.8%)	2.66 (1.77, 3.99)
IV	21 (4.8%)	18 (3.8%)	39 (4.3%)	7.51 (5.04, 11.20)
X	63 (14.4%)	100 (21.4%)	163 (18.0%)	2.40 (1.81, 3.19)
Year of diagnosis				
1988–1992	159 (36.2%)	145 (31.0%)	304 (33.5%)	1.00
1993–1996	132 (30.1%)	156 (33.3%)	288 (31.8%)	1.08 (0.83, 1.41)
1997–2000	148 (33.7%)	167 (35.7%)	315 (34.7%)	0.86 (0.63, 1.18)
Transfer to other department	17 (3.9%)	71 (15.2%)	88 (9.7%)	1.06 (0.71, 1.59)
Study region				
Ibk	261 (59.5%)	153 (32.7%)	414 (45.6%)	1.00
UL	104 (23.7%)	146 (31.2%)	250 (27.6%)	1.00 (0.77, 1.31)
OL	69 (15.7%)	104 (22.2%)	173 (19.1%)	0.77 (0.55, 1.07)
Lz	5 (1.1%)	65 (13.9%)	70 (7.7%)	1.32 (0.89, 1.98)
Department volume				
24–35			439 (48.4%)	1.00
≤11			468 (51.6%)	0.98 (0.78, 1.23)

cancer. For cervical cancer, an improvement was seen in univariate analysis, but not in multivariate analysis. Finally, corpus cancer does not show an improvement in univariate analysis, but only in multivariate analysis. As already mentioned in the discussion of age effects, our cancer register has limited data and therefore is not able to fully explain the observed time trends. Information on primary treatment shows an increase in chemotherapy for breast cancer, but we do not have detailed information on chemotherapy regimen. For cervical cancer, our data show an increased surgical volume in early stages. In general, we see a clear shift towards early stages for breast cancer and cervical cancer which of course improves outcome.

Our general judgement is that the limited data available in our cancer register restrict our ability to analyse in depth some of the trends observed. This is beyond the scope of cancer registers and should be dealt with in specially designed studies.

We did not adjust for treatment. The reason was that adjustment should compensate for factors influencing survival which cannot be influenced by departments, but not for factors chosen by departments. If we consider the case of a department that offers poor treatment, adjusting for treatment could eliminate differences in outcome, which we feel would not be justified. It can be argued that therapy could heavily confound our analysis. Thus, a subanalysis examined basic variables for primary treatment in the model. Compared to our main analysis, the effects for breast cancer (HR for small departments 1.29, 95% CI 1.13, 1.47) and ovarian cancer (HR for small departments 1.26, 95% CI 1.04, 1.53) are a little smaller but still statistically significant. The effect for corpus cancer (HR 0.87, 95% CI 0.67, 1.12) is smaller and not statistically significant, as already shown in the analysis without therapy, and the effect for cervical cancer (HR 0.81, 95% CI 0.61, 1.09) loses statistical significance. In summary, our main results, namely negative effects for small departments for breast and ovarian cancer, change only slightly and remain statistically significant.

External comparison

The question studied here has been of public interest for more than a decade. Some articles also discuss methodological problems like self-interest bias and publication bias. Our general goal was to analyse all gynaecological cancer sites and report all results. Hence, neither biases mentioned above was relevant for our study. Another bias able to distort results is selection bias in the departments, meaning not all cancer patients are included in the analysis, for example only patients qualifying for certain trials. It is well known that patients treated in clinical trials differ in their survival from other patient groups. Again, this did not play a role in our analysis because we analysed a population-based cancer registry data set covering all cancer patients in our population.

Some articles deal with different outcome measures, for example hospital mortality or 30-day mortality and complications after surgery. This was not possible in our analysis, because we included all cancer patients, namely also patients who did not undergo surgery or even curative therapy. Moreover, we had no information on surgeon; this was never part of the Cancer Registry data set.

When comparing our results with published results, one must consider whether a specific study region employs guidelines which contribute to standardised diagnostics and therapy, or whether a country uses the best treatment principle, as in our country. Such guidelines would tend to minimise outcome differences, because small departments usually should not treat patients with advanced cancer.

This analysis obviously cannot answer the question whether department size per se influences patient outcome or whether department size is merely a surrogate measure counting for various factors influencing results.

When comparing our results with published results, we use the term effect as shorthand for negative effect for small departments.

Our results for breast cancer are consistent with published results. Roohan [11] reported an analysis from New York State with a total of 47890 patients hospitalised between 1984 and 1989. In addition to hospital volume, the investigators had information on patient age, surgery type, stage, co-morbidity, race, socioeconomic status and distance to the hospital. For five-year survival, they reported a risk ratio of 1.6 for very low hospital volume (10 or fewer patients) as compared to high hospital volume (151 or more per year). In addition, the investigators discuss a “dose–response” relationship between volume

and survival. However, the study period dates back quite far, which means the results might not be applicable for the most recent decade. Skinner [12] reports a negative effect for small departments too. Two main factors are discussed as being responsible for the effect, namely hospital caseload [11] and surgical specialisation [13]. The UK has guidelines for minimum case-load [14,15]. Our database lacks detailed information on surgical specialisation, so we cannot distinguish between these factors.

Our results for ovarian cancer are also in line with most relevant publications. An analysis from Austria [16] found an effect of similar size. This study also includes information on residual cancer after surgery and covers more than half of the gynaecological units in Austria. Elit [17] for Canada investigated academic status and surgical speciality for cases diagnosed in Ontario from 1992 to 1998 in a total of 3355 patients. Analysis was adjusted for age, co-morbidity and metastatic status. The authors reported an HR of 0.7 for gyn-oncologist and of 0.65 for gynaecologist, each compared to general surgeon. Woodman [18] also investigated effects for surgeons as compared to gynaecologists and transfer to oncologists and found no effect for surgeon volume. For these two studies, the focus is not directly comparable to our study. Ioka [19] investigated 3523 patients newly diagnosed in 1975–1995 in Osaka, Japan. By adjusting for age, histological type and cancer stage, the authors report an HR of 1.6 for very low volume (less than one operation per year) as compared to high volume (average of 9 operations per year). Kumpulainen [20] did a population-based study in Finland with 3851 ovarian cancer patients diagnosed from 1983 to 1994. Hospitals were categorised as university, central or other, and by volume quartile. After adjusting for age and stage, the authors reported a relative risk of 1.06 for other hospitals as compared to university hospitals (nonsignificant) and a relative risk of 1.13 for smallest as compared to largest hospitals when categorised by quartile (significant). Du Bois [21] reported results from a German study group and found an 82% elevated risk for nonstudy hospitals versus study hospitals, but no effect for hospital volume. The discussion mentioned that about 15% of German hospitals participated, and a bias towards participation by centres more interested in quality assurance cannot be ruled out. The main reasons discussed for benefits in large centres are that teaching hospitals are reported to do more accurate staging [22] and, in general, cancer management should be done by a multidisciplinary team [18]. Recommendations for centralisation have been given in England [23,24], Scotland [25] and the United States [26].

For cervical cancer, we found a significant positive effect with an HR of 0.67 for small departments. At first view, this result was unexpected. When breaking down the analysis by stage, we found a nonsignificant positive effect for all stages but stage II (data not shown). Departments in Tyrol have agreed that stages II and III are not expected to be treated in small departments. If we repeat our analysis excluding stages II and III, the result remains unchanged (HR 0.63, 95% CI 0.45, 0.89). Patients are not younger in small departments. All nonhistologically verified cases were observed in small departments and slightly more stage I cases were also observed in small departments. We see many more cases with unknown stage in small departments (29.2% versus 10.5% in large departments). Consequently, the adjustment for staging might not be able to fully compensate differences in stage distribution for cervical cancer. We found no recent publications dealing with centre volume and survival for cervical cancer. This might be attributed to publication bias.

For corpus cancer, we found an HR of 0.82 (95% CI 0.65, 1.01), the effect being near significance. Again, this result was unexpected. When we split the analysis by stage, we saw nonsignificant positive effects for stages III, IV and X, no effect for stage I and a negative effect for stage II, each for small departments as compared to larger departments. Excluding stages II and III (which are unlikely to be treated in small hospitals, as for cervix cancer), the resulting HR is nearly unchanged (0.86, 95% CI 0.66, 1.12). There are no differences in age structure between larger and small departments; all but one nonhistologically verified case were diagnosed in small departments as well as more unknown stages in small departments (21.4% versus 14.4%). Again, adjustment for staging might not be able to fully correct differences in stage distribution due to misclassification of stages.

For both cervix cancer and corpus cancer, additional information is needed in order to shed more light on the unexpected results. This means that we would need more precise information on therapy and multidisciplinary treatment. In our interpretation, we have doubts whether these results are chance findings and would need detailed information on therapy (not only information on whether surgery or chemotherapy was applied but also more details on treatment regimens) as well as on the degree of coordination by various departments, which seems to occur for these cancer sites.

Conclusion

Our analysis demonstrated for small departments significant negative effects for breast cancer and ovarian cancer and significant positive effects for cervical cancer. The analysis is based on Cancer Registry data sets and hence information on confounders is limited. As in every epidemiological analysis, possible confounders are subject to some limitation. However, most of our results are in line with published results. Consequently, it is necessary to carefully discuss results with clinicians and set up guidelines for minimum department case-load, at least for breast cancer and ovarian cancer.

References

[1] Hillner BE, Smith TJ, Desch CE. Hospital and physician volume or specialization and outcomes in cancer treatment: importance in quality of cancer care. J Clin Oncol 2000;18(11):2327–40.
[2] Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas B. Cancer incidence in five continents. Volume VIII. IARC Scientific Publications No. 155 Lyon: IARC, 2002.
[3] Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG. Cancer registration. Principles and methods. Lyon: IARC; 1991.
[4] Oberaigner W, Stühlinger W. Record linkage in the cancer registry of Tyrol. Methods Inf Med 2005;44(5):626–30.

[5] StataCorp. Stata Statistical Software: Release 8. College Station, TX: StataCorp LP; 2003.
[6] Cleves M, Gould W, Gutierrez R. An introduction to survival analysis using Stata, Revised edition. Stata Press; 2004.
[7] Wittekind Ch, Wagner G. TNM Klassifikation maligner Tumoren. 5. Auflage. Berlin: Springer-Verlag; 1997.
[8] Katalinic A, Holzmann M, Uhlenkamp T, Bartel C, Raspe H. Krebs in Schleswig-Holstein 1998. Lübeck: Institut für Krebsepidemiologie i.V.— Registerstelle des Krebsregisters Schleswig-Holstein; 2000.
[9] Schmidtmann I, Husmann G, Krtschil G, Seebauer G. Krebs in Rheinland-Pfalz: Inzidenz und Mortalität im Jahr 2000. Mainz: Krebsregister Rheinland-Pfalz; 2002.
[10] Vercelli M, Capocaccia R, Quaglia A, Casella C, Puppo A, Coeberg JW. Relative survival in elderly European cancer patient: evidence for health care inequalities. The EUROCARE working group. Crit Rev Oncol Hematol 2000;35(3):161–79.
[11] Roohan PJ, Bickell NA, Baptiste MS, Therriault GD, Ferrara EP, Siu AL. Hospital volume differences and five-year survival from breast cancer. Am J Public Health 1998;88(3):454–7.
[12] Skinner KA, Helsper JT, Deapen D, Ye W, Sposto R. Breast cancer: do specialists make a difference? Ann Surg Oncol 2003;10(6):606–15.
[13] Gillis CR, Hole DJ. Survival outcome of care by specialist surgeons in breast cancer: a study of 3786 patients in the west of Scotland. BMJ 1996;312(7024):145–8.
[14] Calman K, Hine D. Policy framework for commissioning cancer services: a report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales. Department of Health. London HM Stationary Office; 1995.
[15] Improving outcomes in breast cancer: guidance for purchasers. London: Department of Health; 1996.
[16] Sevelda P, Obermair A, Oberaigner W, Marth C. Qualitätserfassung bei Ovarialkarzinom. Krebs! Hilfe! 2004;4:48–9.
[17] Elit L, Bondy SJ, Paszat L, Przybysz R, Levine M. Outcomes in surgery for ovarian cancer. Gynecol Oncol 2002;87(3):260–7.
[18] Woodman C, Baghdady A, Collins S, Clyma JA. What changes in the organisation of cancer services will improve the outcome for women with ovarian cancer? Br J Obstet Gynaecol 1997;104(2):135–9.
[19] Ioka A, Tsukuma H, Ajiki W, Oshima A. Influence of hospital procedure volume on ovarian cancer survival in Japan, a country with low incidence of ovarian cancer. Cancer Sci 2004;95(3):233–7.
[20] Kumpulainen S, Grenman S, Kyyronen P, Pukkala E, Sankila R. Evidence of benefit from centralised treatment of ovarian cancer: a nationwide population-based survival analysis in Finland. Int J Cancer 2002;102 (5):541–4.
[21] Du Bois BA, Rochon J, Lamparter C, Pfisterer J. Pattern of care and impact of participation in clinical studies on the outcome in ovarian cancer. Int J Gynecol Cancer 2005;15(2):183–91.
[22] Wolfe CD, Tilling K, Raju KS. Management and survival of ovarian cancer patients in south east England. Eur J Cancer 1997;33(11): 1835–40.
[23] Improving outcomes in gynecological cancers: the research evidence. London: NHS Executive, Department of Health; 1999.
[24] National Cancer Guidance Steering Group: improving outcomes in gynecological cancers: the manual. London: NHS Executive, Department of Health; 1999.
[25] Fighting the silent killer: optimizing ovarian cancer management in Scotland. Accounts Commission for Scotland: The Commission; 1998.
[26] Guidelines for referral to a gynecologic oncologist: rationale and benefits. The Society of Gynecologic Oncologists. Gynecol Oncol 2000;78(3 Pt 2): S1–S13.