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Key words

Abstract

Objectives: To examine the influence of pre-existing psychiatric disorder on the choice of treatment in patients with gynecological cancer.

Materials and methods: The analyses are based on all patients who underwent surgical treatment for endometrial, ovarian or cervical cancer who were registered in the Danish Gynecological Cancer Database in the years 2007 -2014 (3,059 patients with ovarian cancer, 5,100 patients with endometrial cancer, and 1,150 with cervical cancer). Logistic regression model and Cox regression model, adjusted for relevant confounders, were used to estimate the effect of pre-existing psychiatric disorder on the course of cancer treatment. Our outcomes were i) pre-surgical oncological treatment, ii) macroradical surgery for patients with ovarian cancer, iii) radiation/chemotherapy within 30 days and 100 days after surgery, and iv) time from surgery to first oncological treatment.

Results: In the group of patients with ovarian cancer, more patients with a psychiatric disorder received macro-radical surgery vs patients without a psychiatric disorder, corresponding to an adjusted OR of 1.24 (95% CI 0.62-2.41), and the chance for having oncological treatment within 100 days was OR=1.26 (95% CI 0.77- 2.10). AS for patients with endometrial cancer, all outcome-estimates were close to unity. The adjusted OR for oncological treatment within 30 days after surgery in patients with cervix cancer with a history of psychiatric disorder was 0.20 (95% CI 0.03-1.54).

Conclusions: We did not find any significant differences in the treatment of ovarian and endometrial cancer in patients with pre-existing psychiatric diagnoses. When it comes to oncological treatment, we suggest that an increased attention should be paid to patients with cervix cancer having a pre-existing psychiatric diagnosis.

Introduction

Gynecological cancer accounted for approximately 16% of all new cancer cases and 14% of cancer deaths in women, globally, in 2012 (1). The most common gynecological cancers in Denmark are endometrial, ovarian and cervical cancer (2). For endometrial cancer the age-standardized incidence rate is approximately 13 per 100,000, and the mortality rate is less than 2% of cancer deaths in women (3). Early diagnosis is the major factor accounting for the low mortality, and nearly 80% of the cases are diagnosed while the tumor is confined to the uterus (4). Globally, ovarian cancer is the sixth most common cancer in women. Denmark and the other Scandinavian countries have the highest incidence of ovarian cancer in the world. In Denmark, approximately 500 new cases are diagnosed yearly, and the median age of disease onset is 63 years (5). The symptoms in ovarian cancer are unspecific and consequently, in about 70% of cases, ovarian cancer is diagnosed in an advanced stage. Cervical cancer is the most common form of gynecological cancer in premenopausal women, it affects less than 1% of all women, and almost 400 new cases are diagnosed yearly. About 100 Danish women die annually of the disease.

Age, smoking, alcohol, and *obesity* are factors strongly associated with increased cancer mortality (6-8), and moreover, psychiatric illness has been associated with increased tobacco use, obesity, alcohol and substance abuse (9). Some studies have shown that patients with cancer having a psychiatric disorder are diagnosed later, and receive fewer sessions of chemotherapy, surgery and other cancer related treatments, and that they receive their treatments significantly later than patients without a psychiatric disorder (10-15). In 2003, Spiegel et al (16) argued that depression may influence the course of cancer treatment in different ways as some symptoms of depression are similar to symptoms related to cancer, like the vegetative symptoms of sleep and appetite disturbance, fatigue and concentration difficulties. Due to an overlap in symptoms and weak social network, referral for a diagnosis of suspected cancer can potentially be delayed for patients with

depression symptoms. Several factors might contribute to an increased vulnerability in patients with psychiatric disorders compared to those without psychiatric disorders, and when it comes to cancer treatment in patients with psychiatric disorders, the evidence is still sparse. Factors that might contribute to deteriorated outcomes in patients with a psychiatric disorder are less likely to adhere to preventive screening procedures, to receive treatment, to complete treatment (17), and some might refuse surgery (14, 18). Moreover, patients with a psychiatric disorder may be less effective at navigating in the complex healthcare systems (19, 20).

This study aims to investigate the association between psychiatric disorders prior to surgical treatment in women with gynecological cancers and macroradical surgery, the oncological treatment, and the time from surgery to oncological treatment.

Material and Methods

Setting

This study is a population-based nationwide cohort study using data from the Danish national health-care registries. The population-based study design was possible due to equal access to a centralized tax-funded healthcare system for all residents in Denmark. We used 1) the nationwide clinical quality database, the Danish Gynecological Cancer Database (DGCD), to identify all patients with a diagnosis of gynecological cancer, 2) the Danish National Patient Registry (DNPR) to retrieve information regarding relevant psychiatric diagnoses up to ten years prior to a gynecological cancer surgery, and 3) the Income Statistics Register to provide data on the socioeconomic status.

The data were linked by a unique identifier, the civil registration number which all Danish residents are assigned either at birth or when immigrating to Denmark. Linkage of data between registries on

an individual level is therefore possible and valid (21).

The Danish National Patient Registry

The DNPR was established in 1977. This register contains data on all procedures related to the diagnostic evaluation and treatment of patient admissions in Denmark (22). We used the DNPR to include information on oncological treatment for each patient. We also used the DNPR to identify patients with the following psychiatric disorders: schizophrenia, schizotypal disorders and affective disorders (International Classification of Diseases (ICD-10): DF20-29: Schizophrenia, schizotypal and delusional disorders (primary psychotic disorders), or DF30-39: depression and other affective disorders).

The Danish Gynecological Cancer Database

The DGCD was established in January 2005 and includes information on different types of gynecological cancers (5). All gynecological departments in Denmark participating in the diagnosis and treatment of these cancers are required to report to the DGCD. The DGCD includes comprehensive information on each patient, including details on history, surgical procedures, staging, and pathology. We used the DGCD to identify women with a gynecological cancer and included relevant clinical information like type of surgery, tumor stage, cancer diagnosis, and performance status measured as ECOG-PS. ECOG-PS is a scale that was developed by the Eastern Cooperative Oncology Group to describe the patient's level of function in terms of their ability to care for themselves, daily activity, and physical ability. It varies from 0 for "fully active" to 5 for "dead".

The Income Statistics Registry

Using the Income Statistics Registry (23), we included information on the socio-economic status for each patient at the time of cancer surgery. The socio-economic class was defined as the household

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income in the year the patient received surgical treatment for gynecological cancer, adjusted for the number of people in the household. The socio-economic class was divided by the median into two groups, low and high.

Study population

The study population includes all women who were registered in the DGCD with the diagnosis of endometrial, ovarian or cervical cancer within the period 01 January 2007 - 18 September 2014, and who received surgery. We divided the study population by type of cancer (three mutually exclusive groups): ovarian cancer, endometrial cancer, and cervix cancer.

Exposed and unexposed cohorts

The exposed cohorts comprised patients, treated with surgery for the gynecological cancer, who had at least one psychiatric diagnosis (schizophrenia, or schizotypal or affective disorders) within the period of 10 years to 120 days before the date of surgery. This group is now referred to as the group of patients with a psychiatric disorder. The unexposed cohorts comprised all patients, treated with surgery for the gynecological cancer, who did not have a psychiatric diagnosis (schizophrenia, or schizotypal or affective disorders) within the 10 years. This group is now referred to as the group of patients without a psychiatric disorder. To avoid that the psychiatric diagnosis was present solely as a result of the patient´s knowledge of having a cancer, psychiatric disorders diagnosed less than 120 days before the date of the cancer diagnosis were excluded.

Outcomes

The primary outcome was the effect of psychiatric disorders on the course of gynecological cancer treatment with specific attention on i) receiving a pre-surgical (neo-adjuvant) oncological treatment, ii) receiving macroradical surgery, i.e. no visible tumor left (complete cytoreductive

surgery). This outcome will only be calculated for patients with ovarian cancer since more than 90% of patients with endometrial and cervical cancer receive macroradical surgery, iii) receiving either radiation or chemotherapy within 30 days after surgery, iv) receiving either radiation or chemotherapy within 100 days after surgery (24), v) time from surgery to the first oncological treatment given within 100 days.

According to Danish guidelines for treatment of cervix cancer adjuvant radiation therapy and concomitant treatment with cisplatin should be given if one of the following criteria is met: i) positive lymph nodes, ii) invasion of parametria, iii) resection edge is not free. Moreover, adjuvant radiation therapy and concomitant treatment with cisplatin is recommended for patients with negative lymph node if one of the following criteria is met: i) tumor is greater than 3 cm and invasion depth is greater than 2/3, ii) tumor is greater than 2 cm, invasion depth is greater than 1/3 and vascular invasion. According to these guidelines approximately 25% of the cervical cancer patients should receive adjuvant therapy (25).

Statistical analyses and confounders

We used an approximation of the Fisher exact test to compare the baseline characteristics of women with the different types of gynecological cancer with and without a psychiatric disorder.

We used a logistic regression model to estimate the ratio for receiving macroradical surgery in patients with ovarian cancer and a psychiatric disorder versus those without a psychiatric disorder, adjusted for relevant confounders. We also used a logistic regression model to estimate the effect of a psychiatric disorder on receiving oncological treatment within 30 days and 100 days after surgery, adjusted for relevant confounders.

A Cox regression model was used to estimate the effect of a psychiatric disorder on the time from surgery to start of oncological treatment. We used a time window of 100 days from the date of

surgery. Patients who did not survive 30 days or 100 days after surgery were excluded from the corresponding analyses.

The specific confounders were included as follows: *Age* at the time of a gynecological cancer diagnosis, and clinical tumor *stage* according to low (clinical tumor stage I and II) or high (clinical tumor stage III and IV). *Year* of surgery was divided into two time intervals 2007-2010 and 2011-2014. The patient's socio-economic status was defined from the patient's personal income in the year of the gynecological cancer surgery. The personal equivalent disposable income for our study population was from 56,000 DKK (7,500 EUR) to 693,000 DKK (93,000 EUR) per year with a median about 200,000 DKK (26,900 EUR). The s*ocio-economic class* was divided according to low being lower than the median and high as being equal to or higher than the median. *Education* was defined into categories of i) basic school, ii) high school or short cycle tertiary, or iii) higher education including bachelor, masters and doctoral levels. The ECOG-PS was grouped into categories by reported normal activity, yes = 0 and no = 1), s*moking* by no = 0 vs yes = 1, Body Mass Index (*BMI*) by BMI<25, BMI>=25 and BMI<30, and BMI>=30; and *Alcohol abuse as* no vs yes.

For each outcome variable in the multivariate model, confounders were included corresponding to a biological rationale and to a priori decisions.

In sub-analyses we restricted our exposed cohorts only to include those patients who had at least one psychiatric diagnosis within the period of 5 years to 120 days before the date of surgery.

Approvals

The DGCD operates under the Danish law on data protection, with licenses granted by the Danish Data Protection Agency and the Danish Health and Medicines Authority. This specific study has been approved by the Danish Data Protection Agency (jr. nr. 2008-58-0035).

According to Danish law, ethical approval is not required for purely registry-based studies.

Results

From the DGCD, we extracted information on 9,442 patients and nearly all received a surgical treatment, providing us with a total of 9,309 patients. Patients with ovarian cancer comprised 3,059 patients, 5,100 patients had endometrial cancer, and 1,150 had cervical cancer. Eighty-five women with ovarian cancer, 136 with endometrial cancer and 31 with cervix cancer, had a diagnosis of psychiatric disorder within 10 years before the cancer diagnosis (Table 1). Table 1 shows the baseline characteristics of the cohorts. For each cancer type, about 2.8% of the study population had at least one former hospital contact with a psychiatric diagnosis. For all three types of cancers, the mean age of patients with a psychiatric disorder was younger than in patients without a psychiatric disorder. For patients with ovarian cancer, a total of 42.4% of the patients with a psychiatric disorder had low tumor stage vs 35% in patients without a psychiatric disorder; the difference was not statistically significant. There was a significant difference in the socio-economic class distribution across the psychiatric groups for all three cancer types. For patients with ovarian cancer, only 29.4% of the patients with a psychiatric disorder belonged to a high socio-economic class vs 45.2% of the patients without a psychiatric disorder, and the corresponding proportions were 26.5% vs 44.3% for patients with endometrial cancer and 38.7% vs 49.1% for patients with cervix cancer.

From the study population only 97received a pre-surgical (neo-adjuvant) oncological treatment (26 patients with ovarian cancer, 61 patients with endometrial cancer, and 10 patients with cervix cancer), and none of them had a prior psychiatric disorder. Therefore, we did not perform further analyses according to pre-surgical oncological treatment.

Sixty-nine patients with endometrial cancer did not survive 30 days after surgery (3 with a psychiatric disorder and 66 without a psychiatric disorder) and 223 did not survive 100 days after surgery (11 with a psychiatric disorder and 212 without a psychiatric disorder). A total of 117 patients with ovarian cancer did not survive 30 days after surgery (2 with a psychiatric disorder and 115 without a psychiatric disorder) and 278 did not survive 100 days after surgery (4 with a psychiatric disorder and 274 without a psychiatric disorder). Seven patients with cervix cancer did not survive 30 days after surgery (all without a psychiatric disorder) and 38 did not survive 100 days after surgery (all without a psychiatric disorder). Those patients were excluded from the analyses 30 and 100 days of post-surgical oncological treatment, respectively.

Table 2 shows the results for patients with ovarian cancer according to macroradical surgery and post-surgical (adjuvant) oncological treatment, as well as time from the surgery to oncological treatment within 100 days after surgery. A larger number of patients with a psychiatric disorder received macroradical surgery versus patients without a psychiatric disorder (61.2% vs 54%), corresponding to an adjusted OR of 1.24 (95% CI 0.62;41). The results indicated no significant difference in the ratio for oncological treatment within 30 days or within 100 days after surgery (adjusted OR 1.12 (95% CI 0.62; 2.03) and 1.26 (95% CI 0.77; 2.10), respectively). Figure 1 shows the Kaplan-Meier estimates of the oncological treatment within 100 days after surgery. The figure, and the HR presented in table 2, showed no significant difference according to the time from surgery to oncological treatment in patients with psychiatric disorder versus those without.

Table 3 shows the results for patients with endometrial cancer according to post-surgical oncological treatment. The results indicated that there was no significant differences in the ratios for post-surgical oncological treatment for patients with endometrial cancer (adjusted OR 0.82 (95% CI 0.38; 1.77) for oncological treatment within 30 days and within 100 days adjusted OR 1.05 (95% CI 0.55; 1.98)). There was no difference in the median duration from the time of surgery to the

oncological treatment between those with and without a psychiatric diagnosis (adjusted HR 1.03 (95% CI 0.60; 1.76)).

Table 4 shows the results for patients with cervix cancer according to post-surgical oncological treatment, as well as the median for duration in days from time of surgery to oncological treatment within 100 days after surgery. Patients with a psychiatric disorder had a statistically non-significantly lower chance of receiving the oncological treatment within 30 days, as well as 100 days, after surgery (adjusted OR 0.20 (95% CI 0.03; 1.54) and adjusted OR 0.40 (95% CI 0.12; 1.36), respectively). Figure 1 illustrates that patients with a psychiatric disorder waited longer for oncological treatment after surgery than patients without a psychiatric disorder (adjusted HR= 0.42 (0.14; 1.35)).

We also performed sub-analyses where the exposed cohorts were restricted to comprise patients who had at least one psychiatric diagnosis within the period of 5 years before the date of surgery, and the results were similar to those from the main analyses (data not shown). Moreover we performed an additional analysis without tumor stage as an adjustment variable; the estimated effect of psychiatric disorder was very similar to our main result.

Discussion

Our study showed that patients with ovarian cancer and pre-existing psychiatric disorder did not have a lower ratio for macro-radical surgery and oncological treatment compared to the patients without a psychiatric disorder. The ratio for oncological treatment for patients with endometrial cancer was not influenced by a pre-existing psychiatric disorder. When it comes to oncological treatment for patients with cervix cancer and pre-existing psychiatric disorder we found a tendency towards a reduced ratio for oncological treatment.

In this study we examined the effect of pre-existing psychiatric disorder on post-surgical treatment in patients with gynecological cancers. The study was restricted to women with ovarian, endometrial and cervix cancer who had received surgical treatment. Approximately 3% of the study population had at least one hospital contact with a psychiatric diagnosis preceding the cancer diagnosis. This corresponds to the general Danish female population (26, 27). We did not find that patients with ovarian cancer with pre-existing psychiatric disorder had a lower chance of receiving a macro-radical surgical treatment or oncological treatment. For patients with endometrial cancer, we did not find a statistically significant lower chance for oncological treatment either. However, in patients with cervix cancer, our data suggest (although our results were not statistically significant) that patients with a pre-existing psychiatric diagnosis had a lower chance of receiving oncological treatment compared to patients without a psychiatric diagnosis.

Other studies have shown that patients with both cancer and psychiatric disorders have a lower chance of receiving oncological treatment compared to patients with cancer without psychiatric disorders (28, 29). Results from the present study indicate the same tendency for patients with cervix cancer. Moreover, we found a potential delay in the time for oncological treatment in patients with cervix cancer having a pre-existing psychiatric disorder. In general, patients with a psychiatric disorder have an increased sensitivity to stress factors which might cause a depression episode in this patient group. Depression affects the patient's cognitive function and might therefore

reduce compliance to oncological treatment. This could explain both the lower ratio of oncological treatment and the potential delay. Moreover, it could be difficult for women with psychiatric disorders to follow the national screening program for cervix cancer, which might be caused by a general lack of disease knowledge. In general, they are younger and their psychiatric disorder might not be as well treated at the time of diagnosis as in the older age groups.

Our study has several strengths. To our knowledge, this is the first study, based on nationwide data, providing adjusted risk estimates for treatment outcomes in patients with gynecological cancers. The validity of our results depends on the size of the study, accurate classification of exposure and the outcome data, and the ability to take into account the influence of confounders. We used DGCD to identify gynecological cancer patients, and multiple studies reported that data in the DGCD are both valid and complete, and provide a solid base for research (5). Using exclusively nationwide register-data leads to a high completeness of the study populations and minimizes the risk for selection bias due to independently collected data. In the DNPR we had access to mandatory registration of all in- and outpatient diagnoses and in general the validity of the diagnoses in the DNPR is high. Our outcome data on treatment procedures in the DNPR have both very high completeness and validity (22). Also, our outcome data were obtained independently of the hypothesis examined, preventing differential misclassification of our outcome assessment. The information on several important confounders was an important strength. As we expected for all cancer types, women with a psychiatric disorder were younger, had a lower socio-economic status and lower education level.

Our study also has limitations. The limitation of register data is that they do not contain detailed information about health behavior and details according to treatments. In patients with psychiatric disorders we included all patients who had been diagnosed with schizophrenia, schizotypal disorders and affective disorders within 10 years before cancer diagnosis. Some of them can be

cured of their psychiatric disorder long before they had a cancer diagnosis. Restricting the period to patients with a psychiatric disorder within 5 years before cancer diagnosis did, however, not change our results. Also, we included only psychiatric patients with hospital contact as it was not possible for us to have access to data from the general practitioners. A psychiatric diagnosis only given by the general practitioners would therefore not be detected in our study and these patients would be categorized as unexposed. Such cases could potentially lead to underestimation of the effect of psychiatric disorders on cancer treatment. Another weakness in our study is that we could not perform a separate analysis according to different groups of psychiatric disorders because of the small number of patients with psychiatric disorders.

The majority of patients receiving a cancer diagnosis might react with depressive symptoms as this is a powerful stress factor (30). We therefore only looked at pre-existing psychiatric disorders which were diagnosed within the period of 10 years to 120 days before the date of surgery.

The positive finding in our study is that we did not find any difference in the treatment of patients with ovarian and endometrial cancer who had a pre-existing psychiatric disorder. We did, however, find differences in the treatment for cervix cancer in those with a pre-existing psychiatric disorder. It is necessary to pay special attention to these patients with a pre-existing psychiatric disorder to ensure that they receive the same treatment and as quickly as patients without psychiatric disorder. In 2013 The Danish Health Authorities introduced a need based follow up program instead of the earlier timetabled follow up program. This means that women with a low risk of gynecological cancer receive less attention at the hospital and the resources are redirected to the women with a special need for close follow up.

Possible explanations to the variation in treatment between women with a psychiatric diagnosis prior to cancer and women without can be lack of referral if the patients are considered not fit for treatment due to

individual psychical or psychological factors or inability to adhere to treatment. It is also important to notice that some psychotropic drugs can interact with specific drugs used in oncological treatment resulting in severe side effects and in some cases death (31). Specific psychotropic drugs such as clozapine have been found to cause blood dyscrasia such as leukopenia or neutropenia, which can result in life-threatening infections (32, 33). This is another factor for clinicians to consider before initiating treatment. Another suggested possibility is that depression is an indication of global brain dysfunction. This central nervous system dysregulation produces a greater risk for morbidity which weakens a patient's chance of receiving an oncological treatment (34). Moreover, depression has a double feedback loop whereby it promotes poor function and poor function in return promotes depression, which makes models delineating the exact mechanism of how depression influences diagnosis and makes treatment problematic (35).

 Although our results are reassuring regarding patients with ovarian and endometrial cancer, they should be examined in other study populations. Until our results on patients with cervix cancer are confirmed special attention should be given to patients with cervix cancer having a pre-existing psychiatric disorder when it comes to oncological treatment.

Table 1: Baseline characteristics of women diagnosed ovarian, endometrial or cervix cancer in 2007-2014 according to psychiatric disorders

	Ovarian cancer (N= 3,059)		Endometrial cancer (N= 5,100)		Cervix cancer (N=1,150)	
	With psychiatric disorder	Without psychiatric disorder	With psychiatric disorder	Without psychiatric disorder	With psychiatric disorder	Without psychiatric disorder
N	85	2,974	136	4,964	31	1,119
Age, mean (sd)	57.6 (15.9)	62.3 (15.1) *	59.1 (16.4)	62.6 (15.2) *	57.5 (18.5)	60.6 (14.3)
Stage						
Low	36 (42.4%)	1,041(35.0%)	52 (38.2%)	1,822 (6.7%)	28 (90.3%)	992 (88.7%)
High	49 (57.7%)	1,933 (65.0%)	8 (5.9%)	301 (6.1%)	3(9.7%)	104 (9.3%)
missing			76 (55.9%)	2,841 (57.2%)	0	23 (2.1)
BMI						
Normal	41 (48.2%)	1,517(51.0%)	55(40.4%)	1,669 (33.6%)	14 (45.2%)	620 (55.4%)
Overweight	26 (30.6%)	802 (26.9%)	32 (23.5%)	1,434 (28.9%)	14 (45.2%)	285 (25.5%)
Obese	14 (16.5%)	452 (15.2%)	45 (33.1%)	1,716 (34.6%)	3 (9.7%)	190 (16.9)
missing	4 (4.7%)	203 (6.8%)	4 (2.9%)	145 (2.9%)	0	24 (2.1%)
ECOG-PS		*				
Low	46 (54.1%)	1,427(47.9%)	83 (61.0%)	2,998 (60.4%)	24 (77.4%)	819 (73.2%)
High	37 (43.5%)	1,535(51.6%)	52 (38.2%)	1,935 (38.9%)	3 (9.7%)	133 (11.9%)
missing					4 (12.9%)	167 (14.9%)
Year				*		
2007-2010	54 (63.5%)	1,833(61.6%)	68 (50.0%)	2,904 (58.5%)	22 (70.8%)	663 (59.3%)
2011-2014	31 (36.5%)	1,141(38.4%)	68 (50.0%)	2,060 (41.5%)	9 (29.0%)	456 (40.8%)
Socio		*		*		*
Low	55 (64.7%)	1,357(45.6%)	82 (60.3%)	2,236 (45.0%)	19 (61.3%)	473 (42.3%)
High	25 (29.4%)	1.345(45.2%)	36 (26.5%)	2,198 (44.3%)	12 (38.7%)	549 (49.1%)
missing	5 (5.9%)	272 (9.2%)	18 (13.2%)	530 (10.7%)	0 (0%)	97(8.7%)
Education						
Low	34 (44.0%)	1,113(37.4%)	62 (45.6%)	1,799 (36.2%)	13 (41.9%)	387 (34.6%)
Medium	29 (34.1%)	1,044(35.1%)	41 (30.2%)	1,705 (34.4%)	11 (35.5%)	414 (37.0%)
High	19 (22.4%)	588 (19.8%)	22 (16.2%)	999 (20.1%)	6 (19.4%)	243 (21.7%)
missing	3 (3.5%)	229 (7.7%)	11 (8.1%)	461 (9.3%)		
Smoking						

No	67 (78.8%)	2,327(78.2%)	118 (86.8%)	4,190 (84.4%)	25 (80.7%)	772 (68.9%)
Yes	15 (17.7%)	562 (18.9%)	17 (12.5%)	734 (14.8%)	6 (19.4%)	339 (30.3%)
missing	3 (3.5%)	85 (2.9%)	1 (0.7%)	40 (0.8%)	0 (0.0%)	8 (0.7%)
Alcohol		*				
No	65 (76.5%)	1,963(66.0%)	94 (69.1%)	3,266 (65.8%)	22 (70.9%)	731 (65.3%)
Yes	18 (21.2%)	721 (24.2%)	28 (20.6%)	1,294 (26.1%)	8 (25.8%)	304 7.2%)
missing			14 (10.3%)	404 (8.1%)		

*p-value < 0.05

ECOG-PS   ; forklar hvad det betyder (også selv om det har været forklaret I teksten)

Table 2: Distribution of treatment by psychiatric disorder status for patients with *ovarian cancer* and risk estimates from logistic regression analyses (for type of surgery and chance of receiving oncological treatment) and Cox regression analyses (days from surgery to first oncological treatment)

Ovarian cancer	With psychiatric disorder	Without psychiatric disorder	Crude OR/HR (95% CI)	Adjusted OR/HR (95%CI)*
Macroradical surgery **(n=3,059)**			1.52 (0.90; 2.53)	1.24 (0.62; 2.41)
Yes	52 (61.2%)	1.607 (54.0%)		
No	21 (24.7%)	986 (33.2%)		
Oncological treatment within a 30 days after surgery **(n=2,942)**			1.06 (0.60; 1.87)	1.12 (0.62; 2.03)
Yes	15 (18.1%)	492 (17.2%)		
No	68 (82.0%)	2,367 (82.8%)		
Oncological treatment within a 100 days after surgery **(n=2,781)**			1.18 (0.73; 1.91)	1.26 (0.77; 2.10)
Yes	24 (29.6%)	711 (26.3%)		
No	57 (70.4%)	1,989 (73.7%)		
Time from surgery to oncological treatment within a 100 days			1.14 (0.76; 1.72)	1.21 (0.79; 1.84)
median (25% fractal; 75% fractal)	17.5 (6; 43)	15 (6; 43)		

*Adjusted for age, tumor stage, year of surgery, socio-economic class, BMI, ECOG-PS, smoking, alcohol consumption and level of education

Table 3: Distribution of treatment by psychiatric disorder status for patients with *endometrial cancer* and risk estimates from logistic regression analyses (chance of receiving oncological treatment) and Cox regression analyses (days from surgery to first oncological treatment)

| Endometrial cancer	With psychiatric disorder	Without psychiatric disorder	Crude OR/HR (95% CI)	Adjusted OR/HR (95%CI)*
Oncological treatment within a 30 days after surgery (**n=5,028**)			0.96 (0.59; 1.57)	0.82 (0.38; 1.77)
Yes	19 (14.3%)	723 (14.8%)		
No	114 (85.7%)	4,172 (85.2%)		
Oncological treatment within a 100 days after surgery (**n=4,876**)			0.97 (0.64; 1.48)	1.05 (0.55; 1.98)
Yes	29 (23.2%)	1,127 (23.7%)		
No	96 (76.8%)	3,624 (76.3%)		
Time from surgery to oncological treatment within a 100 days median (25% fractal; 75% fractal)	20 (9; 37)	19 (6; 49)	0.97 (0.67; 1.40)	1.03 (0.60; 1.76)

*Adjusted for age, tumor stage, year of surgery, socio-economic class, BMI, ECOG-PS, smoking, alcohol consumption and level of education

Table 4: Distribution of treatment by psychiatric disorder status for patients with *cervix cancer* and risk estimates from logistic regression analyses (and chance of receiving oncological treatment) and Cox regression analyses (days from surgery to first oncological treatment)

Cervix cancer	With psychiatric disorder	Without psychiatric disorder	Crude OR/HR (95% CI)	Adjusted OR/HR (95%CI)*
Oncological treatment within a 30 days after surgery (**n=1,143**)			0.38 (0.09; 1.63)	0.20 (0.03; 1.54)
Yes	2(6.5%)	169 (15.2%)		
No	29 (93.6%)	943 (84.8%)		
Oncological treatment within a 100 days after surgery (**n=1,112**)			0.46 (0.16; 1.34)	0.40 (0.12; 1.36)
Yes	4 (12.9%)	262 (24.2%)		
No	27 (87.1%)	819 (75.8%)		
Time from surgery to oncological treatment within a 100 days median (25% fractal; 75% fractal)	27 (10; 54.5)	17 (6; 52)	0.49 (0.18; 1.33)	0.42 (0.14; 1.35)

*Adjusted for age, tumor stage, year of surgery, socio-economic class, BMI, ECOG-PS, smoking, alcohol consumption and level of education

Figure 1. Kaplan-Meier estimates for chemotherapy within 100 days after surgery, by psychiatric groups
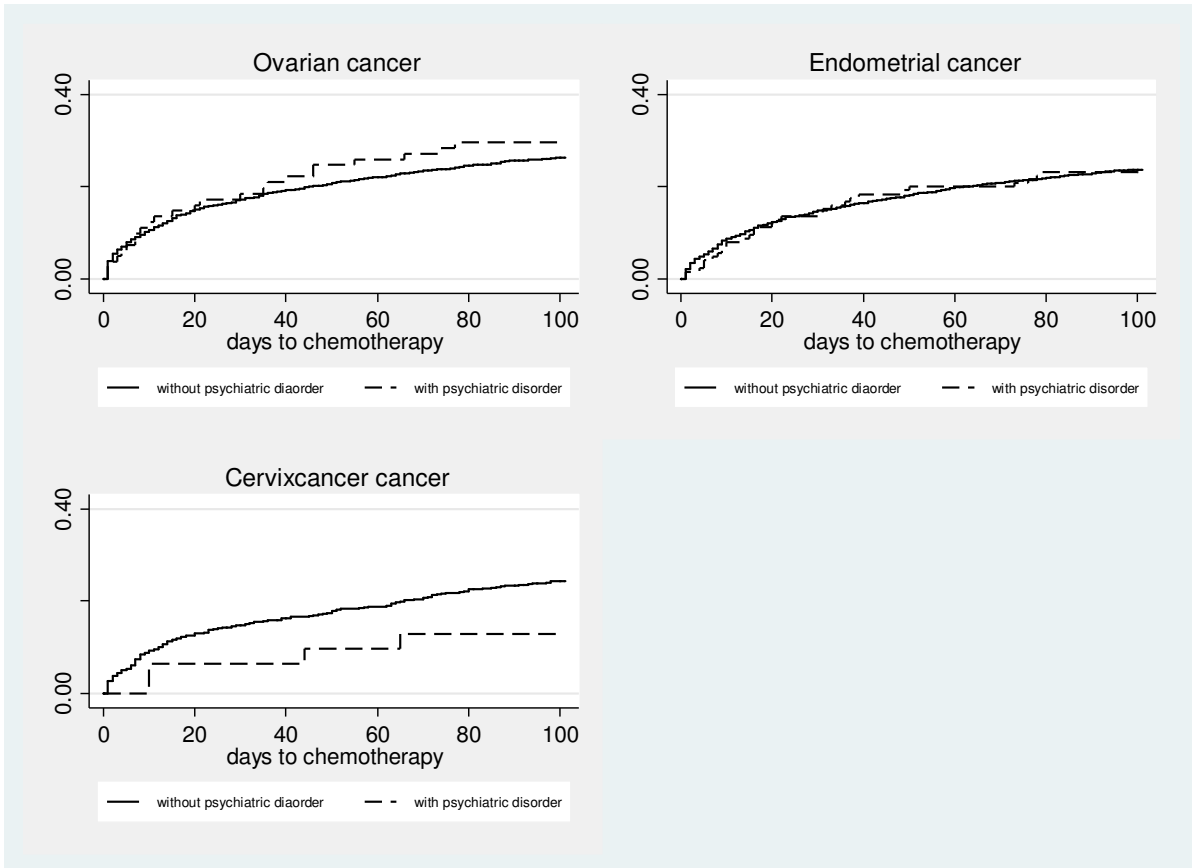
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