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How many patients enter endometrial cancer surgery with psychotropic medication prescriptions, and how many receive a new prescription perioperatively?

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HIGHLIGHTS

- One in eight patients already had psychotropic medications prescribed before surgery for early stage endometrial cancer.
- Previous history of cancers increases the odds for psychotropic medications is a novel finding of this study.
- Multiple comorbidities are associated with increasing prevalence of prescription of psychotropic medications.

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ABSTRACT

Objective. Psychotropic medications including antidepressants and anxiolytics are used to treat anxiety and depression in cancer patients; however, little is known about the prescription practices in endometrial cancer. This study aimed to determine the prevalence, type, dose, frequency and timing of psychotropic medications prescribed to endometrial cancer patients. A secondary aim was to study sociodemographic and clinical characteristics associated with receiving a psychotropic medication prescription.

Methods. Secondary data analysis of an international, multicentre, prospective randomised controlled trial was conducted. Patients aged >18 years diagnosed with Stage I endometrial cancer were included. Logistic regression models were fitted to estimate the association of receiving psychotropic medications with patient's socio-demographic and clinical characteristics.

Results. The overall prevalence of patients prescribed one or more psychotropic medications was 16.8% (n = 121/719) comprising antidepressants (12.6%, n = 91/719) and anxiolytics (5.8%, n = 42/719). The majority of patients (78.1%, n = 71/91) were already receiving antidepressants before cancer diagnosis, the remaining medications were newly prescribed perioperatively (21.9%, n = 20/91). Patients of younger age (18–50 years, OR (Odds Ratio): 2.61), who had hypertension (OR: 0.61), history of a previous cancer (OR: 1.96), and ≥2 comorbidities (2–3, OR: 2.97; 4–5, OR: 7.85; ≥6, OR: 9.13) were significantly ($p < 0.05$) more likely to receive a prescription of psychotropic medications.

Conclusions. While one in eight patients already had psychotropic medications prescribed before surgery for early stage endometrial cancer, only few women received a new prescription after surgery. The overall prescription rates were similar to other patients with cancer, but higher than those observed in the general population, likely reflecting the comorbidity burden of patients who develop endometrial cancer. Qualitative data could be used in future research to explore the psychological and quality of life impacts of endometrial cancer.

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1. Introduction

Endometrial cancer is the most commonly diagnosed gynaecological cancer in developed countries [1]. Globally, the incidence rate of endometrial cancer is higher in more developed regions (13.0/100,000) such as Northern America, Europe and Australia compared to less developed regions (5.9/100,000) such as Africa [2]. The majority of cases (>90%) are diagnosed in women 50 years or older and surgery is the primary treatment for early stage cancer [3,4]. Overweight or obesity is the main risk factor for endometrial cancer [5]. Compared with other gynaecological cancers, women diagnosed with endometrial cancer often present with multiple chronic comorbid conditions, such as diabetes, hypertension or arthritis [6]. After a diagnosis of cancer, many patients experience anxiety or depression which may continue throughout the cancer survival period [7]. Anxiety and depression has been reported to be the third prioritised problem after worry and focusing on getting well in patients with endometrial cancer [8]. Using the Hospital Anxiety and Depression Anxiety sub-scales, it has been reported that before surgery, patients more commonly experience symptoms of anxiety (19.5%, n = 25/132) than depression [9]. Symptoms of anxiety and depression continue for many women beyond the period of primary treatment of endometrial cancer [9,10].

Psychotropic medications such as antidepressants and anxiolytics are recommended for the treatment of moderate to severe anxiety or depression [11]. Across the world, the current prescription prevalence rate of antidepressants to patients with cancer more broadly is 15.6%, with a higher prevalence of prescribing observed in female patients and patients with breast cancer (22.0%) [12]. Fortuny et al., 2009 [13] found in the United States of America that within the first year after an endometrial cancer diagnosis the prevalence of antidepressant prescriptions (Serotonin selective reuptake inhibitors only) and anxiolytics (Benzodiazepines only) was 10.2% (n = 48/469) and 5.1% (n = 24/469), respectively. Recently, Lin et al., 2016 [14] specifically focused on antidepressant prescriptions among a nationwide endometrial cancer population in Taiwan and found that 19.2% (n = 1612/8392) of patients were prescribed an antidepressant. However, these studies aimed to assess if medications increased the risk of developing endometrial cancer; and provided little information about the details of the prescription characteristics, such as type or timing of prescriptions relative to the endometrial cancer diagnosis. Given the reported high prevalence of psychological distress in patients with endometrial cancer, more details about the patterns of psychotropic medication prescribing including overall prevalence, reasons for prescription, time of initiation of medications, and details of prescription characteristics are needed. There is also a lack of research focusing on sociodemographic and clinical characteristics associated with the prescription of psychotropic medications. Many prevalence studies combine gynaecological cancers and remain unfocused on individual tumour types or stage of disease.

To address these gaps, we conducted a secondary analysis of data from a large prospective clinical trial that enrolled patients diagnosed with stage 1 endometrial cancer to determine- 1) the prevalence and characteristics of psychotropic medications prescribed to patients with endometrial cancer; and 2) sociodemographic and clinical characteristics associated with receiving a psychotropic medication prescription.

2. Methods

2.1. Site and timeline

Data were extracted from an international, multicentre prospective randomised controlled trial (The Laparoscopic Approach to Cancer of the Endometrium (LACE) trial; ClinicalTrials.gov: NCT00096408; Australian New Zealand Clinical Trials Registry: CTRN12606000261516). LACE commenced in October 7, 2005 and recruited to June 30, 2010, then followed patients for 4.5 years. Patients diagnosed with endometrial cancer were enrolled from 20 tertiary gynaecological oncology centres in Australia, New Zealand, Scotland and Hong Kong [15]. Data used for these secondary analyses were collected in detail during the pre and perioperative period and then one-week, four-week, three-month and six-month postoperatively.

2.2. Patient recruitment

The details of recruitment were described elsewhere [15,16].

Briefly, women were eligible to enrol, if they were 18 years or older, had histologically confirmed endometrioid adenocarcinoma of the endometrium of any grade, an Eastern Cooperative Oncology Group score of less than one/two, and imaging studies (computed tomography, CT) of the abdomen and pelvis and chest radiograph or chest CT suggesting the absence of extrauterine disease. Patients were excluded if they had histological cell type other than endometrioid on curettage, clinically advanced disease (stage II–IV).

Overall 760 women were recruited for the clinical trial and underwent either total abdominal or total laparoscopic hysterectomy surgery. For this secondary analysis, patients were eligible if sociodemographic and clinical characteristics as well as information on psychotropic medication prescriptions were available.

2.3. Sociodemographic and clinical characteristics

The following sociodemographic characteristics were collected: age, height and weight, education, employment, employment location, marital status, insurance, birth country and ethnicity. Body mass index (BMI) was calculated and grouped according to World Health Organisation (WHO) using weight and height data [17]. Clinical characteristics included hysteroscopy date (used as a proxy for the date of endometrial cancer diagnosis), surgical stage of cancer, perioperative medical history of comorbidities (hypertension, obesity, diabetes, gastro-oesophageal reflux disease (GORD), arthritis, asthma, hyperlipidaemia/hypercholesterolemia), number of comorbidities, previously diagnosed cancer type and number, comorbidity and new cases of anxiety and depression, types of surgery (total abdominal or total laparoscopic hysterectomy), and adjuvant treatment (radiotherapy and/or chemotherapy).

2.4. Details of medication data collection

Antidepressants and anxiolytics (name, dose, frequency, unit, start date and end date of prescription) were recorded by the trial nurse at pre, peri, and post-operative assessments. They were classified using the Anatomical Therapeutic Chemical (ATC) Classification System [18]. This classification system is the gold standard for international drug utilisation research and is maintained by the WHO Collaborating Centre for Drug Statistics Methodology. Anatomical Therapeutic Chemical codes used were: NO5B (anxiolytics) and N06A (antidepressant) [18].

2.5. Statistical analysis

Descriptive statistics were used to determine the prevalence and distribution of dependent and independent variables. Normality for continuous variables was tested and accepted when the mean was within ±10% of the median, skewness and kurtosis coefficients were within ±2 and the histogram was approximately symmetrical and bell-shaped. Univariate logistic regression models were used to determine socio-demographic and clinical characteristics potentially associated with the use of any psychotropic medications (antidepressants and/or anxiolytics) as the dependent variable. The set of variables showing statistically significant ($p < 0.05$) associations with the use of psychotropic medications were then tested in multivariable logistic regression models using backward model selection for their independent contribution [19]. Results are presented as odds ratio (OR) with corresponding 95% confidence intervals (CIs) for both univariate and multivariable analyses. All analyses were performed SPSS software version 23.0.

3. Results

3.1. Patients characteristics

Sociodemographic and clinical characteristics of the 719 patients included in these analyses are presented in Table 1. The mean age of patients was 62.7 (range from 31 to 93). Only 13.1% (n = 91/696) had a BMI of ≤25 kg/m^2 (normal category), the remaining patients (86.9%, n = 605/696) were overweight or obese. Half of the patients (49.9%, n = 359/719) completed senior high school or less, over 60% (n = 440/719) were retired. Less than one-third of patients were employed full time or part-time/casual (27.1%, n = 195/719) and held private health insurance (26.6%, n = 191/719). The majority of patients were born in Australia (65.1%, n = 468/719) and were of European ancestry (75.2%, n = 541/719).

Many patients (89.3%, n = 626/701) had one or more comorbidity, for example, 52.5% (n = 368/701) had hypertension. Around 10% (n = 66/701) were previously diagnosed with another cancer, about half of these (n = 33/66) with breast or skin cancer (n = 27/66). Overall, 12.9% (n = 93/719) patients had either a medical history (n = 82/93) of anxiety or depression or were new cases diagnosed post-surgery (n = 11/93). Of the 82 patients with a history, most had a diagnosis of depression alone (n = 57/82) or comorbid depression with anxiety (n = 7/82). One-quarter of the patients (n = 185/719) received chemotherapy and/or radiotherapy as adjuvant treatment (Table 1).

3.2. Prescription characteristics of psychotropic medications

Characteristics of the psychotropic medications are presented in Table 2. The overall prevalence of patients with endometrial cancer during the six-month study period of having been prescribed one or more psychotropic medications was 16.8% (Table 2A). A total of 137 prescriptions of psychotropic medications were recorded for 121 patients (Table 2A and B). Among these, the prevalence of patients prescribed with antidepressants and anxiolytics was 12.6% (n = 91/719) and 5.8% (n = 42/719), respectively (Table 2A). Type, dose and change of dose are presented in Supplementary Table S2. Sertraline (n = 20/94) was the most delivered antidepressant prescription followed by venlafaxine (n = 17/94), paroxetine (n = 16/94) and citalopram (n = 13/94). Oxazepam (n = 17/43) was the most prescribed anxiolytic followed by diazepam (n = 15/43) and lorazepam (n = 10/43).

Time point of initial psychotropic medications and their continuation in the timeline of this study are presented in Table 2C and D, respectively. Majority of the patients (n = 71/91) patients were already receiving antidepressant prescriptions before cancer diagnosis, whereas the number (n = 24/42) was higher for anxiolytics during perioperatively (Table 2C). 98/137 of the psychotropic medication prescriptions were continued by patients until 6-month post-surgery. Anxiolytics were more commonly initiated in the early post-operative phase than antidepressants, and half of the anxiolytics prescriptions (n = 22/42) were stopped within the first 6-month post-surgery (Table 2D).

The reasons for the prescription of psychotropic medications and whether or not psychological treatment was also received, are presented in the Table 2E and F, respectively. Overall, 62.8% (n = 76/121) of the patients were prescribed one or more psychotropic medications for the treatment of depression and/or anxiety. Almost the same proportion of antidepressants (n = 29/121) and anxiolytics (n = 28/121) were prescribed to patients without anxiety or depression. Notably, 25 patients with a long medical history (n = 19/25) of anxiety (n = 6/19), depression (n = 11/19) or both (n = 2/19) did not receive psychotropic medications (Table 2E). Only 6% (n = 43/719) of patients visited a psychiatrist, psychologist or other mental health counsellor during the first six months after surgery. The majority of these patients (n = 31/43; 72.1%) only attended one or two sessions with a mental health professional (Table 2F).

Table 1
Sociodemographic and clinical characteristics of the 719 patients diagnosed with endometrial cancer.

Characteristics	n (%)
Age at diagnosis (n = 716) (mean, SD)	62.7, 10.1
18–50	71 (9.9)
51–70	486 (67.9)
71+	159 (22.2)
BMI (n = 696)	
Normal (18.50–24.99)	91 (13.1)
Overweight (25.00–29.99)	162 (23.3)
Obesity class I (30.00–34.99)	155 (22.3)
Obesity class II (35.00–39.99)	134 (19.2)
Obesity class III (≥40)	154 (22.1)
Education	
Did not complete primary school	31 (4.3)
Completed primary school	112 (15.6)
Completed junior/senior high school	359 (49.9)
Trade or technical certificate	86 (12.0)
University or college degree	77 (10.7)
Other[a]	54 (7.5)
Employment	
Employed full-time	97 (13.5)
Employed part-time or casual	98 (13.6)
Home duties/home-carer	133 (18.5)
Retired	304 (42.3)
Other[b]	87 (12.1)
Employment location (n = 698)	
Indoors	434 (62.2)
Outdoors	28 (4.0)
Both indoors and outdoors	236 (33.8)
Marital status	
Married/living together	455 (63.3)
Divorced/separated	106 (14.7)
Widowed	101 (14.0)
Other[c]	57 (7.9)
Insurance[d]	
Yes, cover hospital/extra/other	72 (10)
Yes, cover hospital and extra	119 (16.6)
No	528 (73.4)
Income	
<AUS$40,000	468 (65.1)
AUS$40,001+	165 (22.9)
Not reported	86 (12.0)
Birth country	
Australia	468 (65.1)
Other	251 (34.9)
Ethnicity (n = 718)	
European	541 (75.2)
Indigenous Australian	17 (2.4)
Other[e]	160 (22.3)
Surgical stage (n = 716)	
I	594 (83.0)
II	72 (10.0)
III	44 (6.1)
IV	6 (0.9)
Comorbidities (n = 701)	
Hypertension	368 (52.5)
Hyperlipidaemia/hypercholesterolemia	179 (25.5)
Diabetes	157 (22.4)
Arthritis	124 (17.7)
Obesity	112 (16)
Asthma	94 (13.4)
GORD	84 (12.0)
Number comorbidities (n = 701)	
Nil	75 (10.4)
1	140 (19.5)
2	147 (20.4)
3	128 (17.8)
4	87 (12.1)
5	62 (8.6)
6	31 (4.3)
7	16 (2.2)
≥8	15 (2.0)
History of previous cancer	66 (9.2)
Single	62 (8.9)
Two or more	4 (0.6)
Previously diagnosed cancer type	

Table 1 (*continued*)

Characteristics	n (%)
Breast	33 (4.6)
Skin	27 (3.7)
Blood and renal each	6 (0.8)
Other[f]	4 (0.5)
Anxiety & depression	93 (12.9)
Before diagnosis of cancer	82 (11.4)
Depression	57
Anxiety	18
Anxiety & depression	7
New case after surgery	11 (1.5)
Depression	9
Anxiety	2
Surgery[g] (n = 718)	
Abdominal hysterectomy	327 (45.5)
Laparoscopic hysterectomy	391 (55.5)
Adjuvant treatment	
Chemotherapy	12 (1.7)
Radiotherapy	131 (18.2)
Both	42 (5.8)
No further treatment	534 (74.3)

SD—standard deviation, BMI—Body-mass index, GORD—gastro-oesophageal reflux disease.

[a] Not stated or informed different education level.

[b] Student, unemployed or looking for work, permanently ill/unable to work or other.

[c] Included single/never married or other.

[d] Public insurance is universally available for all Australian citizen and permanent residence.

[e] Included Australian, Asian or other.

[f] Included colorectal, bowel and choriocarcinoma.

[g] One surgery was abandoned.

3.3. Characteristics associated with the prescription of psychotropic medications

Socio-demographic and clinical characteristics associated with the prescription of psychotropic medications are presented in Table 3. Univariate analyses showed that younger age (18–50), having GORD or asthma, ≥2 comorbidities, and having a medical history or being newly diagnosed with anxiety and/or depression were associated with the prescription of psychotropic medications (Table 3). In a mutually adjusted multivariable model (excluding a medical history or new diagnosis of anxiety and/or depression), younger age (18–50 years, OR 2.61), hypertension (OR 0.61), history of previous diagnosed cancer (OR 1.96) and ≥2 comorbidities (2–3, OR 2.97; 4–5, 7.85 and ≥6, 9.13) remained significantly associated ($p < 0.05$) with having a prescription of psychotropic medications (Table 4).

4. Discussion

This large international multicentre study identified that the prevalence of psychotropic medications was 16.8%, comprised of antidepressants (12.6%) and/or anxiolytics (5.8%). This prevalence rate of antidepressants (12.6%) was similar to those reported by previous studies on female patients 12.5% [20], but higher than the 10.2% observed in a study in endometrial cancer patients that focused on SSRIs only [13]. Conversely, the prevalence of antidepressants was a little lower than in a recent Taiwanese population-based study (19.2%), which collected medication data from prescriptions filled, including all classes of antidepressants [14]. The observed rate of anxiolytics was similar to the 5.1% observed by Fortuny et al. (2009) [13] although that study included benzodiazepines only.

Considering the time of initiation of the psychotropic medication, most prescriptions (77.6%, n = 73/94) of antidepressants were already provided to patients before the diagnosis of endometrial cancer, and few new prescriptions were Initiated peri- (n = 5/94) or post-operatively (n = 16/94) (Table 2C). This is similar to the original Psychosocial Collaborative Oncology Group (PSYCOG) study conducted by Derogatis et al., 1983 [21], which found that only 11% of psychiatric disorders arose after the cancer, with most mental health morbidity having predated the diagnosis. This suggests that either the majority of patients

Table 2
Prescription characteristics of psychotropic medications (n = 719)[a].

A. Overall prevalence of patients prescribed with psychotropic medication from baseline to 6-month post-surgery period

Prevalence of patients with one or more psychotropic medications	121 (16.8%)
Prevalence of AD	91 (12.6%)
Prevalence of AX	42 (5.8%)

B. Number of psychotropic medications prescription

Number of prescriptions (including changed & double prescription)	137
Number of double prescription of AD and/or AX	16
Change of ADs	2
Double ADs or AXs	2
Both ADs & AXs	12

C. Time-point of initial psychotropic medication prescription

Number of patient	Before diagnosis of endometrial cancer	Perioperative	Post-surgery			
			W1	W4	M3	M6
AXs (n = 42)	18	5	14	2	2	1
ADs (n = 91)	71	4	6	4	4	2
Total	89[b]	9	20	6	6	3

D. Continuation of psychotropic medications from perioperative to six-month post-surgery

Prescription	Ongoing	Discontinued	Then recommenced
AD & AX (n = 137)	98	36	3
ADs	78	14[c,d]	2
AXs	20	22[d]	1

E. Reasons for psychotropic medications prescription before diagnosis of endometrial cancer and new cases

Reason	AX[e] (n = 42)	AD[e] (n = 91)	Total (AX & AD)	No AD or AX
Depression	7	49	56	15
Anxiety	5	8	13	8
Anxiety and depression	2	5	7	2
Other than anxiety and depression[f]	28	29	–	–
Total			76	25[g]

F. Psychological treatment (n = 43)

Visited a psychiatrist, psychologist or other mental health counsellor	Number of visits for treatment		
	One visit	Two visits	3 to 12 visits (mean: 6)
Comorbid with anxiety or depression, no AD or AX (n = 2)	1	1	–
Prescribed with ADs and/or AX with anxiety and depression (n = 6)	1	4	1
Prescribed with ADs and/or AXs (n = 6)	2	1	3
No anxiety or depression or AD/AX (n = 22)	8	9	5
Other (n = 7)[h]	3	1	3
Total (n = 43)	15	16	12

AD—antidepressant, AX—anxiolytics, W—week, M—month.

[a] Measurement of each characteristic is presented in the Supplementary Table S1.

[b] Six patients prescribed with both antidepressants and anxiolytics.

[c] Two patients were discontinued due to change of AD and five patients were discontinued after diagnosis of cancer.

[d] Limited duration of prescription (1–4 days) was identified in AD (n = 3/14) and AX (n = 19/22).

[e] 9/42 of AX and 52/91 of AD were prescribed before diagnosis of cancer to treat anxiety and depression.

[f] The most commonly prescribed medications were diazepam, lorazepam, citalopram, venlafaxaine, etc.

[g] 19/25 patients had long medical history of anxiety and/or depression (mean: 5 years) after considering year of endometrial cancer diagnosis and as well as anxiety and/or depression.

[h] Included schizophrenia, delusional/bipolar disorder, etc.

are coping well with their endometrial cancer diagnosis and do not require psychotropic medications, given that the cohort involves patients with early stage disease whose goal of treatment is cure, or that there is an under-recognition and under-treatment of psychological problems. When we assessed the overlap between antidepressant prescriptions with the patients' psychological status as comorbidities, we found that 52 patients had a medical history of anxiety and/or depression (Table 3E). Pre-existing, long-term chronic medical health issues and risk factors of endometrial cancer (such as abnormal uterine bleeding, obesity, menopausal syndrome) may lead to psychological distress and treatment with antidepressants [22–26]. In contrast, 24/42 anxiolytics were newly prescribed after diagnosis of cancer for anxiety and/or depression (Table 2C). This may reflect the fact that anxiolytics are often used for other purposes such as to overcome insomnia or neuropathic pain [27–32].

After matching the comorbid conditions of anxiety and/or depression with psychotropic medications, 25 patients did not receive medication despite having a long-term (2 to 10 years) medical history (n = 19) or being a new case (n = 6) of depression and/or anxiety (Table 2E). This may either reflect a lack of awareness of the symptoms by health care professionals, or that alternative management options are being pursued instead of psychotropic medications. Almost all participants (89.3%, n = 644/719) had one or more comorbidities. Therefore, it is also possible that treatment was focused of the many physical conditions presented by the patients rather than their psychological well-being [33]. Use of secondary data did not allow us to distinguish between the aforementioned potential explanations regarding non-use of medications for depression and/or anxiety. Only 8 patients reported they received psychological treatment for anxiety and/or depression (Table 2F). Recent clinical guidelines for management of depression and anxiety in adult cancer patients [11] emphasise the importance of psychological care for these conditions.

A very short duration (one to four days) of anxiolytic (n = 19/22) or antidepressant (n = 3/14) prescriptions was observed for some patients (Table 2D). This indicates that they may have been prescribed for symptom relief including to treat insomnia [30,31], pain [29–32], nausea or vomiting [27,28] (Table 2D), or that side-effects emerged. Our data shows that 28 anxiolytic (such as diazepam, lorazepam) and 29 antidepressant prescriptions (such as citalopram, venlafaxaine) were received by patients for reasons other than anxiety and depression (Table 2E). Possible indications besides anxiety and depression were identified in a previous study by Stiefel et al., (1990) [34], including to overcome fear of procedure (anxiolytics), or insomnia (antidepressants). Additionally, venlafaxine is considered the safest medication for the treatment of hot flashes [35] and also used to reduce neuropathic pain [36].

Several characteristics were associated with the prescription of psychotropic medications in the multivariable analyses including- 1) age, 2) history of previous cancer and 3) number of comorbidities, while hypertension was associated with lower risk. It is well known that younger patients have more difficulty adjusting to the existential threat of cancer. Alternatively, they may also be more likely or willing to seek help for mental health concerns than older patients [37]. As the population ages, the development of second and third cancers is becoming more common. Our finding that the need for psychotropic medications seems to increase with the number of cancer diagnoses is a novel finding of our study. Multiple cancer diagnoses may increase the complexity of treatment or may overwhelm patients coping ability more than a first diagnosis of cancer does. A further important outcome of this study is the recognition of comorbidities increasing the likelihood of psychiatric disorders occurring. The burden of medical illnesses can take its toll on patients' capacity to cope. Ashbury et al., 2003 [38] showed that patients with breast cancer and comorbid physical disorders had 2.15 higher odds of antidepressant prescriptions. Similar results (≥3 comorbidities, OR: 4.74) were also reported in an international multicentre study with advanced cancer patients [39], but here we confirm importance

Table 3
Univariate analysis of characteristics associated with the prescription of psychotropic medications.

Characteristics	OR (95% CI)	*p* value
Age (n = 716)		
18–50	1.61 (0.81–3.20)	0.17
51–70	0.98 (0.60–1.59)	0.93
71+	1.00	
BMI (n = 696)		
Normal (18.50–24.99)	1.00	
Overweight (25.00–29.99)	1.65 (0.78–3.48)	0.18
Obesity class I (30.00–34.99)	1.14 (0.52–2.49)	0.74
Obesity class II (35.00–39.99)	1.67 (0.77–3.59)	0.19
Obesity class III (≥40)	1.91 (0.91–4.00)	0.08
Education		
Did not complete primary school	1.08 (0.37–3.12)	0.88
Completed primary school	0.98 (0.46–2.08)	0.95
Completed junior or senior high school	0.92 (0.48–1.74)	0.80
Trade or technical certificate	0.80 (0.35–1.83)	0.60
University or college degree	1.00	
Other	0.67 (0.25–1.79)	0.42
Employment		
Employed full-time	1.00	
Employed part-time or casual	0.72 (0.34–1.57)	0.41
Home duties/home-carer	1.14 (0.58–2.25)	0.70
Retired	0.97 (0.53–1.77)	0.92
Other	0.83 (0.37–1.82)	0.63
Employment location (n = 698)		
Indoors	1.21 (0.80–1.83)	0.36
Outdoors only or both	1.00	
Marital status		
Married/living together	1.00	
Divorced/separated	1.02 (0.59–1.78)	0.93
Widowed	0.63 (0.33–1.21)	0.16
Other	1.00 (0.48–2.06)	0.99
Birth country		
Australia	1.00	
Other	1.08 (0.72–1.62)	0.71
Surgical stage (n = 716)		
1	1.00	
≥2	0.91 (0.53–1.55)	0.73
Hypertension		
No	1.00	
Yes	0.94 (0.63–1.39)	0.76
Obesity		
No	1.00	
Yes	1.29 (0.78–2.15)	0.32
Diabetes		
No	1.00	
Yes	1.17 (0.74–1.86)	0.48
Gastro-oesophageal reflux disease		
No	1.00	
Yes	2.46 (1.48–4.11)	0.00
Arthritis		
No	1.00	
Yes	1.26 (0.77–2.06)	0.34
Asthma		
No	1.00	
Yes	1.68 (1.00–2.82)	0.05
Hyperlipidaemia/hypercholesterolemia		
No	1.00	
Yes	1.36 (0.88–2.09)	0.16
Number of comorbidities (n = 701)		
Nil or one	1.00	
2–3	1.92 (1.07–3.44)	0.03
4–5	4.44 (2.44–8.08)	0.00
6 or more	4.83 (2.34–9.98)	0.00
History of previous cancer (n = 701)		
No	1.00	
Yes	1.61 (0.88–2.94)	0.12
Medical history or new cases of anxiety and/or depression (n = 701)		
No	1.00	
Yes	26.44 (15.53–45.01)	0.00
Surgery (n = 718)		
Total abdominal hysterectomy	1.08 (0.73–1.59)	0.70
Total laparoscopic hysterectomy	1.00	
Adjuvant treatment		
No	1.00	
Yes	0.99 (0.63–1.55)	0.97

OR—odds ratio, CI—confidence interval.

of comorbidities in early stage endometrial cancer. Presence of hypertension was associated with 0.61 lower odds prescription of psychotropic medications. Possible explanation may be that the use of beta-blockers and other anti-hypertensive medications has been found to reduce the incidence of anxiety [40].

4.1. Study strengths and limitations

Strengths of this study are its large sample size and detailed record of medications. Limitations include lack of data to identify who prescribed psychotropic medications (i.e. the general practitioner, psychiatrist or oncologist), and what type of psychological treatment was received. Patient-reported medical history and comorbid conditions entered by the study nurse were used to identify the comorbidities of anxiety and depression, rather than through a formal clinical interview. Using data from a surgical clinical trial means that the study includes a relatively homogenous patient population of relatively well patients with early stage cancer and this is a limitation of this study. However, given that over 80% of endometrial cancers are diagnosed at early stages this should still capture the patient experience well.

4.2. Future research

This research found that the prevalence rate of psychotropic medications was high before the diagnosis of endometrial cancer and only few patients were initiated on psychotropic medications after surgery. This suggests that surgical treatment of endometrial cancer is well tolerated psychologically by most women although under-recognition and under-treatment of mental illness post-surgery cannot be excluded. There was some mismatching between prescriptions and noted diagnosis of anxiety or depression, and future research should consider patients' symptom factors to better explain the prescribing or otherwise of psychotropic medications to women treated for endometrial cancer. Qualitative data could be used in future research to explore in greater depth the psychological conditions and life impacts during long survival.

Table 4
Multivariable logistic regression of variables associated with the prescription of psychotropic medications[a].

Characteristics	OR (95% CI)	*p* value
Age		
18–50	2.61 (1.18–5.76)	0.01
51–70	1.30 (0.77–2.20)	0.32
71+	1.00	
Hypertension		
No	1.00	
Yes	0.61 (0.39–0.98)	0.04
History of previous cancer		
No	1.00	
Yes	1.96 (1.01–3.82)	0.04
Number of comorbidities		
Nil or one	1.00	
2–3	2.97 (1.55–5.68)	0.00
4–5	7.85 (3.93–15.67)	0.00
≥6	9.13 (3.97–20.98)	0.00

OR—odds ratio, CI—confidence interval.
[a] Adjusted for all variables in the model excluding medical history or new cases of anxiety and/or depression.

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Conflict of interests

The authors have declared no conflicts of interest.

Author contribution

Conception and design: Saira Sanjida, Monika Janda.
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Critical revision and final approval of manuscript: All authors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2018.11.018.

References

[1] J. Ferlay, I. Soerjomataram, R. Dikshit, S. Eser, C. Mathers, M. Rebelo, et al., Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012, Int. J. Cancer 136 (5) (2015) E359–E386 (2015 Mar 1).
[2] D.W. Cramer, The epidemiology of endometrial and ovarian cancer, Hematol. Oncol. Clin. North Am. 26 (1) (2012 Feb) 1–12.
[3] N. Colombo, E. Preti, F. Landoni, S. Carinelli, A. Colombo, C. Marini, C. Sessa, et al., Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, Ann. Oncol. 22 (6) (Oct 2013) vi35–39.
[4] T.S. Sannes, S.E. Jensen, S.M. Dodd, S.M. Kneipp, S. Garey Smith, S.M. Patidar, et al., Depressive symptoms and cortisol variability prior to surgery for suspected endometrial cancer, Psychoneuroendocrinology 38 (2) (2013 Feb) 241–249.
[5] M.A. Onstad, R.E. Schmandt, K.H. Lu, Addressing the role of obesity in endometrial cancer risk, prevention, and treatment, J. Clin. Oncol. 34 (35) (2016 Dec 10) 4225–4230.
[6] J.W. Wang, L. Sun, J. Li, X.H. Cong, X.F. Chen, Z. Tang, et al., Comorbid chronic diseases and their associations with quality of life among gynecological cancer survivors, BMC Public Health 15 (Sep 25 2015) 965–971.
[7] G.T. Deimling, K.F. Bowman, S. Sterns, L.J. Wagner, B. Kahana, Cancer-related health worries and psychological distress among older adult, long-term cancer survivors, Psychooncology 15 (4) (2006) 306–320 (2006 Apr).
[8] M.M. Jeppesen, O. Mogensen, P. Dehn, P.T. Jensen, Needs and priorities of women with endometrial and cervical cancer, J. Psychosom. Obstet. Gynaecol. 36 (3) (2015) 122–132.
[9] G. Ferrandina, M. Petrillo, G. Mantegna, G. Fuoco, S. Terzano, L. Venditti, et al., Evaluation of quality of life and emotional distress in endometrial cancer patients: a 2-year prospective, longitudinal study, Gynecol. Oncol. 133 (3) (2014) 518–525 (2014 Jun).
[10] I.J. Rowlands, M. Janda, L. McKinnon, P.M. Webb, V.L. Beesley, Australian National Endometrial Cancer Study Group, Prevalence, predictors, and correlates of supportive care needs among women 3–5 years after a diagnosis of endometrial cancer, Support Care Cancer 23 (5) (May 2015) 1205–1214.
[11] P. Butow, M.A. Price, J.M. Shaw, J. Turner, J.M. Clayton, P. Grimison, et al., Clinical pathway for the screening, assessment and management of anxiety and depression in adult cancer patients: Australian guidelines, Psychooncology 24 (2015) 987–1001.
[12] S. Sanjida, M. Janda, D. Kissane, J. Shaw, S.A. Pearson, T. DiSipio, et al., A systematic review and meta-analysis of prescribing practices of antidepressants in cancer patients, Psychooncology 25 (9) (2016 Sep) 1002–1016.
[13] J. Fortuny, C. Sima, S. Bayuga, H. Wilcox, K. Pulick, S. Faulkner, et al., Risk of endometrial cancer in relation to medical conditions and medication use, Cancer Epidemiol. Biomark. Prev. 18 (5) (2009 May) 1448–1456.
[14] C.F. Lin, H.L. Chan, Y.H. Hsieh, H.Y. Liang, W.C. Chiu, K.Y. Huang, et al., Endometrial cancer and antidepressants: A nationwide population-based study, Medicine (Baltimore) 95 (29) (Jul 2016) e4178–e4184.
[15] M. Janda, V. Gebski, L.C. Davies, P. Forder, A. Brand, R. Hogg, et al., Effect of total laparoscopic hysterectomy vs total abdominal hysterectomy on disease-free survival among women with stage I endometrial cancer: a randomized clinical trial, JAMA 317 (12) (2017 Mar 28) 1224–1233.
[16] M. Janda, V. Gebski, P. Forder, D. Jackson, G. Williams, A. Obermair, LACE Trial Committee, Total laparoscopic versus open surgery for stage 1 endometrial cancer:

the LACE randomized controlled trial, Contemp. Clin. Trials 27 (4) (Aug 2006) 353–363.
[17] World Health Organization (WHO), Global database on Body Mass Index, Retrieved from http://apps.who.int/bmi/index.jsp?introPage=intro_3.html 2006, Accessed date: 19 September 2017.
[18] ATC/DDD Index 2017, WHO collaborating centre for drug statistics methodology web site, http://www.whocc.no/atc_ddd_index/ 2015, Accessed date: 15 June 2017.
[19] Z. Bursac, C.H. Gauss, D.K. Williams, D.W. Hosmer, Purposeful selection of variables in logistic regression, Source Code Biol. Med. 3 (2008 Dec 16) 17.
[20] C.G. Ng, M.P.M. Boks, H.M. Smeets, N.Z. Zainal, N.J. de Wit, Prescription patterns for psychotropic drugs in cancer patients; a large population study in the Netherlands, Psycho-Oncology 22 (2013) 762–767.
[21] L.R. Derogatis, G.R. Morrow, J. Fetting, D. Penman, S. Piasetsky, A.M. Schmale, et al., The prevalence of psychiatric disorders among cancer patients, JAMA 249 (6) (1983 Feb 11) 751–757.
[22] L.S. Cohen, C.N. Soares, A.F. Vitonis, M.W. Otto, B.L. Harlow, Risk for new onset of depression during the menopausal transition: the Harvard study of moods and cycles, Arch. Gen. Psychiatry 63 (4) (2006 Apr) 385–390.
[23] P.K. Dalal, M. Agarwal, Postmenopausal syndrome, Indian J. Psychiatry 57 (Suppl. 2) (2015 Jul) S222–S232.
[24] A. Grundy, M. Cotterchio, V.A. Kirsh, N. Kreiger, Associations between anxiety, depression, antidepressant medication, obesity and weight gain among Canadian women, PLoS One 9 (6) (2014 Jun 16), e99780. .
[25] F. Kayhan, H. Alptekin, A. Kayhan, Mood and anxiety disorders in patients with abnormal uterine bleeding, Eur. J. Obstet. Gynecol. Reprod. Biol. 199 (2016 Apr) 192–197.
[26] W.J. Koh, N.R. Abu-Rustum, S. Bean, K. Bradley, S.M. Campos, K.R. Cho, et al., Uterine neoplasms, version 1.2018, NCCN Clinical Practice Guidelines in Oncology, J. Natl. Compr. Cancer Netw. 16 (2) (Feb 2018) 170–199.
[27] P.L. Triozzi, D. Goldstein, J. Laszlo, Contributions of benzodiazepines to cancer therapy, Cancer Investig. 6 (1) (1988) 103–111 (1988).
[28] R.E. Kast, Mirtazapine may be useful in treating nausea and insomnia of cancer chemotherapy, Support Care Cancer 9 (6) (Sep 2001) 469–470.
[29] J.C. Coyne, S.C. Palmer, P.J. Shapiro, R. Thompson, A. DeMichele, Distress, psychiatric morbidity, and prescriptions for psychotropic medication in a breast cancer waiting room sample, Gen. Hosp. Psychiatry 26 (2004) 121–128.
[30] E.S. Cankurtaran, E. Ozalp, H. Soygur, D.I. Akbiyik, L. Turhan, N. Alkis, Mirtazapine improves sleep and lowers anxiety and depression in cancer patients: superiority over imipramine, Support Care Cancer 16 (11) (2008) 1291–1298.
[31] L. Traeger, J.A. Greer, C. Fernandez-Robles, J.S. Temel, W.F. Pirl, Evidence-based treatment of anxiety in patients with cancer, J. Clin. Oncol. 30 (11) (Apr 10 2012) 1197–1205.
[32] M.J. Fisch, F. Zhao, J. Manola, A.H. Miller, W.F. Pirl, L.I. Wagner, Patterns and predictors of antidepressant use in ambulatory cancer patients with common solid tumors, Psycho-Oncology 24 (2015) 523–532.
[33] J. Turner, B. Kelly, Emotional dimensions of chronic disease, West. J. Med. 172 (2) (2000 Feb) 124–128.
[34] F.C. Stiefel, A.B. Kornblith, J.C. Holland, Changes in the prescription patterns of psychotropic drugs for cancer patients during a 10-year period, Cancer 65 (4) (Feb 15 1990) 1048–1053.
[35] C. Stubbs, L. Mattingly, S.A. Crawford, E.A. Wickersham, J.L. Brockhaus, L.H. McCarthy, Do SSRIs and SNRIs reduce the frequency and/or severity of hot flashes in menopausal women, J. Okla. State Med. Assoc. 110 (5) (2017 May) 272–274.
[36] R. Aiyer, R.L. Barkin, A. Bhatia, Treatment of neuropathic pain with venlafaxine: a systematic review, Pain Med. 18 (10) (Oct 1 2017) 1999–2012.
[37] A. Stark, H. Kaduszkiewicz, J. Stein, W. Maier, K. Heser, S. Weyerer, et al., A qualitative study on older primary care patients' perspectives on depression and its treatments - potential barriers to and opportunities for managing depression, BMC Fam. Pract. 19 (1) (2018 Jan 3) 2.
[38] F.D. Ashbury, L. Madlensky, P. Raich, M. Thompson, G. Whitney, K. Hotz, et al., Antidepressant prescribing in community cancer care, Support Care Cancer 11 (2003) 278–285.
[39] E. Janberidze, M.J. Hjermstad, C. Brunelli, J.H. Loge, H.C. Lie, S. Kaasa, et al., Euro impact. The use of antidepressants in patients with advanced cancer—results from an international multicentre study, Psychooncology 23 (10) (2014 Oct) 1096–1102.
[40] S.A. Steenen, A.J. van Wijk, G.J. van der Heijden, R. van Westrhenen, J. de Lange, A. de Jongh, Propranolol for the treatment of anxiety disorders: systematic review and meta-analysis, J. Psychopharmacol. 30 (2) (2016 Feb) 128–139.