Received: 11 February 2018 | Accepted: 9 June 2018

DOI: 10.1111/aogs.13413

ORIGINAL RESEARCH ARTICLE

Use of prescription drugs among women diagnosed with epithelial ovarian cancer in Denmark

Anton Pottegård[1] | Søren Friis[2,3] | Freija Verdoodt[2] | Christian Dehlendorff[2] | Jesper Hallas[1] | Susanne K. Kjær[2,4]

[1]Clinical Pharmacology and Pharmacy, Department of Public Health, University of Southern Denmark, Odense, Denmark

[2]Danish Cancer Society Research Center, Danish Cancer Society, Copenhagen, Denmark

[3]Department of Public Health, University of Copenhagen, Copenhagen, Denmark

[4]Department of Gynecology, Rigshospitalet University Hospital, University of Copenhagen, Copenhagen, Denmark

Correspondence: Anton Pottegård, Clinical Pharmacology and Pharmacy, Department of Public Health, University of Southern Denmark, JB Winsløwsvej 19, 2, 5000 Odense C, Denmark (apottegaard@health.sdu.dk).

Funding information
Freija Verdoodt is funded by the Sapere Aude-program of the Independent Research Fund Denmark (grant 6110-00596B).

Abstract

Introduction: Epithelial ovarian cancer patients often suffer from chronic diseases requiring drug treatment. We assessed temporal patterns of drug use among women with ovarian cancer.

Material and methods: We identified all postmenopausal women with epithelial ovarian cancer in Denmark 2005-2012 and a comparison cohort of age-matched women without cancer. We calculated rates of new drug treatment and total drug use and examined use of new and prevalent drugs before and after diagnosis. Analyses were stratified by histological type and stage of epithelial ovarian cancer.

Results: We identified 2742 patients. The rate of new drug treatment increased from 3 to 5 months before diagnosis and peaked in the first month after diagnosis at 99 new types of drug therapy per 100 individuals (mainly antiemetics, proton-pump inhibitors, hypnotics, and opioids). Although declining, the rate of new drug use remained substantially higher among epithelial ovarian cancer patients than among controls throughout the 3-year postdiagnosis follow-up period. The number of prevalent drugs increased slightly from a median of 4 drugs (interquartile range 2-7) before diagnosis to 5 drugs (interquartile range 2-8) shortly after the diagnosis. The use of preventive drugs decreased only slightly after diagnosis. In stratified analyses, we found limited variation according to histological type, whereas patterns were slightly more pronounced among women with nonlocalized disease compared with localized disease.

Conclusions: Drug use among postmenopausal women with epithelial ovarian cancer was substantial and varied considerably in relation to the time of cancer diagnosis, although only limited changes were seen in the use of preventive medicines.

KEYWORDS
drug utilization, histology, neoplasm staging, ovarian neoplasms, pharmacoepidemiology

1 | INTRODUCTION

Epithelial ovarian cancer (EOC) is typically a disease of elderly women and most often diagnosed in an advanced stage and has a poor prognosis, with an overall 5-year survival around 40%-50%.[1] Elderly EOC patients often suffer from chronic diseases at the time of the diagnosis.[2] Hence, drug use for prophylaxis or treatment of concomitant disease is considerable at diagnosis of EOC.[3] Many EOC patients initiate drug therapy, either as adjuvant therapy to the standard cancer therapy or as part of the clinical workup for the cancer diagnosis. Among patients dying from EOC,

Abbreviations: ATC, anatomic therapeutic chemical; EOC, epithelial ovarian cancer; ICD, International Classification of Diseases.

end-of-life care may involve discontinuation of drugs, except for palliative drug therapy (eg, strong analgesics, steroids, and anxiolytics). Women with EOC are therefore prone to polypharmacy of varying magnitude during the course of the disease and with relation to the prognosis.

Polypharmacy is associated with an increased risk of adverse drug interactions and events,[4] which may affect the quality of care in women with EOC. Further, polypharmacy and discontinuation of concomitant drugs pose substantial challenges for pharmacoepidemiological research aimed at evaluating potential associations with cancer risk or prognosis of commonly used drugs for chronic conditions, eg, aspirin, statins, or metformin, as changes in adherence to these drugs may directly or indirectly influence cancer risk or outcomes.

A comprehensive assessment of drug therapy among EOC patients would provide important guidance for future clinical practice, safety, prognosis, and quality of life for these women, and provide important information for pharmacoepidemiological studies of EOC prognosis. Presently, however, only limited knowledge is available on prevalence, trends, and factors associated with drug use among EOC patients. We therefore aimed to describe drug utilization among postmenopausal women with EOC, with focus on temporal patterns in drug use and consideration of tumor characteristics and clinical stage.

Key Message

Drug use among postmenopausal patients with epithelial ovarian cancer is substantial, with the rate of new drug treatments increased 3-5 months before diagnosis. Only limited changes were seen after diagnosis in use of preventive medicines.

2 | MATERIAL AND METHODS

We obtained data from nationwide Danish health and demographic registries on all women with postmenopausal EOC. Using descriptive statistics, we examined use of prescription drugs preceding and following the EOC diagnosis.

2.1 | Data sources

The nationwide Danish registries hold information for the entire population on demographic parameters and health data, including cancer incidence and use of prescription drugs. Unambiguous linkage between registries can be accomplished using the CPR-number, a unique personal identifier assigned by the Danish Civil Registration System to all residents in Denmark.[5] The Danish Civil Registration System contains information on date of birth and dates of migration and death for all Danish citizens.[5] In the present study, we also obtained data from the Danish Cancer Registry,[6] the Danish National Prescription Registry,[7] and the Danish Patient Registry.[8]

The Danish Cancer Registry[6] offers accurate and almost complete registration of incident cancer in Denmark since 1943. Cancer diagnoses are recorded according to the International Classification of Diseases, version 10 (ICD-10), and the ICD for Oncology (ICD-O-1-3) for details on topography and morphology. Relevant codes for EOC are provided in Appendix S1.

The Danish National Prescription Registry[7] contains data on all prescription drugs dispensed to Danish residents since 1995. The data include the type of drug, date of dispensing, and quantity. The dosing schedule and the indication for prescribing are not available. Drugs are categorized according to the Anatomic Therapeutic Chemical (ATC) index, a hierarchical classification system developed by the World Health Organization.[9]

The Danish National Patient Register[8] contains detailed data on all somatic hospital admissions in Denmark since 1977 and on all outpatient hospital contacts and psychiatric admissions since 1995. Discharge/contact diagnoses are coded according to ICD-8 (1977-1993) and ICD-10 (since 1994).

2.2 | Patient population

We included all women aged ≥ 55 years diagnosed with histologically verified EOC between 2005 and 2012. Women with previous cancer (except non-melanoma skin cancer) were excluded. All patients were followed from 3 years before the EOC diagnosis until date of death, migration, or 3 years after the diagnosis. For each patient using risk set sampling, we randomly selected four women (controls) without cancer at the date of diagnosis of the patient from the general female population with same birth year as the case patients, thereby establishing a cancer-free comparison cohort.

2.3 | Study drugs

We considered drug treatment at the fourth level of the ATC system, corresponding to drug classes, eg, proton-pump inhibitors (ATC A02BC). Prescriptions for antibiotics (ATC J01) were excluded from analysis, as antibiotic therapy is rarely chronic. New (incident) drug treatment was defined as a prescription within a specific drug class, filled by a patient with no previous prescription within the same drug class for the preceding 2 years.

2.4 | Statistical analyses

In analyses of both new and total drug use, we evaluated drug use from 36 months before to 36 months after the date of EOC diagnosis. First, we described the overall incidence rate of treatment initiation with prescription drugs over time within the population of EOC patients. Specifically, we estimated the monthly incidence rate of new drug treatment per 100 persons per 'person-month'. Similar analyses were performed for the cancer-free comparison cohort. We further described total use of prescription drugs by estimating the

total number of unique drug classes used by each patient/control woman within 3-month exposure windows, depicting the distribution of number of drugs used over time (median, 25th and 75th centile, and 10th and 90th centiles).

Second, we described overall trends in exposure to the most commonly used drugs around the time of diagnosis. Specifically, we identified the most used drug classes during the first 6 months after diagnosis and described the proportion of patients using these drugs in 6-month intervals. In this analysis, drug use in each time-interval was defined as at least one prescription within the time-interval.

In secondary analyses, we repeated the analyses stratified by histological type of epithelial cancer (serous, endometrioid, clear cell, and mucinous) and by tumor stage (localized, nonlocalized, unknown).

All analyses were performed using STATA Release 14.2 (StataCorp, College Station, TX, USA).

2.5 | Ethical approval

The Danish Health Data Authority approved the study (approval 2015-57-0008). According to Danish law, ethical approval is not required for registry-based studies.[10]

3 | RESULTS

We identified 4119 women with EOC between 2005 and 2012. After exclusions [post-mortem diagnosis (n = 38), non-epithelial/no histology (n = 338), age < 55 years (n = 760), and previous cancer (n = 241)], the final study population comprised 2742 patients with incident EOC. The median age was 69 years (interquartile range 62-76 years). The majority of patients had serous EOC (59.5%) and about one-half (49.2%) had verified non-localized disease at the time of diagnosis (Table 1).

The analysis of initiation of new drug treatment (Figure 1) showed an increase from 3-5 months before the time of diagnosis, peaking at 99 new drug treatments per 100 individuals during the first month after the diagnosis. Compared with the control women, EOC patients had a consistently higher rate of new drug treatment, which persisted up to 3 years after the diagnosis (Figure S1). In post-hoc exploratory analysis, we identified the most common drug classes driving this increase in new drug therapy among the EOC patients, defined as new drugs initiated in the period from 3 months before the diagnosis to 6 months after the diagnosis (ie, corresponding to the peak observed in Figure 1). This analysis showed that a wide range of drugs contributed, with antiemetics, proton-pump inhibitors, hypnotics, and opioids being the most common (Table 2).

The number of drug classes used by the EOC patients increased in the period immediately following the diagnosis (Figure 2). While the median use only increased slightly, a more noticeably increase was seen for the 75th and 90th percentiles of drug users.

TABLE 1 Baseline characteristics of women with epithelial ovarian cancer in Denmark, diagnosed during 2005-2012

	Patients (n = 2742)
Age (years)	
Median (IQR)	69 (62-76)
55-65	1020 (37.2%)
66-75	971 (35.4%)
> 75	751 (27.4%)
Clinical stage	
Localized	1004 (36.6%)
Nonlocalized	1348 (49.2%)
Unknown	390 (14.2%)
Histology	
Serous	1632 (59.5%)
Mucinous	186 (6.8%)
Endometrioid	321 (11.7%)
Clear cell	107 (3.9%)
Other epithelial	496 (18.1%)

IQR, interquartile range.

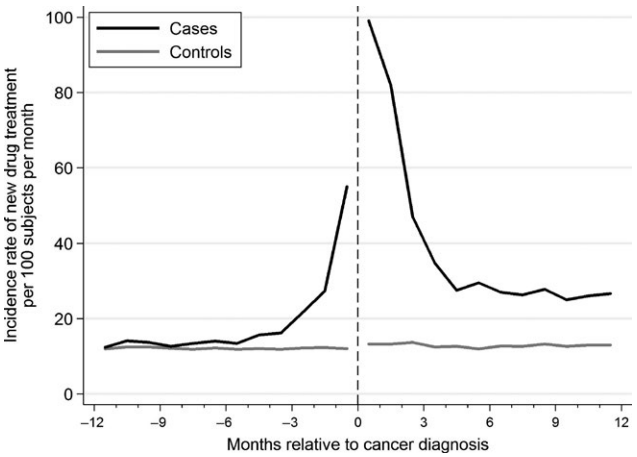

FIGURE 1 The incidence rate of new prescription drug treatment in 1-month intervals within 12 months before to 12 months after epithelial ovarian cancer diagnosis (black) or among age-matched cancer-free women (gray)

The analysis of overall exposure trends of the most commonly used drug classes (top 20 listed in Table 3) showed a marked increase in the use of specific drug classes, including antiemetics and proton-pump inhibitors (in line with the above findings). Most of the drug classes that displayed a peak immediately after the time of diagnosis, however, declined somewhat during the subsequent time intervals. As an example, the prevalence of proton-pump inhibitor use increased from 10% 2 years before diagnosis to 30% immediately after the diagnosis and fell to 24% 2 years after the diagnosis. Similar trends were seen for, eg, antiemetics (1%, 20%, and 7%), opioids (2%, 17%, and 10%), and benzodiazepine-related

TABLE 2 Drug classes initiated among epithelial ovarian cancer patients between 3 months before and 6 months after the diagnosis, corresponding to the period of highest incidence rate of new drug treatment. The table includes the 20 drug classes with highest absolute differences in proportion of users among cases compared with controls

ATC	Name of drug class[a]	Proportion of cases (%)	Proportion of controls (%)
A03FA	Propulsives (antiemetics)	24.9	1.2
A02BC	Proton-pump inhibitors	24.3	3.3
N05CF	Benzodiazepine-related drugs (hypnotics)	21.5	1.8
N02AA	Natural opium alkaloids (opioids)	20.6	1.2
N02AX	Other opioids (mainly tramadol)	16.6	3.0
N02BE	Anilides (mainly paracetamol)	16.7	3.3
A06AD	Osmotically acting laxatives	14.0	1.0
N05BA	Benzodiazepine derivatives (hypnotics)	13.5	1.7
J02AC	Triazole derivatives (antimycotics)	10.1	1.0
A06AB	Contact laxatives	9.2	0.7
C03CA	Sulfonamides, plain (high-ceiling diuretics)	9.7	1.6
A12BA	Potassium	8.9	1.5
H02AB	Glucocorticoids	9.6	2.2
N02AB	Phenylpiperidine derivatives (mainly fentanyl)	6.6	0.3
A04AA	Serotonin (5HT3) antagonists (antiemetics)	6.1	0.0
C03DA	Aldosterone antagonists	6.1	0.5
A02AA	Magnesium compounds	5.3	0.6
A07AA	Antibiotics (intestinal anti-infectives)	5.0	0.4
M01AB	Acetic acid derivatives and related substances (nonsteroidal anti-inflammatory drugs)	6.5	2.3
C05AA	Corticosteroids (antihemorroidals)	5.5	1.4

[a]The official WHO name is used, with specification provided in parentheses.

drugs (9%, 30%, and 17%). In contrast, the use of other drug classes, notably statins and certain antihypertensive agents (eg, angiotensin-converting enzyme inhibitors), showed a different pattern, with a smaller increase up to the time of diagnosis, and only a slight decline thereafter. As an example, statins increased from 18% 2 years before the diagnosis to 21% just prior to the diagnosis, and dropped to the same level as 2 years before the diagnosis (17%) in the first period after the diagnosis. Corresponding numbers for angiotensin-converting enzyme inhibitors were 10%, 11%, and 9%. A table similar to Table 3, but with data from 36 months before to 36 months after the diagnosis, and the 50 most commonly used drugs (instead of 20) is provided in Table S1. Of note, use of hormone replacement therapy showed a marked decrease from 17% in the 6 months before the diagnosis to 8% in the 6 months after the diagnosis, and increasing to about 12% thereafter (Table S1).

Secondary analyses stratified by histological type revealed results similar to those of the main analysis, ie, a peak around the time of diagnosis for a number of drugs and a subsequent decline to levels somewhat higher than those before the diagnosis (Table S2A-D). In analyses stratified according to clinical stage, the general pattern of drug use before, around, and after the diagnosis was generally more pronounced among EOC patients with non-localized disease compared with localized disease. This included a larger spike in the rate of new drug treatment around the time of diagnosis (Figure S2A-C) and a slightly larger drop in the use of preventive drugs after the diagnosis had been established (Table S3A-C).

4 | DISCUSSION

In our nationwide study, we have documented a substantial use of drugs among postmenopausal women with EOC that begins to deviate from age-matched controls within 3-5 months before the time of diagnosis. A spike in new drug treatments, driven by symptomatic drugs such as antiemetics, opioids, and hypnotics, was seen around the time of diagnosis, and the rate of new drug treatment remained increased among patients with EOC compared with controls up to 3 years after the diagnosis. Conversely, the use of prophylactic drugs such as statins and antihypertensive agents dropped only slightly during the 3-year postdiagnosis follow-up period.

An important strength of our study was the nationwide approach, minimizing selection bias and misclassification, and the use of high-quality registry data on cancer incidence[6] and prescription drug use.[7] Some limitations, however, also need to be considered. The primary weakness of our study was the lack of data on complementary and

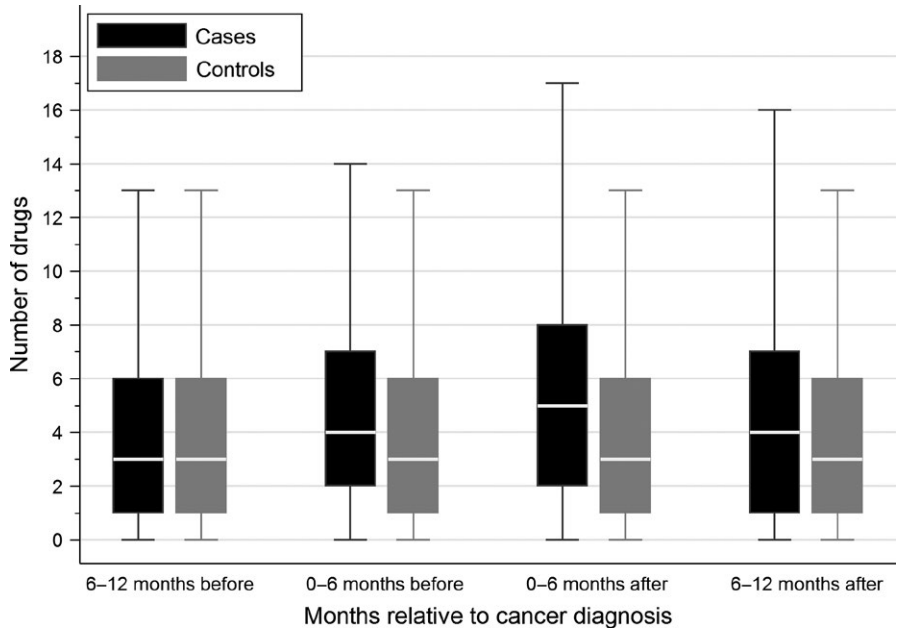

FIGURE 2 The distribution of number of different drug classes used per woman in 6-month intervals (median, 25th and 75th centile, and 10th and 90th centiles) within 12 months before to 12 months after epithelial ovarian cancer diagnosis (black) and among age-matched cancer-free women (gray)

alternative medicines reported to be used by a considerable proportion of patients with cancer,[11-13] as well as over-the-counter medication, which is also frequently used.[14,15] Another limitation was the lack of data on the reasons for discontinuation of drug treatment. Although our staging information allowed some assessment of trends associated with prognosis, more specific proxies such as data on which patients entered palliative care would have allowed for more detailed analyses. Further, we did not have access to prescriber data, ie, whether drug therapy was initiated or managed in primary care or by hospital physicians. Lastly, our analyses did not incorporate data on diagnoses, ie, the underlying reasons for drug treatment.

Our findings have some clinical implications. Our results emphasize that the time of EOC diagnosis was associated with a considerable increase in new drug therapy, largely driven by drugs related to managing symptoms from the cancer or its treatment (antiemetics, proton-pump inhibitors, opioids, mild analgesics etc.) or psychological effects of the establishment of the diagnosis (eg, hypnotics). A different pattern was seen for preventive medications (eg, statins, angiotensin-converting enzyme inhibitors, etc.). While establishment of a diagnosis of a potentially lethal disease can be seen as an opportunity for evaluating if preventive drug therapy should be continued,[4,16,17] we found only very limited changes in the postdiagnosis use of preventive medications. This is in full accordance with previous studies on end-of-life drug use, both among patients with advanced cancer disease[18] and among patients with limited life expectancy in general.[19]

One specific and increasingly recognized issue is the risk of drug-drug interactions, which is of particular concern among cancer patients due to the typical narrow therapeutic index of chemotherapeutic agents.[20,21] Examples of drug-drug interactions with chemotherapeutic agents used in EOC therapy include the interaction between antidepressant drugs and platin-based chemotherapy[22] and the increased toxicity observed among patients receiving paclitaxel with a concomitant use of the common antiplatelet drug clopidogrel.[23,24] However, drug-drug interactions are not the only concern associated with polypharmacy among patients with cancer, as drug-related adverse events are both more common[4] and more often of higher severity among cancer patients compared with other patients.[25]

Our findings also have some important implications for pharmacoepidemiological studies on women with EOC and cancer patients in general. First, the markedly increased use of drugs leading up to the date of the EOC diagnosis infers a risk of reverse causation bias (protopathic bias) in cancer risk studies, ie, that drug use assessed close to the diagnosis may be erroneously associated with an increased cancer risk, when in fact the drug use was caused by an as yet undiagnosed cancer. However, as shown in our previous study,[26] a average lag-time of 6 months seems sufficient to avoid such bias. Studies on cancer prognosis is another increasingly common but inherently difficult[27-29] pharmacoepidemiological discipline. As illustrated by our study, drug use around the time of an EOC diagnosis cannot be perceived as a random event. Rather, new drug use after the diagnosis is, for the majority, closely related to cancer symptoms and use of preventive medicines around and after the cancer diagnosis is governed by increased medical surveillance, prediagnosis comorbidity, and, to some extent, cancer prognosis. As such, comparison of cancer survival among users vs nonusers of a certain drug after the EOC diagnosis may be confounded by (the typically incompletely assessed) baseline prognosis, and careful evaluation of the influence of temporal exposure patterns in relation to the time of diagnosis on the studied association is warranted.

TABLE 3 Use of the 20 most commonly used prescription drugs, defined by their prevalence of use in the 6-month period immediately after diagnosis, in 6-month intervals from 24 months before to 24 months after epithelial ovarian cancer diagnosis. Sorted by ATC code

		Time relative to epithelial ovarian cancer diagnosis							
		Months before diagnosis				Months following diagnosis			
ATC	Name of drug class[a]	24 to 18 (n = 2742)	18 to 12 (n = 2742)	12 to 6 (n = 2742)	6 to 0 (n = 2742)	0 to 6 (n = 2243)	6 to 12 (n = 1969)	12 to 18 (n = 1731)	18 to 24 (n = 1557)
A02BC	Proton-pump inhibitors	10%	11%	12%	22%	30%	24%	23%	24%
A03FA	Propulsives (antiemetics)	1%	1%	1%	8%	20%	7%	6%	7%
A06AD	Osmotically acting laxatives	1%	1%	1%	4%	11%	7%	6%	7%
A12BA	Potassium	6%	7%	7%	9%	13%	10%	10%	10%
B01AC	Platelet aggregation inhibitors excluding heparin	17%	17%	18%	19%	16%	15%	16%	16%
C03AB	Thiazides and potassium in combination	15%	15%	15%	16%	15%	13%	14%	13%
C03CA	Sulfonamides, plain (high-ceiling diuretics)	7%	7%	7%	11%	13%	10%	9%	9%
C07AB	Beta-blocking agents, selective	11%	12%	12%	12%	13%	12%	12%	11%
C08CA	Dihydropyridine derivatives (calcium-channel blockers)	11%	11%	12%	13%	11%	12%	11%	13%
C09AA	Angiotensin-converting enzyme inhibitors, plain	10%	10%	11%	11%	9%	9%	9%	9%
C10AA	HMG CoA reductase inhibitors (statins)	18%	19%	20%	21%	17%	17%	18%	18%
H02AB	Glucocorticoids	4%	4%	4%	5%	9%	7%	7%	8%
J02AC	Triazole derivatives (antimycotics)	1%	1%	1%	2%	10%	5%	5%	4%
M01AE	Propionic acid derivatives (mainly ibuprofen)	9%	10%	9%	10%	12%	10%	9%	9%
N02AA	Natural opium alkaloids (opioids)	2%	1%	2%	6%	17%	10%	9%	10%
N02AX	Other opioids (mainly tramadol)	7%	7%	6%	12%	18%	11%	10%	10%
N02BE	Anilides (mainly paracetamol)	13%	13%	15%	18%	28%	20%	20%	23%
N05BA	Benzodiazepine derivatives (hypnotics)	9%	9%	9%	14%	19%	14%	13%	13%
N05CF	Benzodiazepine-related drugs (hypnotics)	9%	9%	9%	15%	30%	18%	16%	17%
N06AB	Selective serotonin reuptake inhibitors	7%	7%	7%	8%	10%	10%	10%	10%

[a]The official WHO name is used, with specification provided in parentheses.

In conclusion, we have shown that drug use is frequent among postmenopausal women with EOC, with a considerable increase of new drug therapy around the time of the cancer diagnosis but only limited changes in the use of preventive medicines following the EOC diagnosis.

ACKNOWLEDGMENTS

Martin T. Ernst (University of Southern Denmark) is acknowledged for valuable help with data management.

CONFLICTS OF INTEREST

The authors report no conflicts of interest.

ORCID

Anton Pottegård http://orcid.org/0000-0001-9314-5679

Freija Verdoodt http://orcid.org/0000-0002-8243-697X

Jesper Hallas http://orcid.org/0000-0002-8097-8708

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. *Cancer J Clin*. 2017;67:7-30.
2. Tetsche MS, Dethlefsen C, Pedersen L, et al. The impact of comorbidity and stage on ovarian cancer mortality: a nationwide Danish cohort study. *BMC Cancer*. 2008;8:31.
3. Verdoodt F, Kjaer Hansen M, Kjaer SK, et al. Statin use and mortality among ovarian cancer patients: a population-based cohort study. *Int J Cancer*. 2017;141:279-286.
4. Lees J, Chan A. Polypharmacy in elderly patients with cancer: clinical implications and management. *Lancet Oncol*. 2011;12:1249-1257.
5. Schmidt M, Pedersen L, Sørensen HT. The Danish Civil Registration System as a tool in epidemiology. *Eur J Epidemiol*. 2014;29:541-549.
6. Gjerstorff ML. The Danish Cancer Registry. *Scand J Public Health*. 2011;39:42-45.
7. Pottegård A, Schmidt SAJ, Wallach-Kildemoes H, Sørensen HT, Hallas J, Schmidt M. Data resource profile: The Danish National Prescription Registry. *Int J Epidemiol*. 2017;46:798-798f.
8. Schmidt M, Schmidt SAJ, Sandegaard JL, Ehrenstein V, Pedersen L, Sørensen HT. The Danish National Patient Registry: a review of content, data quality, and research potential. *Clin Epidemiol*. 2015;7:449-490.
9. WHO Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC Classification and DDD Assignment 2016*. Oslo, Norway: WHO; 2016.
10. Thygesen LC, Daasnes C, Thaulow I, Brønnum-Hansen H. Introduction to Danish (nationwide) registers on health and social issues: structure, access, legislation, and archiving. *Scand J Public Health*. 2011;39:12-16.
11. Posadzki P, Watson L, Alotaibi A, Ernst E. Prevalence of complementary and alternative medicine-use by UK cancer patients: a systematic review of surveys. *J Integr Oncol*. 2012;1:102.
12. Fremd C, Hack CC, Schneeweiss A, et al. Use of complementary and integrative medicine among German breast cancer patients: predictors and implications for patient care within the PRAEGNANT study network. *Arch Gynecol Obstet*. 2017;295:1239-1245.
13. Berretta M, Della Pepa C, Tralongo P, et al. Use of complementary and alternative medicine (CAM) in cancer patients: an Italian multicenter survey. *Oncotarget*. 2017;8:24401-24414.
14. Hanigan MH, Dela Cruz BL, Thompson DM, Farmer KC, Medina PJ. Use of prescription and nonprescription medications and supplements by cancer patients during chemotherapy: questionnaire validation. *J Oncol Pharm Pract*. 2008;14:123-130.
15. Maggiore RJ, Gross CP, Hurria A. Polypharmacy in older adults with cancer. *Oncologist*. 2010;15:507-522.
16. Lord S, Hall PS, Seymour MT. Concomitant medications in cancer patients: should we be more active in their management? *Ann Oncol*. 2010;21:430.
17. Todd A, Husband A, Andrew I, Pearson SA, Lindsey L, Holmes H. Inappropriate prescribing of preventative medication in patients with life-limiting illness: a systematic review. *BMJ Support Palliat Care*. 2017;7:113-121.
18. Cashman J, Wright J, Ring A. The treatment of co-morbidities in older patients with metastatic cancer. *Support Care Cancer*. 2010;18:651-655.
19. Poudel A, Yates P, Rowett D, Nissen LM. Use of preventive medication in patients with limited life expectancy: a systematic review. *J Pain Symptom Manage*. 2017;53:1097-1110.e1.
20. Scripture CD, Figg WD. Drug interactions in cancer therapy. *Nat Rev Cancer*. 2006;6:546-558.
21. Riechelmann RP, Del Giglio A. Drug interactions in oncology: how common are they? *Ann Oncol*. 2009;20:1907-1912.
22. Engelmann BJ, Ryan JJ, Farrell NP. Antidepressants and platinum drugs. *Anticancer Res*. 2014;34:509-516.
23. Bergmann TK, Filppula AM, Launiainen T, Nielsen F, Backman J, Brosen K. Neurotoxicity and low paclitaxel clearance associated with concomitant clopidogrel therapy in a 60-year-old Caucasian woman with ovarian carcinoma. *Br J Clin Pharmacol*. 2016;81:313-315.
24. Agergaard K, Mau-Sørensen M, Stage TB, et al. Clopidogrel-paclitaxel drug-drug interaction: a pharmacoepidemiologic study. *Clin Pharmacol Ther*. 2017;102:547-553.
25. Puts MTE, Costa-Lima B, Monette J, et al. Medication problems in older, newly diagnosed cancer patients in Canada: how common are they? A prospective pilot study. *Drugs Aging*. 2009;26:519-536.
26. Pottegård A, Hallas J. New use of prescription drugs prior to a cancer diagnosis. *Pharmacoepidemiol Drug Saf*. 2017;26:223-227.
27. Suissa S. Randomized trials built on sand: examples from COPD, hormone therapy, and cancer. *Rambam Maimonides Med J*. 2012;3:e0014.
28. Weberpals J, Jansen L, Carr PR, Hoffmeister M, Brenner H. Beta blockers and cancer prognosis – The role of immortal time bias: a systematic review and meta-analysis. *Cancer Treat Rev*. 2016;47:1-11.
29. Weberpals J, Jansen L, van Herk-Sukel MPP, et al. Immortal time bias in pharmacoepidemiological studies on cancer patient survival: empirical illustration for beta-blocker use in four cancers with different prognosis. *Eur J Epidemiol*. 2017;32:1019-1031.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Pottegård A, Friis S, Verdoodt F, Dehlendorff C, Hallas J, Kjær SK. Use of prescription drugs among women diagnosed with epithelial ovarian cancer in Denmark. *Acta Obstet Gynecol Scand*. 2018;00:1–7. https://doi.org/10.1111/aogs.13413