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*Published in:*  
Gynecologic Oncology

*DOI:*  
[10.1016/j.ygyno.2022.04.017](https://doi.org/10.1016/j.ygyno.2022.04.017)

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*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2022

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Broekman, K. E., van der Aa, M. A., Nijman, H. W., Jalving, M., & Reyners, A. K. L. (2022). End-of-life care for patients with advanced ovarian cancer in the Netherlands: A retrospective registry-based analysis. *Gynecologic Oncology*, 166(1), 148-153. <https://doi.org/10.1016/j.ygyno.2022.04.017>

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Contents lists available at ScienceDirect

## Gynecologic Oncology

journal homepage: [www.elsevier.com/locate/ygyno](http://www.elsevier.com/locate/ygyno)

## Research Paper

## End-of-life care for patients with advanced ovarian cancer in the Netherlands: A retrospective registry-based analysis

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## HIGHLIGHTS

- Medical care use near end-of-life was analysed for 1775 ovarian cancer patients.
- The study reports the lowest percentages of five indicators of aggressive care.
- During the last 6 months of life, half of the patients were admitted to hospital.
- Chemotherapy use near the end-of-life was infrequent: 12% in the last month.
- Surgery and ICU admissions in the final 6 months of life were rare (<10%).

## ARTICLE INFO

## Article history:

Received 3 March 2022

Received in revised form 19 April 2022

Accepted 21 April 2022

Available online 26 May 2022

## Keywords:

End-of-life

Ovarian cancer

Aggressive medical care

## ABSTRACT

**Objective.** Patients with advanced ovarian cancer have a poor prognosis and can experience debilitating symptoms in the last phase of life. Several analyses, mainly performed in the United States (US), show high rates of chemotherapy administration and hospital visits near the end-of-life in this patient category. No large European studies are available, while the organisation of palliative care differs between the US and Europe. We aimed to analyse the intensity of inpatient care near the end-of-life in the Netherlands and perform a cross-study comparison with previous reports.

**Methods.** All patients with ovarian cancer that died in 2016 and 2017 were identified from the Vektis database, a data warehouse including all insurance declarations in the Netherlands. For the last 6 months of life the following parameters of aggressive care were extracted: administration of chemotherapy, emergency room (ER) visits, surgical procedures, hospital and intensive care unit (ICU) admissions. The intensity of inpatient care was compared to previously reported European and US data.

**Results.** Data on medical care use was available for 1775 patients. During the last 6 months of life, half of the ovarian cancer patients were admitted to hospital. Chemotherapy administration near the end-of-life was infrequent: 12% in the last month of life. Surgery and ICU admissions in the final 6 months of life were rare (<10%). Our cohort showed the lowest percentages of all five indicators of aggressive care reported thus far.

**Conclusion.** Aggressive medical care use in the final 6 months of life in this Dutch cohort of ovarian cancer patients was lower than in other previously reported cohorts.

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## 1. Introduction

Patients with ovarian cancer (OC) are usually diagnosed with advanced stage disease, with the majority of women eventually dying of their disease. Ovarian cancer-specific survival at 5 years is 40% for

stage III disease and only 20% for stage IV disease [1]. Patients can experience debilitating symptoms during the last phase of life [2]. Aggressive medical care near the end-of-life, including hospital and intensive care unit (ICU) admissions, is associated with worse patient's quality of life [3].

The US National Quality Forum (NQF) defined indicators of 'aggressive medical care', namely: chemotherapy administration within the last 14 days of life, more than one emergency room (ER) visit in the last 30 days of life, more than one hospital admission in the last 30 days of life, more than 14 days spent admitted to the hospital during

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the last 30 days of life, ICU admission during the last 30 days of life, death in a hospital and hospice admission during the last 3 days of life [4]. The majority of studies on end-of-life care use some or all of these metrics.

Several large registry-based studies from the United States (US) show high rates of medical care in the final months of life in patients with ovarian cancer, including chemotherapy administrations, ER visits, hospital admissions and ICU admissions [5,6]. There is only one, small, retrospective study in which end-of-life care in European patients was analysed. This Italian study included 101 patients, 77% and 38% of patients received chemotherapy in the last three and final month of life, respectively [7]. No European studies reporting ER visits or ICU admissions are available.

In the Netherlands, the general practitioner (GP) has the primary responsibility for palliative care near the end-of-life and there is a network of outpatient palliative care teams which can be consulted for advice [8,9]. This contrasts with the organisation of palliative care in other European countries and the US, where specialised palliative care physicians either in hospital or in outpatient hospices treat symptoms near the end-of-life. In this study, we aimed to analyse the end-of-life care use in a cohort of ovarian cancer patients in the Netherlands (2016–2017) and compared this to previously reported data.

## 2. Methods

### 2.1. Patient selection and data collection

All patients dying with ovarian cancer in 2016 and 2017 were selected from the Vektis database, a data warehouse including all insurance declarations in the Netherlands. The Vektis database includes information on all patients treated in-hospital and is used to calculate

reimbursement of hospitals by the insurance companies and includes data regarding diagnosis and hospital care use (for example diagnostic procedures and treatments). Patients with a diagnosis registered as 'malignancy ovary/tuba' and 'malignancy ovary' in the group of 'gynaecological tumours' were included. For these patients, the following five parameters of 'aggressive medical care' were retrieved: administration of chemotherapy, ER visits, surgical procedures, hospital and ICU admissions. Data were collected for the final 6, 3, 2 and last month of life. Data was available for the total cohort and for three age groups: <60 years, 60–75 years, >75 years. For privacy reasons, data was not extracted at a patient level but as percentages of the total cohort. For the same reason, data was not available if there were < 10 events per represented category. Patient demographics and disease characteristics are not available in the Vektis database. To give a general overview of the characteristics of the population of patients with ovarian cancer in the Netherlands, baseline characteristics for all patients dying with ovarian cancer in 2016 and 2017 were retrieved from the database of the Netherlands Cancer Registry. This database includes the same, but a larger number of patients than the Vektis database, because patients not treated in-hospital are also included in the Netherlands Cancer Registry. Data from the Vektis database and the Netherlands Cancer Registry could not be matched on a patient level. The  $n = 1775$  patients for whom insurance data were available, can therefore be considered a large sample from the entire cohort of ovarian cancer patients from 2016 to 2017 that are included in the Netherlands Cancer Registry ( $n = 2172$ ).

### 2.2. Literature search

A PubMed search was performed in November 2021 using the following MESH terms: 'end of life' AND 'ovarian cancer', yielding 110

**Table 1**  
Inpatient care use near the end-of-life.

	N	6 m	3 m	2 m	1 m
<b>A Chemotherapy</b>					
Age					
<60	350	50.9% (45.6–56.1)	31.7% (26.8–36.6)	22.3% (17.9–26.7)	10.6% (7.4–13.8)
60–75	902	60.8% (57.6–63.9)	41.6% (38.4–44.8)	30.0% (27.1–33.0)	14.2% (11.9–16.5)
>75	523	42.6% (38.4–46.9)	26.2% (22.4–30.0)	18.2% (14.9–21.5)	9.4% (6.9–11.9)
Total (95% CI)	1775	53.5% (51.1–55.8)	35.1% (32.9–37.3)	25.0% (23.0–27.0)	12.1% (10.5–13.6)
<b>B Emergency room visits</b>					
Age					
<60	350	32.3% (27.4–37.2)	24.3% (19.8–28.9)	19.1% (15.0–23.3)	12.0% (8.6–15.4)
60–75	902	31.5% (28.5–34.5)	23.4% (20.6–26.2)	19.7% (17.1–22.3)	12.0% (9.9–14.1)
>75	523	20.8% (17.4–24.3)	14.9% (11.9–18.0)	13.2% (10.3–16.1)	8.4% (6.0–10.8)
Total (95% CI)	1775	28.5% (26.4–30.6)	21.1% (19.2–23.0)	17.7% (15.9–19.5)	10.9% (9.5–12.4)
<b>C Surgery</b>					
Age					
<60	180	13.9% <sup>‡</sup> (8.8–18.9)	6.1% <sup>‡</sup> (2.6–9.6)		
60–75	902	8.2% (6.4–10.0)	5.0% (3.6–6.4)	3.3% (2.2–4.5)	
>75	523	10.7% (8.1–13.4)	5.7% (3.7–7.7)	4.8% (3.0–6.6)	
Total (95% CI)	1605	9.7% (8.2–11.1)	5.4% (4.3–6.5)	3.9% (2.9–4.9)	
<b>D Hospital admissions</b>					
Age					
<60	350	55.1% (49.9–60.4)	40.9% (35.7–46.0)	32.6% (27.7–37.5)	22.6% (18.2–27.0)
60–75	902	51.0% (47.7–54.3)	39.4% (36.2–42.6)	33.9% (30.8–37.0)	24.5% (21.7–27.3)
>75	523	41.3% (37.1–45.5)	28.5% (24.6–32.4)	25.4% (21.7–29.2)	19.3% (15.9–22.7)
Total (95% CI)	1775	49.0% (46.6–51.3)	36.5% (34.2–38.7)	31.2% (29.0–33.3)	22.6% (20.7–24.5)
<b>E ICU admissions</b>					
Age					
<60	180	9.4% <sup>‡</sup> (5.2–13.7)	7.8% <sup>‡</sup> (3.9–11.7)	6.7% <sup>‡</sup> (3.0–10.3)	
60–75	902	7.3% (5.6–9.0)	5.7% (4.2–7.2)	4.9% (3.5–6.3)	4.0% (2.7–5.3)
>75	276	5.8% <sup>‡</sup> (3.0–8.6)	4.4% <sup>‡</sup> (1.9–6.8)	4.0% <sup>‡</sup> (1.7–6.3)	4.0% <sup>‡</sup> (1.7–6.3)
Total (95% CI)	1358	7.3% (5.9–8.7)	5.7% (4.4–6.9)	4.9% (3.8–6.1)	4.0% (2.9–5.1)

If <10 events were recorded no number was available, therefore no summary data is presented. For some variables, data was only available for the cohort of patients that died in 1 year, these variables are marked †. Age categories for which the percentage has a statistically significant difference compared to the other age categories are highlighted with an asterisk. For surgery and ICU-admissions the numbers were too low to perform a comparison between categories.

results. All abstracts were screened by the first author (KEB) and all papers reporting analysis of one or more NQF indicators of aggressive medical care in ovarian cancer patients were retrieved. Review articles were screened for additional relevant studies.

### 2.3. Statistical analysis

Demographic characteristics of the patient cohort were summarised using descriptive statistics. The five parameters of aggressive medical care reported at four different time points were represented as percentages with 95% confidence intervals (CIs). To assess the difference between the age categories, we calculated the mean and standard error of the difference, assuming a normal distribution of the reported percentages so that variances could be computed from the reported 95% CIs and added together. A *p*-value <0.05 was considered statistically significant.

For some age categories for the variables 'surgery' and 'ICU admissions', data were only available for one of the years (i.e. 2016 or 2017) because for the other year the number of events was <10. Therefore, for these categories, only data from 1 year was used to calculate a point estimate and 95% CI for the different time points and compare these between age groups.

## 3. Results

### 3.1. Study cohort

In the Netherlands Cancer Registry, there were 2172 patients dying with ovarian cancer in 2016 and 2017. The available demographic characteristics of this cohort are shown in Supplementary Table 1. Parameters of aggressive medical care were available for 1775 patients from the health insurance records in the Vektis database.

### 3.2. Hospital care use in the last months of life

For the entire cohort, chemotherapy was administered to half of the patients in the final 6 months of life, but only 12% of patients received systemic treatment in the month before death.

Approximately one third of patients visited the ER in the final 6 months of life; and only 11% in the last month of life. Surgery was rarely performed in our cohort of patients: 10% in the final 6 months of life, and only 4% in the final 2 months of life. Data for the last month of life was not available because there were < 10 events per represented category.

Hospital admissions were frequent in the final 6 months of life, with at least one admission in almost half of the patients. Approximately one fifth of the patients were admitted to the hospital during the last month of life. In contrast, admission to the ICU was rare in our patient cohort, with 7% of patients admitted to the ICU in the final 6 months of life. Admissions closer to death, e.g. in the last 1 or 2 months of life, were rare.

The frequency of inpatient care in the final 6, 3, 2 and last month of life is shown in Table 1.

### 3.3. Comparisons between age groups

The rate of chemotherapy administration was highest in patients 60–75 years of age compared to younger or older patients in the final 6, 3 and 2 months of life (see Table 1a). Furthermore, ER visits in the 6 and 3 months before death (see Table 1b) and hospital admissions at 6, 3 and 2 months before death (see Table 1d) were less frequent in patients >75 years of age compared to the younger age groups. For the other variables, there were no statistically significant differences between age groups.

### 3.4. Comparison with literature

Taking into account the reports with comparable definitions for the five parameters of aggressive medical care only, our cohort showed the lowest percentages of all five indicators of aggressive care (Table 2). The frequency of inpatient care use was compared between our cohort and the cohorts described in the literature. The largest absolute difference was seen for hospital admissions and chemotherapy use. Surgical procedures and ICU admissions were rare in our population. Of note, most other studies also included data on parameters of aggressive medical care use in the last 14 days of life, but this data was not available for our cohort. Furthermore, some reports only provided data on emergency room visits and hospital admissions for patients with more than one event.

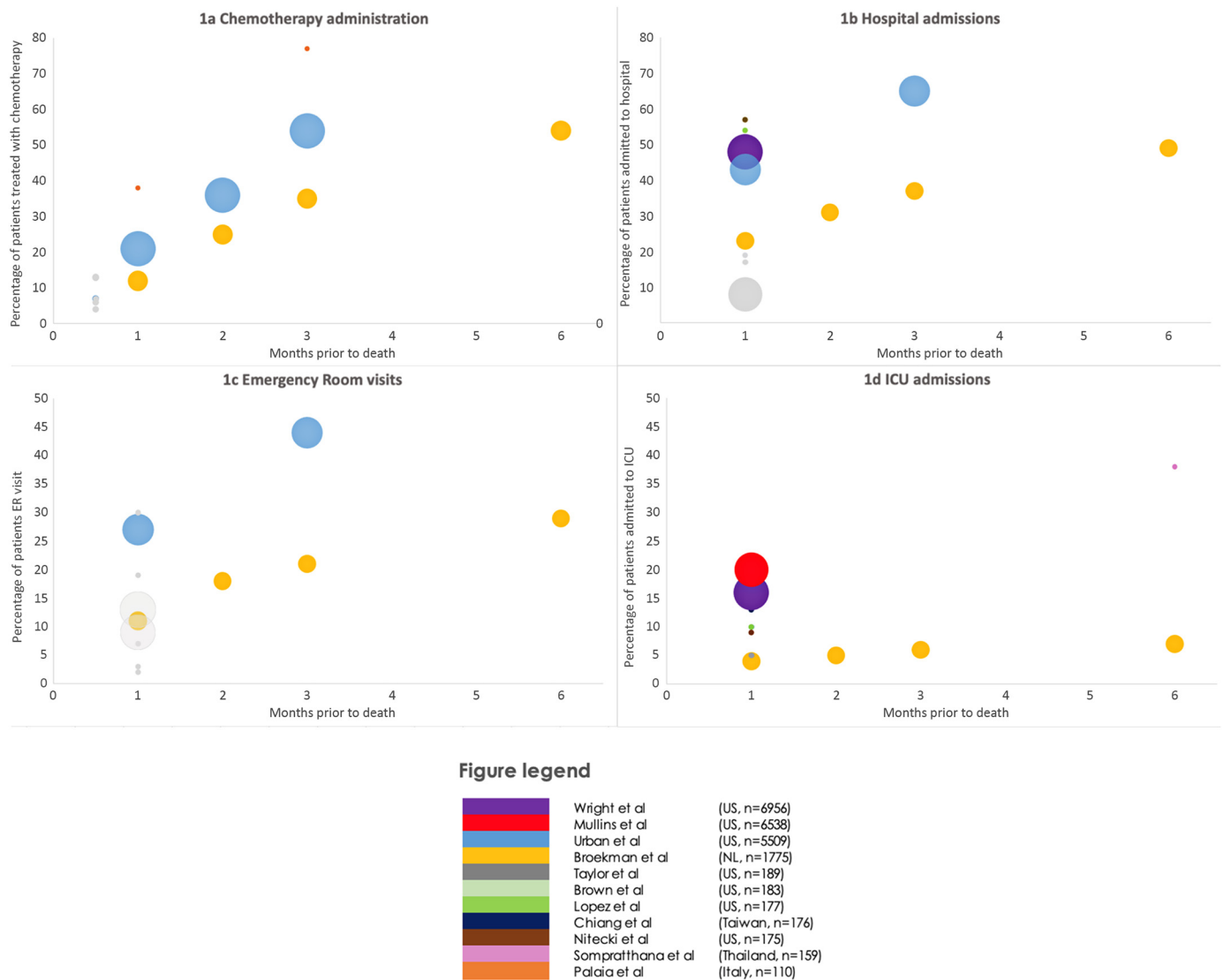
Use of chemotherapy, ER visits, hospital and ICU admissions in the different ovarian cancer patients cohorts from literature are visualised

**Table 2**  
Frequencies of aggressive medical care parameters near the end-of-life from literature.

Study	Country	n	6 m	3 m	2 m	1 m	14d
<b>Chemotherapy</b>							
Palaia	Italy	110		77.0%		38.0%	
Urban	US	5509		53.7%	36.0%	21.2%	
<b>Broekman</b>	<b>Netherlands</b>	<b>1775</b>	<b>53.5%</b>	<b>35.1%</b>	<b>25.0%</b>	<b>12.1%</b>	
Nitecki	US	175					12.6%
Lopez	US	177					7.0%
Brown	US	183					7.0%
Sompratthana	Thailand	159					6.9%
Chiang	Taiwan	176					6.2%
Mullins	US	6538					5.2%
<b>Emergency room visits</b>							
Taylor	US	189					30.0%*
Urban	US	5509		43.9%			27.4%
Brown	US	183					19.0%*
Wright	US	6956					13.0%*
<b>Broekman</b>	<b>Netherlands</b>	<b>1775</b>	<b>28.5%</b>	<b>21.1%</b>	<b>17.7%</b>	<b>10.9%</b>	
Mullins	US	6538					9%*
Nitecki	US	175					6.9%*
Chiang	Taiwan	176					2.8%*
Lopez	US	177					2.0%*
<b>Surgery</b>							
Lopez	US	177					36.0%
Nitecki	US	175		36.0%			
Urban	US	5509		19.3%			10.4%
Sompratthana	Thailand	159	22.6%				
<b>Broekman</b>	<b>Netherlands</b>	<b>1775</b>	<b>9.7%</b>	<b>5.4%</b>	<b>3.9%</b>		
<b>Hospital admissions</b>							
Nitecki	US	175					57.0%
Lopez	US	177					54.0%
Wright	US	6956					47.5%
Urban	US	5509		62.5%			43.2%
<b>Broekman</b>	<b>Netherlands</b>	<b>1775</b>	<b>49.0%</b>	<b>36.5%</b>	<b>31.2%</b>	<b>22.6%</b>	
Chiang	Taiwan	176					19.3%*
Brown	US	183					17.0%*
Taylor	US	189					10.0%*
Mullins	US	6538					7.9%*
<b>ICU admissions</b>							
Sompratthana	Thailand	159	38.4%				
Mullins	US	6538					19.8%
Wright	US	6956					16.0%
Chiang	Taiwan	176					12.5%
Lopez	US	177					10.0%
Brown	US	183					10.0%
Nitecki	US	175					8.6%
Taylor	US	189					5.0%
<b>Broekman</b>	<b>Netherlands</b>	<b>1775</b>	<b>7.3%</b>	<b>5.7%</b>	<b>4.9%</b>	<b>4.0%</b>	

\*more than one visit \*more than one admission.

Bold highlights the results from the current study. Results for studies using slightly different parameters compared to the current study (i.e. frequencies in the final 14 days of life for chemotherapy administration and more than 1 hospital admission or ER visit) are displayed in *italics* and cannot be directly compared to the current results.



**Fig. 1.** Indicators of aggressive medical care near the end-of-life as reported in literature.

Frequency of chemotherapy administration (1a), hospital admission (1b), emergency room visits (1c) and ICU admission (1d) in the final 6, 3, 2 and last month of life as reported in the literature. Each study is depicted by a bubble (for colour codes see figure legend) with its size representing study sample size. Results for studies using slightly different parameters compared to the current study (i.e. frequencies in the final 14 days of life for chemotherapy administration (1a) and more than 1 hospital admission (1b) or ER visit (1c)) are colored light grey and cannot be directly compared to the current results.

in Fig. 1. Data on surgical procedures was not included, because this parameter is not described extensively in the existing literature.

#### 4. Discussion

In this large, retrospective study of patients with ovarian cancer, aggressive medical care use during the last months of life, defined by chemotherapy and surgical treatment, and admission to hospital, the ER or ICU, was low compared to previous reports.

The percentages for chemotherapy use in the last months of life in our cohort are lower than those reported in a large retrospective database study performed in the US including 5509 patients [6]. Several, mainly smaller, studies reported chemotherapy treatment in the last 14 days of life, with percentages varying between 5 and 13% [10–15], whereas it was 12% in the last month of life in our study. In a cohort of 110 Italian patients, a much higher percentage of chemotherapy use in the final 3 and last month of life (77% and 38% respectively) was reported [7]. One in four patients in our cohort was treated with chemotherapy in the last 2 months of life, which might reflect the difficulty in predicting which patients will respond to chemotherapy treatment.

If treatment fails, symptoms usually progress quickly leading to death shortly after cessation of systemic treatment [16].

Almost a quarter of patients were admitted to hospital in the last month of life. This percentage is lower than those previously reported, which ranged from 43% to 57% [6,10]. Approximately 10% of patients visited the ER in the last month of life, which can be considered low. In the only other study reporting the percentage of patients visiting the ER in the last month of life, it was 27.4% [6]. All the other studies only report data on patients requiring more than one ER visit, with percentages ranging from 2 to 30% [11,17]. Although GPs can manage most symptoms at home, these hospital and ER admissions could be for treatment of difficult to manage symptoms, such as drainage for symptomatic ascites, intensified pain management or symptomatic treatment of bowel obstruction [18]. Such hospital visits should not necessarily be considered harmful to patients, but could be part of good collaboration between hospital specialists and the GP [19]. Unfortunately, the reason for ER visits or hospital admissions could not be retrieved from our database.

ICU admissions and surgical procedures were rare in our population. Data on ICU admissions and surgical procedures are scarce in the literature. Reported ICU admissions in the final month of life range from 5 to 20%,

with our percentage being the lowest [15,17]. Only four studies reported data on surgical procedures on any time point in the final 6 months of life, all reporting higher percentages than in our cohort of patients.

There are some limitations to the comparison of our findings to previous analyses. Most other reports on end-of-life care use parameters with slightly different definitions. This complicates a cross study comparison for these parameters. Chemotherapy use is mainly reported for the last 14 days of life, but in our dataset treatment in the final months of life was recorded. Furthermore, our dataset included the percentage of patients with any ER visit, whilst for most studies patients with more than one ER visit were counted. However, our percentage was even lower than half of the studies counting patients with more than one ER visit. A strength of our analysis is that it included an unselected nationwide population, whilst other studies used data from patients selected based on their age, place of death, health insurance or region within a country. It should however be noted that data from insurance records were only available for 1775 patients, while 2172 patients dying with ovarian cancer were included in the Netherlands Cancer Registry in 2016 and 2017. A comparison between the characteristics of these two cohorts could not be made, therefore selection bias cannot be excluded. In addition, information on the disease course, previous therapies and response to treatment was not available. It is likely that end-of-life medical care use, for example chemotherapy, differs between patients with a longer disease course and prolonged responses to systemic treatment and patients with more aggressive disease.

A comparable registry-based analysis of chemotherapy use near the end-of-life in patients with gastroesophageal cancer, also performed in the Netherlands, reported slightly lower percentages of chemotherapy use in the last 3 and last month of life compared to our study [20]. ICU admissions were rare in both patient populations. Prevalence of chemotherapy use near the end-of-life in the gastroesophageal cancer population was also lower in the Netherlands compared to other western countries. Previous studies in other European countries found a higher rate of chemotherapy administration in the last month of life compared to the current analysis in patients with various types of cancer [21], and this finding was confirmed recently in patients with metastatic breast cancer [22]. Cancer treatment in general can be considered more conservative in the Netherlands compared to the US, with not all treatments that are approved by the European Medicines Agency (EMA) automatically being used in clinical practice. Instead, the Dutch Society of Medical Oncology has developed criteria to assess clinical benefit of treatments, which are also used to inform reimbursement policy [23].

The results of our analysis need to be viewed against the background of the palliative care system in the Netherlands, where palliative care at the end-of-life is primarily provided at home by the GP and community nurses [9]. In a registry-based study including all patients dying of cancer in the Netherlands in 2017 ( $n = 44,908$ ), only 17% of patients with cancer died in a hospital and 54% died at home. Of these patients dying at home, 89% received intensive palliative care from their GP in the final 2 weeks of life [24]. In an interview analysis of patients' preferences and values regarding high-quality palliative care at home, a focus on the personal views of the patient and relatives and proactivity of healthcare professionals as well as patients were considered essential elements [25]. Openly discussing end-of-life care was highly valued. A European cross-national survey study showed that the percentage of patients that had discussed end-of-life wishes with their GP was highest in the Netherlands [26]. A survey study of Dutch patients with cancer found that almost all patients rated respect for their autonomy as important [27]. Despite a home-based focus of palliative care, 22.6% of patients were admitted to the hospital in the last month of life in the current analysis. Future studies should focus on the impact of home-based versus hospital interventions on patient's quality of life in this setting. Early initiation of palliative care by a dedicated palliative care team can improve patient's and caregiver's quality of life and reduce (unnecessary) aggressive medical treatment near the end-of-life [3,28]. Uptake of such teams, supporting the GP, could be improved in the Netherlands further

reducing hospital visits near the end-of-life. In a nationwide survey supported by the Dutch Federation of Cancer Patient Organisations (NFK), 37% of patients stated that they did not receive additional care after hearing that their cancer was incurable, and half of these expressed a clear need for this support. Contact with a key person within the hospital, even though their GP was the main health care professional providing treatment, was the most requested type of care [29].

## 5. Conclusion

In conclusion, our analysis shows the lowest reported rate of hospital-based 'aggressive medical care' use near the end-of-life of patients with ovarian cancer. Future studies should evaluate the effect of home-based versus hospital palliative interventions on patients' quality of (end of) life.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ygyno.2022.04.017>.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sector.

## Declaration of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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