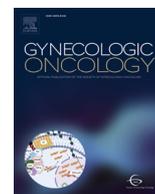




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## Postoperative outcomes of primary and interval cytoreductive surgery for advanced ovarian cancer registered in the Dutch Gynecological Oncology Audit (DGOA)



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### HIGHLIGHTS

- Complications with re-invention were significantly higher in PDS compared to IDS.
- Time to start adjuvant chemotherapy is longer in patients with severe complications.
- Regional variation for severe complications is apparent in the Netherlands

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### ABSTRACT

**Objectives.** The challenge when performing cytoreductive surgery (CRS) is to balance the benefits and risks. The aim of this study was to report short term postoperative morbidity and mortality in relation to surgical outcome in patients undergoing primary debulking surgery (PDS) or interval debulking (IDS) surgery in the Netherlands.

**Methods.** The Dutch Gynecological Oncology Audit (DGOA) was used for retrospective analysis. Patients undergoing PDS or IDS between January 1st, 2015 - December 31st, 2018 were included. Outcome was frequency of postoperative complications. Median time to adjuvant chemotherapy and severity of complications were related to outcome of CRS. Complications with Clavien-Dindo  $\geq 3$  were analyzed per region and case mix corrected. Statistical analysis was performed with R.Studio.

**Results.** 1027 patients with PDS and 1355 patients with IDS were included. Complications with re-invention were significantly higher in PDS compared to IDS (5.7% vs. 3.6%,  $p = 0.048$ ). Complete cytoreduction was 69.7% in PDS and 62.1% IDS,  $p < 0.001$ . Time to adjuvant chemotherapy was 49 days in patients with complete CRS and a complication with re-intervention. Regional variation for severe complications showed one region outside confidence intervals.

**Conclusions.** Higher complete cytoreduction rate in the PDS group indicates that the correct patients have been selected, but is associated with a higher percentage of complication with re-intervention. As result, time to start adjuvant chemotherapy is longer in this group. Maintaining a balance in aggressiveness of surgery and outcome of the surgical procedure with respect to severe complications is underlined. Bench marked data should be discussed nationally to improve this balance.

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## 1. Introduction

The majority of patients with ovarian cancer present with advanced stage disease (FIGO stage IIb-IV) and treatment consists of a combination of cytoreductive surgery (CRS) and (neo)adjuvant chemotherapy (NACT). There is no discussion that removal of all visible disease during CRS provides the best survival outcome for patients [1,2]. Whether primary debulking surgery (PDS) followed by adjuvant chemotherapy is superior to neoadjuvant chemotherapy and interval debulking surgery (IDS) remains subject of continuing debate [3–6]. However, current practice is to perform PDS when findings on pre-operative CT scans predict that complete CRS is feasible. This is based on the fact that the subgroup of patients with complete PDS shows a better survival, and it is unknown whether NACT and IDS is disadvantageous for this specific group [7]. At the same time, complete CRS may only be achievable through more aggressive surgery and the latter may result in a higher complication rates [8]. Factors of influence are the presence of co-morbidity and/or performance status [9].

The challenge in performing CRS therefore is to balance the benefits (obtaining complete cytoreduction) and risks (perioperative complications), especially since delay of adjuvant chemotherapy (more than 42 days) has a negative effect on survival [10]. In addition, a recent systematic review showed a 30-day readmission rate for PDS and IDS ranging from 2.5% to 19.3% with lower percentages for IDS. Although this systematic review also noted small population sizes of some of the studies and not all studies reported the outcome of the cytoreductive surgery, it may indicate that patients undergoing IDS experience fewer postoperative complications [11].

With the aim to improve outcomes for ovarian cancer patients, centralization of surgical care for ovarian cancer patients was implemented in 2012 in The Netherlands [12]. Criteria were set so that only gynecological oncologists could perform cytoreductive surgery in centers performing at least 20 cytoreductive surgeries per year [13]. Nationally, centralization resulted in eight regions consisting of one gynecological center combined with several regional hospitals collaborating in a gynecological network.

To gain insight in the quality of care for patients with a gynecological malignancy, the Dutch Gynecological Oncology Audit (DGOA) was initiated in 2013. By means of this nationwide registration information on surgical outcome and complications of all patients is obtained. Participation in the DGOA is obligatory for all hospitals treating patients with a gynecological malignancy and these centers receive benchmarked feedback on their performance. The aim of this study was to report and compare short term postoperative morbidity and mortality in relation to surgical outcome in patients undergoing PDS or IDS in the eight regions in the Netherlands, with data derived from the DGOA.

## 2. Methods

### 2.1. DGOA

The DGOA is a population based prospective database used for retrospective analysis. The database registers surgical outcomes of four gynecological malignancies: ovarian-, cervical-, endometrial- and vulvar cancer. Data are prospectively collected by the gynecologist or by trained data managers supervised by the gynecologist.

### 2.2. Patients

All patients with advanced ovarian cancer (FIGO IIb-IV) undergoing PDS or IDS between January 1st, 2015 and December 31st, 2018 in the Netherlands and registered in DGOA were included. Patients with a borderline histology were excluded for this analysis.

### 2.3. Procedures

For this study, patients undergoing CRS for ovarian cancer were divided in three categories: patients with single PDS, patients with single IDS and patients with multiple attempted cytoreductive surgeries (MCS). CRS was defined as a procedure with the intention to remove all visible disease including extirpation of the uterus, ovaries and tubes, infracolic and supracolic omentectomy, resection of all macroscopic tumor in the abdomen as well as pathological abdominal retroperitoneal lymph nodes. The result of CRS was defined as: complete CRS (macroscopically no residual tumor), optimal CRS (residual tumor  $\leq 1$  cm largest diameter) and incomplete CRS (residual tumor  $> 1$  cm). IDS is defined as a CRS following at least 3 cycles of neoadjuvant chemotherapy [14].

### 2.4. Outcomes

One outcome of the study was the frequency of postoperative complications registered in the DGOA. The Clavien-Dindo scale was used to define the severity of the complications. Also, 30 day in/out hospital mortality, type of re-interventions, readmissions, length of stay at the Intensive Care Unit (ICU) and complicated course were used. Complicated course was defined as a composite measure capturing all patients with a complication leading to an operative or radiologic re-intervention, admission to the ICU for more than 2 days, prolonged hospital stay and/or 30 day mortality [15]. Prolonged hospital stay was defined as  $\geq 14$  days admission at the hospital. Lastly, median time from CRS to first adjuvant chemotherapy in relation to result of CRS and complications were calculated.

### 2.5. Statistical analysis

Patient and tumor characteristics and postoperative outcomes were described for three groups (PDS, IDS and MCS) using frequencies and percentages. Comparison between PDS and IDS was made with chi-square test. Statistical significance was considered at  $p < 0.05$ . Median time to adjuvant chemotherapy was calculated in days for both PDS and IDS.

Univariable and multivariable logistic regression analyses were performed on the risk of developing Clavien-Dindo  $\geq 3$  complications for PDS and IDS separately. Clavien-Dindo was chosen as outcome since this scale is often used in international literature for evaluating surgical complications and allows for international comparison in the future. Patients with single PDS or IDS were included for this analysis, patients with MCS were excluded because of low numbers. Results were expressed as odds ratios with corresponding 95% confidence intervals (CI).

Variables for univariate analysis were chosen based on literature and expert opinion: age, BMI, Charlson Comorbidity Index, FIGO stage, histological type, differentiation grade, debulking result. Variables that were statistically significant in univariate analyses ( $p < 0.1$ ) were then used for multivariable analysis. Degrees of freedom were taken into account in adding factors for multivariable analysis. R statistical package version 1.2.5019 (R Foundation for Statistical Computing, Vienna, Austria) was used to analyze the data.

### 2.6. Comparisons between regions

For each of the eight regions in the Netherlands, the percentage of patients with severe complications, being graded Clavien-Dindo  $\geq 3$ , was adjusted for differences in case mix and presented in observed vs expected funnel plots for PDS and IDS. The case mix adjustment was performed by calculating the “expected” number of Clavien-Dindo  $\geq 3$  complications for each region based on the odds ratios found for the factors in the multivariable analysis. Then the observed/expected (O/E) ratio was calculated and depicted in funnel plots.

### 3. Results

Between January 1st, 2015 and December 31st, 2018, a total of 5569 patients with ovarian cancer were included in the DGOA registry. After meeting the inclusion criteria for the study population, 2382 patients remained in whom 2458 surgical procedures were performed (Fig. 1).

#### 3.1. Procedures and characteristics

From these 2458 surgical records, 1027 patients underwent PDS, 1355 patients underwent IDS, and 76 patients underwent MCS. Table 1 shows patient, tumor and treatment characteristics of the three groups. (See Table 2.)

Median age was significantly different between the PDS and IDS group, 64 and 68 years respectively, with more patients above 70 undergoing IDS (38.4%) compared to PDS (28.9%) [ $P < 0.001$ ]. In addition, FIGO classification was significantly different between PDS and IDS [ $P < 0.001$ ]; patients who underwent IDS had a more advanced FIGO stage compared to PDS. Also, poor differentiation grade was more often seen in patients with IDS (81.9%) compared to patients with PDS (64.7%) [ $P < 0.001$ ].

#### 3.2. Outcomes

Complete cytoreduction rate was higher in PDS compared to IDS (69.7% and 62.1% respectively [ $P < 0.001$ ]). Although PDS had a higher rate of complete cytoreduction, the percentage of women with intestinal surgery with or without construction of a stoma was higher (9.9% and 17.5% for PDS and 7.3% and 15.9% for IDS) [ $p = 0.048$ ].

#### 3.3. Complications in PDS and IDS

The number of complications with a re-intervention showed a significant difference between PDS (5.7%) and IDS (3.6%) [ $P = 0.045$ ].

Otherwise, no differences were found for complications without re-intervention in the two groups (PDS: 32.4% and IDS: 32.6%). Moreover, complications graded as Clavien-Dindo  $\geq 3$ , ICU stay, and 30-day in or out hospital mortality were not statistically different between PDS and IDS.

#### 3.4. Median time to start adjuvant chemotherapy

Fig. 2a-d depicts the time to start adjuvant therapy in days. In total 1842 patients had registered adjuvant chemotherapy; 733 after PDS, and 1109 after IDS. Patients undergoing CRS (both PDS and IDS) without postoperative complications started adjuvant chemotherapy after 28 days (median time), for PDS at 28 days, for IDS at 29 days (Fig. 2a).

Patients with complications without a re-intervention waited 34 days (median time) to start adjuvant chemotherapy (Fig. 2a), being different to patients with a complication with re-intervention. The median time to adjuvant chemotherapy in patients with a complication with re-intervention was 46 days and varied between 45 and 49 days, being the longest interval to adjuvant chemotherapy for all surgical outcomes of PDS and IDS (Fig. 2a). Examining Fig. 2b-d, the same trend is observed for different debulking outcomes. Complications with re-intervention cause the most delay in initiating adjuvant chemotherapy.

#### 3.5. Variation between regions

Fig. 3a and b show two case mix adjusted funnel plots of the eight centralized regions in the Netherlands for PDS and IDS separately. Fig. 3a shows complications with Clavien-Dindo grade  $\geq 3$  for PDS. One hundred-six out of 1027 patients experienced a complication with Clavien-Dindo grade  $\geq 3$ . This meant that we could correct for 10 case mix categories. For this reason, we simplified categories in order to correct for more factors. After univariable and multivariable analysis, we corrected for differences in age, BMI, Charlson Comorbidity Index, FIGO stage, histology type and result of CRS procedure between the

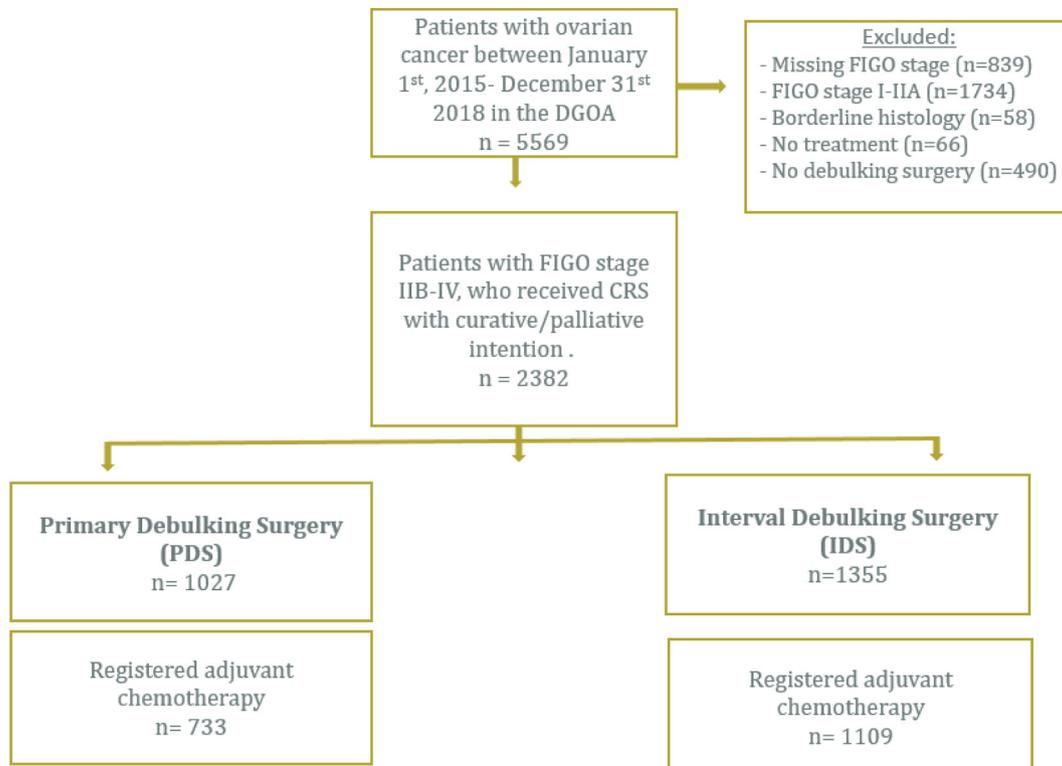


Fig. 1. Flowchart on included patients registered in the DGOA.

**Table 1**  
Patient, tumor and procedural characteristics of cytoreductive surgery in the Netherlands between January 1st, 2015– December 31st, 2018.

	Primary debulking surgery	Interval debulking surgery	p	Multiple debulking surgery <sup>a</sup>
n (%)	1027	1355		76
Age (median [range])	64.0 [17.0, 94.0]	68.0 [17.0, 90.0]	<0.001	63.5 [21.0, 79.0]
Age (%)				
<70	729 (71.0)	835 (61.6)	<0.001	59 (77.6)
70+	297 (28.9)	520 (38.4)		17 (22.4)
NA	1 (0.1)	0 (0.0)		
BMI				
<25	500 (48.7)	672 (49.6)	0.876	38 (50.0)
≥ = 25	495 (48.2)	644 (47.5)		35 (46.1)
NA	32 (3.1)	39 (2.9)		3(3.9)
ASA classification				
0–1	760 (74.0)	1040 (76.8)	0.170	
2–4	62 (6.0)	108 (8.0)		
Unknown <sup>b</sup>	205 (20.0)	207 (15.3)		
Charlson Comorbidity Index				
Charlson 0	773 (75.3)	996 (73.5)	0.326	57 (75.0)
Charlson 1	191 (18.6)	284 (21.0)		10 (13.2)
Charlson ≥2	63 (6.1)	75 (5.5)		9 (11.8)
FIGO Classification				
IIB	199 (19.4)	15 (1.1)	<0.001	1 (1.3)
IIC	47 (4.6)	4 (0.3)		1 (1.3)
IIIA	64 (6.2)	9 (0.7)		3 (3.9)
IIIB	153 (14.9)	26 (1.9)		4 (5.3)
IIIC	489 (47.6)	800 (59.0)		52 (68.4)
IV	75 (7.3)	500 (36.9)		15 (19.7)
X	0 (0.0)	1 (0.1)		0 (0.0)
Histology Type				
epithelial	953 (92.8)	1333 (98.4)	<0.001	73 (96.1)
non- epithelial	26 (2.5)	1 (0.1)		1 (1.3)
mixed form	48 (4.7)	21 (1.5)		2 (2.6)
Differentiation grade				
not specified	142 (13.8)	156 (11.5)	<0.001	8 (10.5)
good	141 (13.7)	48 (3.5)		6 (7.9)
moderate	70 (6.8)	36 (2.7)		5 (6.6)
poor	664 (64.7)	1110 (81.9)		57 (75.0)
undifferentiated	10 (1.0)	5 (0.4)		0 (0.0)
Result of cytoreductive surgery				
incomplete	134 (13.0)	139 (10.3)	<0.001	12 (15.8)
optimal	166 (16.2)	372 (27.5)		20 (26.3)
complete	716 (69.7)	841 (62.1)		44 (57.9)
Missing	11 (1.1)	3 (0.2)		0 (0.0)
Cytoreductive procedure including intestinal surgery				
No	736 (71.7)	1032 (76.2)	0.048	47 (61.8)
Yes, with stoma	102 (9.9)	99 (7.3)		10 (13.2)
Yes, without stoma	180 (17.5)	216 (15.9)		18 (23.7)
Missing	9 (0.9)	8 (0.6)		1 (1.3)

<sup>a</sup> Patients undergoing multiple debulking procedures are not included in statistical analysis.

<sup>b</sup> Patients of this category were not included in statistical analysis.

regions (supplement S1). After case mix correction, the risk of complications graded Clavien-Dindo ≥3 in one region was almost twice as high as the national average (O/E = 1.83). All other regions performed within confidence intervals.

Fig. 3b shows the case mix corrected funnel plot with Clavien-Dindo grade ≥ 3 for IDS, being 123 out of 1355 patients. In IDS we corrected for differences in age, BMI, Charlson Comorbidity Index, FIGO stage, differentiation grade and result of CRS procedure between the regions (supplement S2). After adjusting for case mix, two regions performed outside the confidence intervals. In one region, the risk for a Clavien-Dindo grade ≥ 3 complication was almost twice as high (O/E = 1.89)

**Table 2**  
Complications shown for primary, interval and multiple debulking surgery in the Netherlands between January 1st, 2015– December 31st, 2018.

	PDS	IDS	p	MDS
n (%)	1027 (43)	1355 (57)		76 <sup>a</sup>
Complications				
No complication	635 (61.8)	864 (63.8)	0.045	48 (63.2)
Complication without re-intervention	333 (32.4)	442 (32.6)		25 (32.9)
Complication with re-intervention	59 (5.7)	49 (3.6)		3 (3.9)
Re-intervention type				
Reoperation	48 (4.7)	45 (3.3)	0.028	3 (3.9)
Endoscopic intervention	1 (0.1)	1 (0.1)		0 (0.0)
Radiological intervention	10 (1.0)	3 (0.2)		0 (0.0)
Clavien-Dindo ≥3	106 (10.3)	122 (9.0)	0.311	6 (7.9)
Complicated course <sup>a,b</sup>	82 (15.8)	72 (10.2)	0.005	4 (10.5)
Hospital stay <sup>b</sup>				
Hospital stay <14 days	452 (86.9)	646 (91.6)	<0.001	35 (92.1)
Hospital stay ≥14 days	56 (10.8)	32 (4.5)		2 (5.3)
Missing	12 (2.3)	27 (3.9)		1(2.6)
ICU stay				
≥2 days	60 (5.8)	82 (6.1)	0.899	5 (5.3)
30-day mortality	5 (0.5)	11 (0.8)	0.479	0 (0.0)
Complication type				
Technical	6 (0.6)	12 (0.9)	0.547	0 (0.0)
Systemically				
Mistake with medication	1 (0.1)	0 (0.0)	0.225	0 (0.0)
Side effect of medication	3 (0.3)	1 (0.1)		0 (0.0)
Functional				
Urinary retention	2 (0.2)	2 (0.1)	0.476	0 (0.0)
Ileus	21 (2.0)	21 (1.5)		0 (0.0)
Kidney/liver disorder	3 (0.3)	9 (0.7)		0 (0.0)
Thrombosis				
Thrombosis	2 (0.2)	1 (0.1)	0.701	0 (0.0)
Pulmonary embolus	8 (0.8)	11 (0.8)		0 (0.0)
Blood loss				
Perioperative>1 l	206 (20.1)	214 (15.8)	0.021	12 (15.8)
Hemorrhage	10 (1.0)	18 (1.3)		2 (2.6)
wound defect				
Wound dehiscence	18 (1.8)	14 (1.0)	0.179	0 (0.0)
Platzbauch	8 (0.8)	6 (0.4)		0 (0.0)
Injury				
Injury/obstruction/fistula of great vessel	4 (0.4)	1 (0.1)	0.018	0 (0.0)
Injury/obstruction/fistula of intestine	20 (1.9)	24 (1.8)		2 (2.6)
Injury/obstruction/fistula of bladder	16 (1.6)	20 (1.5)		1 (1.3)
Injury/obstruction/fistula of ureter	14 (1.4)	4 (0.3)		0 (0.0)
Infection				
Local infection	32 (3.1)	33 (2.4)	0.301	2 (2.6)
Organ level	22 (2.1)	38 (2.8)		3 (3.9)
Systemical	26 (2.5)	24 (1.8)		3 (3.9)

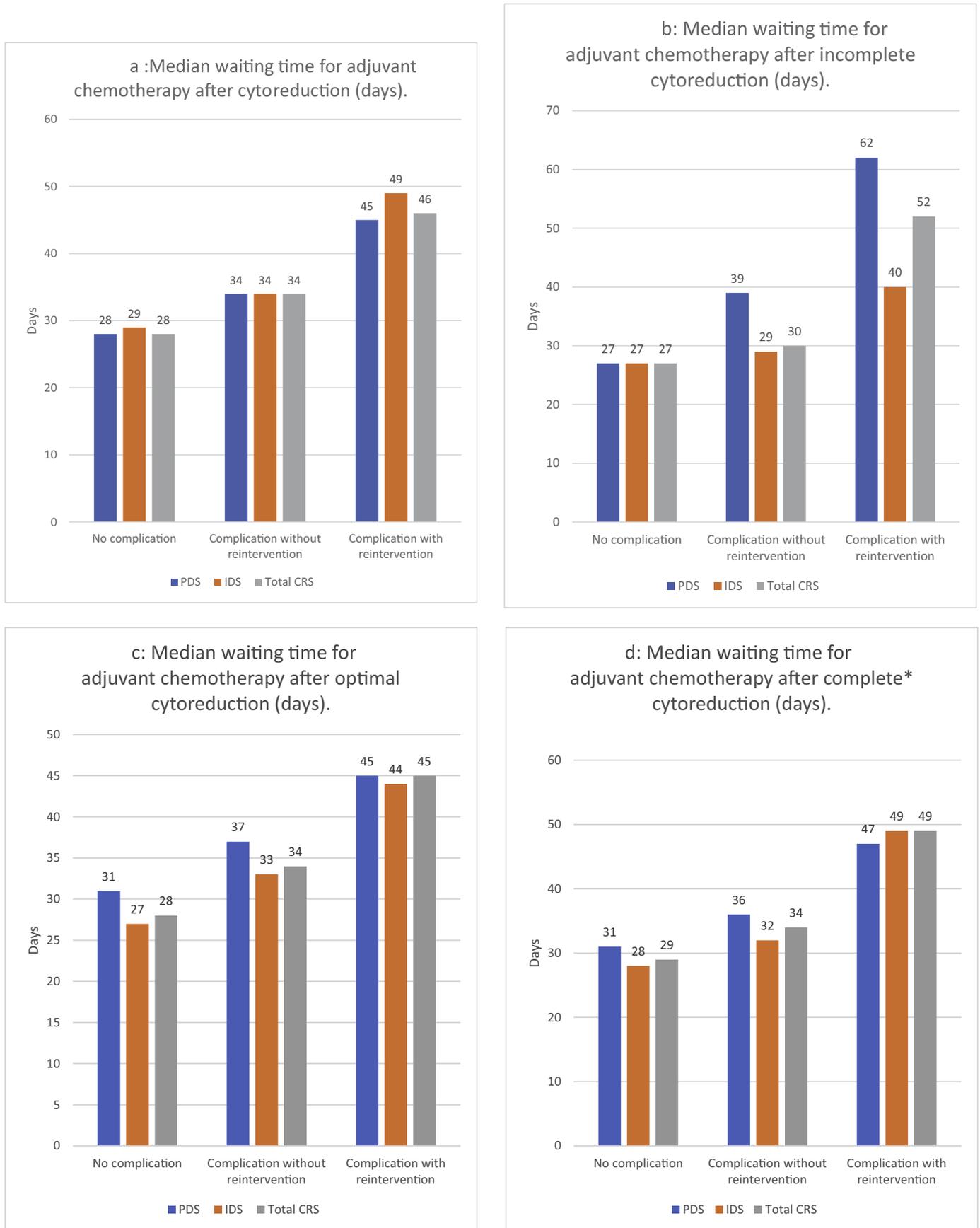
<sup>a</sup> Complicated course: Clavien-Dindo ≥3 and hospital stay of more than 14 days.

<sup>b</sup> Complicated course/hospital stay is shown only for the patients from 2017 to 2018 since date of discharge was mandatory from that year on. The total number of patients is 520 PDS, 705 IDS and 38 s procedure group.

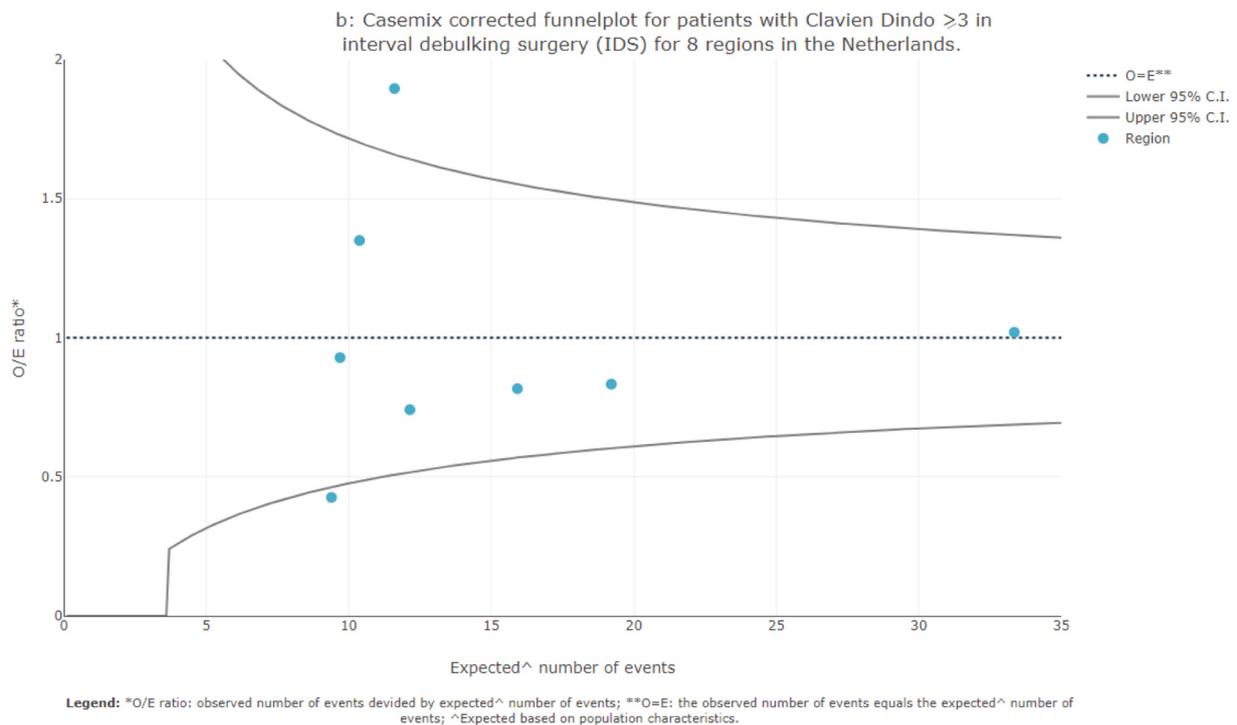
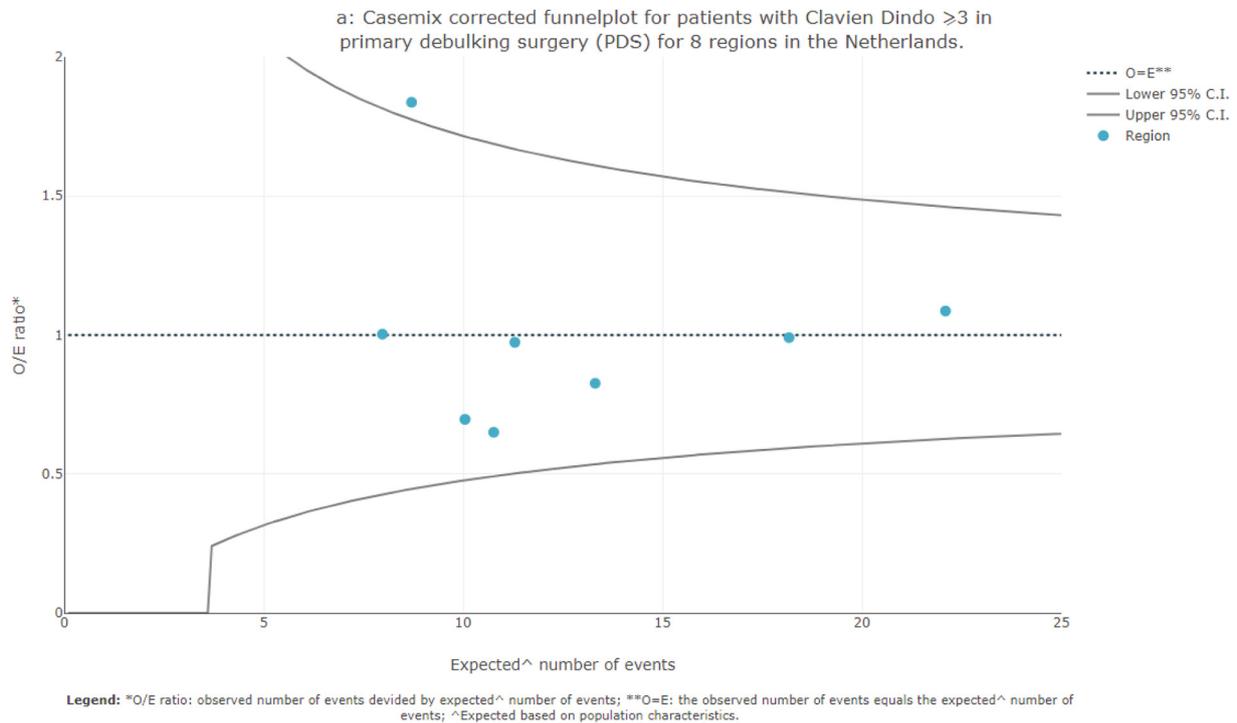
compared to the mean of all regions. The other region had a significantly lower risk of Clavien-Dindo grade ≥ 3 complications, compared to the national average (O/E = 0.42).

#### 4. Discussion

This is the first prospective population-based study on postoperative outcomes in relation to CRS outcomes for patients with advanced ovarian cancer in the Netherlands. Although the percentage of Clavien-Dindo ≥3 complications in the PDS and IDS did not differ significantly, the percentage of patients having a complication with re-intervention was significantly higher for PDS than for IDS (p = 0.045). These findings



**Fig. 2.** a. Median waiting time for adjuvant chemotherapy after cytoreduction (days).  
 b. Median waiting time for adjuvant chemotherapy after incomplete\* cytoreduction (days).  
 c. Median waiting time for adjuvant chemotherapy after optimal\* cytoreduction (days).  
 d. Median waiting time for adjuvant chemotherapy after complete\* cytoreduction (days).



**Fig. 3.** a. Casemix corrected funnelplot for patients with Clavien Dindo  $\geq 3$  in primary debulking surgery (PDS) for 8 regions in the Netherlands. b. Casemix corrected funnelplot for patients with Clavien Dindo  $\geq 3$  in interval debulking surgery (IDS) for 8 regions in the Netherlands.

are in line with previous literature, in which more complications are reported in PDS compared to IDS [3,16].

Moreover, patients with complete CRS with complication and re-intervention waited 49 days (47 days PDS- 49 days IDS) to reinitiate adjuvant chemotherapy. Timmermans et al. Described improved survival when starting adjuvant chemotherapy within 42 days [10]. In our study population all patients with a complication with re-intervention started

chemotherapy later than 42 days. This illustrates the importance of balancing the goal of achieving maximum surgical outcome by aggressive surgery that improves survival but has a higher risk of complications with re-intervention and subsequently a delay in starting adjuvant chemotherapy.

Another notable result was that in case of PDS, more patients had a “complicated course” compared to patients undergoing IDS. This is

mainly due to a longer hospital stay in PDS, defined as  $\geq 14$  days admission at the hospital compared to IDS. The difference in results between complications measured with the Clavien-Dindo classification (being comparable for IDS and PDS) and ‘complicated course’ as a composite measure (being statistical different for IDS and PDS), shows how hospital stay can influence the measuring and reporting of complications and can add another dimension to investigate postoperative complications and their effects [15,17].

Differently to our findings, a single center study which also used Clavien-Dindo, reported significant higher rates of grade 3 and 4 complications in PDS compared to IDS in advanced ovarian cancer [16]. Although this study used the same grading method for complications as our study, its population size is too small to use as comparative literature (PDS 106 patients vs IDS 49 patients).

We identified one region with a nearly two-fold higher risk of receiving a complication graded Clavien-Dindo  $\geq 3$  in both PDS and IDS. We did not expect such a large difference, especially after case mix correction, since regions already balance out a population by geography. This striking difference could be caused by a registration artefact (e.g. more accurate registration by this region). But the region concerned also had the longest interval to start adjuvant chemotherapy (35 days). With these results the clinical audit could analyze the region more closely and identify possible causes to decrease regional variation in the future.

It should be taken into account that similarities and differences between outcomes in PDS and IDS are subject to confounding by indication. The Dutch guideline advises PDS over IDS when complete PDS is feasible based on preoperative findings [14]. In our study, patients who underwent IDS were older, had a higher ASA classification, and had a more advanced FIGO stage compared to patients treated with PDS. This could have influenced the treatment plan but also the surgical aggressiveness and therefore contribute to confounding by indication. This confounding by indication is also illustrated by the significant higher rate of completeness in PDS compared to IDS as several studies actually describe the opposite, where complete IDS is more often achieved compared to PDS [16,18]. A possible explanation is the better selection of patients suitable for PDS/IDS as there is a higher FIGO stage with more extensive disease and poorer differentiation grades of patients undergoing IDS and therefore starting with NACT.

Also interesting are the high numbers of complete cytoreduction in PDS and IDS compared to other studies. A recent study by Palmqvist et al. examined survival before and after centralization in a population based cohort in Sweden [6]. They mentioned complete cytoreduction in PDS of 36% before centralization and 48% after centralization ( $p = 0.016$ ), combined with a better relative survival after centralization [6]. Since 2014, ovarian cancer care is centralized in the Netherlands and our complete PDS percentage is 69.7% between 2015 and 2018. It is hard to compare these results as the initial treatment arms are not comparable (decision to choose for either PDS or IDS). The specific population in Sweden contained 190 patients with PDS (82%) and 41 patients with IDS (18%) after centralization, whereas our study contained more equal division of population sizes 1027 (43%) vs 1355 (57%), respectively. It would be interesting to compare the results of CRS in high volume and low volume centers in the Netherlands with high- and low volume centers in other countries to gain insight how the results of CRS relate to the number of procedures in different countries. Furthermore, it should be noted that a better selection of patients undergoing PDS is made beforehand, which is reflected in the different FIGO stage distribution between patients with a PDS (higher percentage of FIGO stage IIB–IIIB) and IDS (higher percentage of FIGO stage IIIC–IV). In our study there was a rather small group of patients ( $n = 76$ ) with multiple debulking efforts. This may be due to the fact the majority of ‘other surgery’ (Fig. 1) were diagnostic laparoscopies, likely to estimate if a debulking procedure was feasible. Besides the different population sizes and diagnostic procedures, factors such as surgical accreditations, surgical skills and education could also

be of influence adding to the percentage of completeness. Unfortunately, the DGOA cannot report on the survival rates yet as this data is not complete.

The strength of the present study is that, to our knowledge, no population-based comparison of postoperative complications between IDS and PDS in relation to adjuvant treatment have been reported in literature yet. This study gives valuable insights on how the nation performs in relation to surgical outcome, and second on how postoperative outcomes vary between regions.

A possible limitation of the present study includes that either gynecologists or trained data managers perform registration in the DGOA. There could be a discrepancy in the way these two groups interpret the patient files or how strict they are in registering a complication. Data entered by data managers are however checked by gynecologists. To exclude a difference, a sub-analysis was performed which showed that complication rate did not differ between both data sources (data not shown).

It should also be mentioned that in the first years of registration not all adjuvant chemotherapy treatments were added if the patient received chemotherapy in the next year (e.g. surgery in December 2014 and chemotherapy in January 2015). Moreover, in the Netherlands patients can receive chemotherapy in their regional hospital. We encourage the centralized hospital to register the chemotherapy but this is sometimes done by the regional hospital. Unfortunately, due to GDPR (General Data Protection Regulation) we cannot trace patients that are registered in different hospitals. These shortcomings most likely explains our low percentage of patients with adjuvant chemotherapy (76%).

In conclusion, a higher complete cytoreduction rate is achieved in PDS compared to IDS. This is associated with a higher complication with re-intervention rate in the PDS group. The higher rate of complication with re-intervention is subsequently correlated with a delay in starting adjuvant chemotherapy. When performing cytoreductive surgery these advantages and disadvantages should be balanced.

In addition, regional variation in postoperative outcomes exist within the Netherlands. Reporting postoperative outcomes on a national and a regional level (benchmarking) is important, as this information can initiate the discussion to improve surgical outcome and reduce complications which finally leads to an improved outcome for patients with advanced ovarian carcinoma [11].

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## Author contributions

N.M.S. BaldewpersadTewarie- Formal analysis, data curations, investigation, methodology, visualization, original draft writing.

W.J.van Driel – conceptualization- supervision-review & editing.

M.van Ham conceptualization- supervision-review & editing.

M.W.Wouters- conceptualization- supervision-review & editing.

R.Kruitwagen conceptualization- supervision-review & editing.

## Declaration of Competing Interest

There was no conflict of interest.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ygyno.2021.05.030>.

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