



## Original Research

# No improvement in long-term survival for epithelial ovarian cancer patients: A population-based study between 1989 and 2014 in the Netherlands



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## KEYWORDS

Epithelial ovarian cancer;  
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**Abstract Aim:** This study investigates changes in therapy and long-term survival for patients with epithelial ovarian cancer (EOC) in the Netherlands.

**Methods:** All patients with EOC, including peritoneal and fallopian tube carcinoma, diagnosed in the Netherlands between 1989 and 2014 were selected from the Netherlands Cancer Registry. Changes in therapy were studied and related to overall survival (OS) using multivariable Cox regression models.

**Results:** A total of 32,540 patients were diagnosed with EOC of whom 22,047 (68%) had advanced stage disease. In early stage, lymph node dissection as part of surgical staging procedures increased over time from 4% in 1989–1993 to 62% in 2009–2014 ( $P < 0.001$ ). In advanced stage, the number of patients receiving optimal treatment with surgery and chemotherapy increased from 55% in 1989–1993 to 67% in 2009–2014 ( $P < 0.001$ ). Five-year survival rates improved in both early stage (74% versus 79%) and advanced stage (16% versus 24%) as well as in all patients combined (31% versus 34%). Ten-year survival rates, however, slightly improved in early stage (62% versus 67%) and advanced stage (10% versus 13%) but remained essentially unchanged at 24% for all patients combined.

**Conclusion:** Despite intensified treatment and staging procedures, long-term survival for women with EOC has not improved in the last 25 years. The observed improvements in 5-year

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OS reflect a more prolonged disease control rather than better chances for cure. Furthermore, the apparent better long-term outcome, when early and advanced stage patients are analysed separately, is largely due to improved staging procedures and the ensuing stage migration. These effects disappear in a combined analysis of all patients.

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## 1. Introduction

Epithelial ovarian cancer (EOC) is the most lethal gynaecologic cancer worldwide [1]. The 5-year overall survival (OS) rates range between 30% and 46% [2,3]. Due to a lack of specific symptoms, patients are often diagnosed with advanced stage disease, which is associated with poor prognosis and 5-year OS rates of 14–29% [2,4].

Patients who are diagnosed with early stage disease are recommended to undergo a complete staging procedure, consisting of inspection of the abdominal cavity, omentectomy, adequate lymph node sampling and several prescribed biopsies. If patients cannot be staged properly adjuvant chemotherapy is recommended [5,6].

Current management for advanced EOC patients consists of debulking surgery in combination with platinum- and taxane-based chemotherapy. Complete resection of all macroscopic tumour is an independent factor for prolonged survival and is therefore an important goal during debulking surgery [7,8]. The timing of surgery is an ongoing topic of debate; patients were traditionally treated with primary debulking surgery (PDS), but neoadjuvant chemotherapy followed by interval debulking surgery (NACT-IDS) could be an alternative for advanced stage patients [9,10].

Improvements in therapy and diagnostic work-up should ultimately lead to better disease-free survival and OS for EOC patients. Multiple international studies were conducted, which analysed trends in survival. Outcomes varied, but most studies reported improved 5-year survival rates [11–28] (S7). In combination with a decline in incidence for ovarian cancer, among others due to the introduction of the oral contraceptive pill, these studies often result in decreasing ovarian cancer mortality rates [28–31].

The population-based study of van Altena *et al.* [19] analysed trends in relative survival for both early and advanced stage EOC until 2009 in the Netherlands. Since this publication, the role of adequate staging surgery for early stage patients and the introduction of NACT for advanced stage patients have been put forward as important factors for prolonged OS [5,32]. Therefore, we analysed whether long-term survival has indeed improved for both early and advanced stage patients with respect to these changes in treatment.

## 2. Methods

Patients were selected from the Netherlands Cancer Registry (NCR), which is a population-based registry with coverage of all newly diagnosed malignancies in the Netherlands since 1989. Dedicated registration clerks routinely extract patient information from medical records within the hospitals. Information on vital status and date of death were obtained from the municipal demography registries [33].

### 2.1. Study population

All consecutive patients diagnosed with EOC, including peritoneal and fallopian tube carcinoma (International Classification of Diseases for Oncology (ICD-O) codes C48.1, C48.2, C56.9 and C57.0), in the Netherlands between 1989 and 2014 were selected from the NCR [34]. Trends in therapy and survival were studied separately for early (International Federation of Gynaecologists and Obstetricians (FIGO) IA–IIA) and advanced stage patients (FIGO IIB–IV). FIGO stage 2009 was derived from the tumour-nodal-metastasis (TNM) staging system and based on postoperative findings [35]. If patients did not receive surgery or when patients underwent NACT-IDS, clinical tumour stage was used to avoid downstaging. Debulking surgery is registered nationwide from 2004, and outcome of surgery was defined as optimal if macroscopic residual lesions were smaller than one centimetre in maximal diameter. In 2010, complete debulking surgery was implemented in the NCR defined as no macroscopic residual disease.

### 2.2. Statistical analysis

Patients were distributed among period groups according to their date of diagnosis to analyse differences over time for the following time periods; 1989–1993, 1994–1998, 1999–2003, 2004–2008 and 2009–2014. Trends in therapy were analysed using the Cochrane–Armitage test for trends, and patients were divided in two age groups (<65 years at diagnosis and ≥65 years). OS was defined as the date of diagnosis until death or last follow-up date for patients who were still alive (1 February 2017) and was analysed by Kaplan–Meier survival curves and multi-variable Cox regression models. A separate analysis was performed on the Eindhoven Cancer Registry data to

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