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The association between socioeconomic status and tumour stage at diagnosis of ovarian cancer: a pooled analysis of 18 case-control studies

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Abstract

Purpose—Socioeconomic status (SES) is a known predictor of survival for several cancers and it has been suggested that SES differences affecting tumour stage at diagnosis may be the most important explanatory factor for this. However, only a limited number of studies have investigated SES differences in tumour stage at diagnosis of ovarian cancer. In a pooled analysis, we investigated whether SES as represented by level of education is predictive for advanced tumour stage at diagnosis of ovarian cancer, overall and by histotype. The effect of cigarette smoking and body mass index (BMI) on the association was also evaluated.

Methods—From 18 case-control studies, we obtained information on 10,601 women diagnosed with epithelial ovarian cancer. Study specific odds ratios (ORs) with corresponding 95% confidence intervals (CI) were obtained from logistic regression models and combined into a pooled odds ratio (pOR) using a random effects model.

Results—Overall, women who completed ≤high school had an increased risk of advanced tumour stage at diagnosis compared with women who completed >high school (pOR 1.15; 95% CI 1.03–1.28). The risk estimates for the different histotypes of ovarian cancer resembled that observed for ovarian cancers combined but did not reach statistical significance. Our results were unchanged when we included BMI and cigarette smoking.

Conclusion—Lower level of education was associated with an increased risk of advanced tumour stage at diagnosis of ovarian cancer. The observed socioeconomic difference in stage at diagnosis of ovarian cancer calls for further studies on how to reduce this diagnostic delay.

Keywords

Epidemiology; ovarian cancer; pooled analysis; socioeconomic status; tumour stage

1. Introduction

Ovarian cancer is the 5th most common malignancy among women in developed countries [1]. Furthermore, it is a highly fatal disease with the worst prognosis among the gynaecological cancers because it is often diagnosed at an advanced tumour stage [2]. As tumour stage at diagnosis is among the most important prognostic factors in ovarian cancer, detection at an early stage is essential. However, currently there are no efficient screening tools for ovarian cancer and as most women only experience vague symptoms, the disease is often detected at an advanced stage when survival is poor. Therefore, knowledge on predictors for advanced stage at diagnosis of ovarian cancer is crucial to reduce the mortality for this disease.

Socioeconomic status (SES) is a predictor of incidence and survival of a number of diseases and there is evolving evidence for socioeconomic differences in cancer survival for many

cancer types [3;4]. However, in contrast to breast cancer, relatively few studies have addressed the association between SES and ovarian cancer survival and the results have been inconsistent. Five studies [5–9] found worse survival among women with low SES whereas two studies [10;11] found no association. The reasons for socioeconomic differences in cancer survival in general and ovarian cancer survival in particular are not well-understood [4]. Possible underlying causes can be separated into three groups: tumour characteristics (tumour stage at diagnosis and biological characteristics), health care factors (e.g., types of treatment received, medical expertise and utilization of screening), and patient characteristics (e.g., lifestyle factors and comorbidities) [4]. According to Woods et al. [4], SES differences in tumour stage at diagnosis is likely the most important explanation for differences in cancer survival for a number of cancer types; including breast- [12], endometrial- [13] and cervical cancer [14]. SES differences in tumour stage at diagnosis may be attributable to several reasons, including access to and acceptance of cancer screening technologies, awareness of cancer symptoms, health-seeking behaviour, access to health care, comorbidities, and lifestyle factors.

However, only a limited number of studies have investigated SES differences in tumour stage at diagnosis of ovarian cancer, and whereas the majority found no convincing evidence that tumour stage at diagnosis differed according to SES [15–18], one recent study showed that a lower level of education was associated with advanced tumour stage at diagnosis of ovarian cancer [8]. Many of the previous studies were limited by small sample sizes and lack of individual level SES data, and none of the studies investigated whether the association between SES and tumour stage at diagnosis differed by histotype.

Using data from 18 case-control studies included in the international Ovarian Cancer Association Consortium (OCAC), we performed a pooled analysis in order to evaluate the association between SES (represented by highest obtained level of education) and tumour stage at diagnosis, overall and by histotype. Furthermore, we aimed to investigate to what degree the association between SES and tumour stage at diagnosis was confounded by pre-diagnosis cigarette smoking or by body mass index (BMI).

2. Materials and Methods

The Ovarian Cancer Association Consortium (OCAC) described in details elsewhere [19] is an international collaboration of case-control studies founded in 2005 with the original aim to identify genetic polymorphisms associated with ovarian carcinogenesis. More recently, consortial activities have included the identification of risk factors and prognostic factors for ovarian cancer. In the present study, we obtained data from 18 studies that provided information about level of education and other required variables for the study [20–37] (Table 1). All data were checked for internal consistencies and clarifications were provided by the original investigators if needed. Among women diagnosed with ovarian cancer, we excluded from analyses those with missing data for level of education, those with non-epithelial ovarian tumours or epithelial tumours of low malignant potential (borderline ovarian tumours) and those who lacked information on age, race/ethnicity or tumour stage at diagnosis, leaving 10,601 women for analysis. All individual studies included in OCAC had

institutional review board or ethics committee approvals and all study participants provided informed consent.

2.1. Assessment of level of education

Information on highest attained level of education was obtained either from self-administered questionnaires (n = 8 studies) or from in-person interviews (n = 10 studies). For all included OCAC studies, information on highest level of education was harmonized and parameterized as a dichotomous variable (≤high school versus >high school).

2.2. Statistical analysis

Of the 18 studies included for analyses, 11 (AUS, GER, HOP, MAL, MAY, NCO, NEC, NTH, POL, SEA and UKO) used the FIGO staging system [38], while two studies (CON and NJO) used SEER staging manuals [39] to stage ovarian cancer. Five studies (DOV, HAW, STA, UCI and USC) had information on both FIGO and SEER tumour staging. In the common OCAC dataset, a harmonized summary tumour stage variable was created and reported in the following categories: localized tumour stage, regional tumour stage or distant tumour stage, using the following algorithm: localized = FIGO tumour stage IA, IB, I (not other specified (NOS)) or SEER tumour stage 1; regional = FIGO tumour stage IC, IIA, IIB, IIC, II (NOS) or SEER tumour stage 2, 3, 4, 5; distant = FIGO tumour stage IIIA, IIIB, IIIC, III (NOS), IV or SEER tumour stage 7. For studies with information on both FIGO and SEER tumour staging, the harmonized summary tumour stage variable represents the more advanced of FIGO and SEER tumour stage. In all analyses, the harmonized OCAC tumour stage variable was parameterized as a dichotomous comparison of localized tumour stage or advanced tumour stage (regional or distant).

To compare characteristics of the included women according to tumor stage at diagnosis (localized stage versus advanced stage), a Pearson's chi square statistical test was used when data were normally distributed (histology, level of education, smoking status and race/ethnicity) and a Wilcoxon rank sum statistical test was used when data were not normally distributed (age at diagnosis and BMI). We used a two-stage approach [40] to analyse the association between stage of ovarian cancer and level of education. First, study-specific odds ratios (ORs) were obtained by logistic regression models with adjustments for *a priori* selected potential confounding variables (described below). The study-specific estimates were then combined by random-effects inverse variance-weighted meta-analysis into a pooled odds ratio (pOR) with corresponding 95% confidence intervals (CIs) [41]. Statistical heterogeneity among studies was evaluated using the Cochran Q and I^2 statistics. For all analyses, individual studies were included in the meta-analysis only if the following two requirements were met; i) five cases with complete data were available and ii) each level of the tumour stage variable had one or more subjects.

Two statistical models were fitted to evaluate the association of tumour stage at diagnosis of ovarian cancer according to level of education. Model 1 included adjustments for age at diagnosis (continuous variable) and race/ethnicity (non-Hispanic White, Hispanic White, Black, Asian or other, including unknown races). In Model 2, we additionally adjusted for pre-diagnosis cigarette smoking (never, former or current smoker) and BMI (determined

either at one or five years prior to ovarian cancer diagnosis, depending on the study) as a continuous variable (per 5 kg/m^2). Subgroup analyses were conducted for specific histotypes of ovarian cancers including serous, mucinous, endometrioid and clear cell tumours. Serous tumours were additionally categorized as low- (grade 1) or high- (grade 2+) grade tumours. Finally, we also performed additional sensitivity analyses to investigate whether the association between level of education and tumour stage at diagnosis of ovarian cancer overall differed according to study continent (US versus non-US studies), race/ethnicity (white (non-Hispanic or Hispanic White) versus all other races/ethnicities (Black, Asian and other)) or study type (population-based versus hospital-/clinic-based studies). All analyses were conducted using the environment R, version 3.1.0. A 5% significance level was used for all analysis.

3. Results

Characteristics of the 18 studies that contributed data from 10,601 women with epithelial ovarian cancer are shown in Table 1. Eleven studies were conducted in the United States (US), six in Europe and one in Australia. In the studies, the number of women with ovarian cancer ranged from 183 to 1377. Women were 19–91 years of age at diagnosis between 1989 and 2010. Fifteen studies were population-based and three were hospital/clinic-based. Almost four-fifths of the women (78.6%) had advanced tumour stage (regional or distant) at diagnosis of ovarian cancer.

Table 2 presents characteristics of the women included in the analysis according to tumour stage at diagnosis of ovarian cancer. Among women diagnosed at advanced tumour stage, median age at diagnosis was significantly higher (58.0 years) compared with women diagnosed at localized tumour stage (median age = 53.0 years). Furthermore, women diagnosed at advanced tumour stage of ovarian cancer were more often diagnosed with serous tumours, had completed ≤high school, had higher BMI, were less likely to be Asian and were more often a former smoker, compared with women diagnosed at a localized tumour stage (all p-values < 0.01).

In Table 3 are presented the pooled odds ratios for advanced tumour stage at diagnosis of ovarian cancer overall and within histotypes according to level of education. The table shows pORs based on two analytic models: Model 1 includes adjustment for age and race/ethnicity and Model 2 includes additional adjustment for BMI and cigarette smoking status. Women who completed high school or less had an increased risk of advanced tumour stage at diagnosis of ovarian cancer (pOR 1.15; 95% CI 1.03–1.28) (Table 3, Model 1; Figure 1). The risk estimates for the various histotypes generally resembled that for ovarian cancer overall, though none of the risk estimates reached nominal statistical significance (Table 3, Model 1). Additional adjustments for BMI and cigarette smoking status made virtually no changes to the estimated associations between level of education and tumour stage at diagnosis of ovarian cancer (Table 3, Model 2). Heterogeneity was not evident for any of the analyses included in the present paper (All p-values > 0.4 and all I^2 <5%).

Lastly, we performed sensitivity analyses to investigate whether the association between level of education and tumour stage at diagnosis of ovarian cancer overall differed according

to study continent, race/ethnicity or study type. However, the direction and the magnitude of the associations were not markedly different from the associations obtained in the main analyses (Table 3). Further, the risk estimates did not differ statistically significantly between the US studies (pOR 1.11; 95% CI 0.97–1.28) and the non-US studies (pOR 1.22; 95% CI 1.01–1.47), between women of white race/ethnicity (pOR 1.15; 95% CI 1.02–1.29) and women of other races/ethnicities (pOR 1.13; 95% CI 0.84–1.51), as well as between population-based studies (pOR 1.14; 95% CI 1.01–1.28) and hospital-/clinic-based studies (pOR 1.28; 95% CI 0.88–1.73) (all p-values for pairwise comparisons >0.05).

4. Discussion

Tumour stage is the most important prognostic factor of survival in ovarian cancer. It is therefore important to identify factors that predict tumour stage at diagnosis. A potential candidate is socioeconomic status, which has been found to be associated with tumour stage at diagnosis for other gynaecological cancers [12–14]. The present large study evaluated the association between level of education and tumour stage at diagnosis of epithelial ovarian cancer. Our results showed that women who completed high school or less had a modest (15%) increased risk of advanced tumour stage at diagnosis of ovarian cancer compared with women who completed more than high school. Observed risk estimates for the histotypes resembled those for ovarian cancer overall.

Only a few studies have investigated SES differences in tumour stage at diagnosis of ovarian cancer. Our results are partly in line with results from a recent Danish cohort study. Ibfelt et al. [8], with data of 2873 women diagnosed with ovarian cancer, observed that women with medium level of education (10–12 years) had a 25% increased risk of advanced tumour stage at diagnosis of ovarian cancer compared with women with high level of education (>12 years). However, the authors found no association between risk of advanced tumour stage and short level of education (7–9 years). Other studies have found no convincing associations between various measures of SES and tumour stage at diagnosis of ovarian cancer [15–18]. For example, in the largest study to date using data from 16,228 American women with ovarian cancer, Morris et al. [18] found no association between a census-based measure of SES and tumour stage at diagnosis. An explanation for the divergent results may be that only our study and the study by Ibfelt et al. [8] used individual level measures of SES, whereas all other studies of this question have used various area-based/aggregate measures of SES as surrogates for individual SES. Area-based and aggregate measures of SES are known to be less precise (i.e., have higher risk of misclassification) than individual measures of SES and likely to bias relative risk toward the null in epidemiological studies [42]. No previous studies have examined whether or not the association between SES and tumour stage at diagnosis of ovarian cancer differs by histotype. We observed that the estimated risks for the histotypes of ovarian cancer resembled that for ovarian cancer overall. However, the numbers of cases for some of the histotypes were relatively small and additional confirmation would be warranted.

The observed association between educational level and tumour stage at diagnosis is likely to be explained by a complex interaction between several underlying factors, including patient access to regular health-care check-ups, patient awareness of cancer symptoms,

adequate reaction to symptoms, access, barriers and quality of healthcare, time-period to referral to specialist care, lifestyle factors, and comorbidities. Cancer symptom awareness and interpretation of symptoms is poorer among those who are less educated and those with lower SES [43]. Though some ovarian cancers are asymptomatic, most women experience vague or non-specific symptoms, which are similar to those of other common illnesses [44]. Therefore, it is plausible that more highly educated women could be more aware of and able to recognize potential symptoms compared with less educated women and may therefore be more likely to seek medical care earlier, which would eventually lead to a diagnosis of ovarian cancer in an earlier tumour stage. However, compared with cancers that are generally screenable or present with clear clinical signs, the potential for socioeconomic status to have an influence on awareness of symptoms and health-care seeking in ovarian cancer are likely to be rather limited. Alternatively, women that are more educated might respond more promptly to their apparent signs or symptoms whereas less educated women may be more likely to ignore, discount or deny them until mounting discomfort becomes substantial in advanced tumour stage disease.

Regular visits to a primary care physician and the latency from date of visit at the general practitioner until referral to a gynaecologist are both factors that are potentially predictive for tumour stage at diagnosis of ovarian cancer. As low SES is associated with less frequent use of primary care [45] and likely increased time to referral to a specialist, these factors may combine to explain the observed association between educational level and tumour stage at diagnosis. In the present study, 11 of 18 individual studies were conducted in the USA, representing 65% of the women in our study population. In contrast to Europe and Australia, access to health care in the USA is not uniform and a larger proportion of well-educated American women are privately insured compared with less educated American women. It is plausible that women with private health insurance visit a primary care physician more regularly and are faster referred to a gynaecologist compared with women who are uninsured or covered by governmental insurance programs. Therefore, it would be reasonable to assume that the association between level of education and tumour stage at diagnosis of ovarian cancer would be more pronounced among the US studies than among the non-US studies. However, the results from our additional analysis stratified by study continent were not able to support this.

Finally, low SES is known to be associated with less unhealthy lifestyle, including factors such as poorer diet, less exercise, more cigarette smoking and higher BMI [46–48]. Both cigarette smoking and obesity accelerates carcinogenesis resulting in earlier progression and death, whereas obesity can blur ovarian cancer symptoms and delay diagnosis [49]. However, in the present study, BMI and cigarette smoking status had virtually no effect on the estimated associations between level of education and tumour stage at diagnosis. Therefore, BMI and cigarette smoking do not appear to have substantial influence on tumour stage difference by level of education.

A strength of the present study is the large number of ovarian cancer patients obtained by pooling data from 18 individual case-control studies. This collection strengthened the statistical power of the risk estimates and allowed us to examine associations both overall and separately for the various histotypes of ovarian cancer. In addition, the majority of the

studies were population-based designs with information on education obtained from in-person interviews. The participating studies were not selected from among published studies. Therefore, our analyses included both positive and negative study-specific results, limiting the possibility of publication bias. The present analyses relied on individual data combined into a single dataset following careful central data harmonization. We considered differences in study design and data collection across studies and adjusted for relevant confounding factors across studies. However, we could not adjust for comorbidity, as this information was not available in our data. The degree of comorbidity is known to be inversely correlated with SES [50] and comorbidity may blur symptoms of cancer and may reduce individual resources when it comes to health care seeking. Hence, even though a recent cohort study showed that comorbidity only had a small impact on the differences in ovarian cancer stage and survival by SES [8], we cannot rule out that our results may have been slightly affected by unmeasured confounding from comorbidity. Furthermore, information on tumour stage was abstracted from hospital records or cancer registries and the majority of study sites performed pathology review in order to confirm histotype classifications. Nevertheless, not all ovarian tumours underwent systematic histopathologic review and therefore some degree of misclassification of subtype could have occurred. An additional potential limitation of the present study is that we only included one measure of SES - level of education - as only a limited number of OCAC studies obtained information on other measures such as income or marriage/cohabitation status. Even though a single measure of SES may show an association with the health outcome analysed, it may not encompass the entirety of the effect of SES on health, and inclusion of multiple measures of SES are always preferable [51]. Hence, by including only one measure of SES, we may only partly have explained the true association between SES and stage at diagnosis of ovarian cancer. However, level of education is considered to be a good and valid measure of SES with regard to health because it influences an individuals' SES throughout life and it is highly associated with both income and occupation [6; 52]. Further, knowledge and skills obtained through education may affect cognitive functions and thereby strengthen the individuals' comprehension of health messages and communication with health authorities [51]. Finally and perhaps most importantly, for most individuals, level of education does not change substantially throughout life compared with other measures of SES, including income and occupation, and can therefore be considered to be a robust measure of SES [51].

5. Conclusions

This large pooled analysis showed that lower educational level was associated with advanced tumour stage at diagnosis. BMI and cigarette smoking did not explain the association. Hence, in order to reduce diagnostic delays, it is important to identify which underlying factors (e.g., patient awareness of and response to cancer symptoms, access to healthcare and latency of referral to specialist care, lifestyle factors and comorbidities) that contribute to socioeconomic differences in tumour stage at diagnosis of ovarian cancer.

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Abbreviations

95% CI	95% confidence interval
BMI	Body mass index
OCAC	Ovarian Cancer Association Consortium
OR	odds ratio
pOR	pooled odds ratio
SES	socioeconomic status

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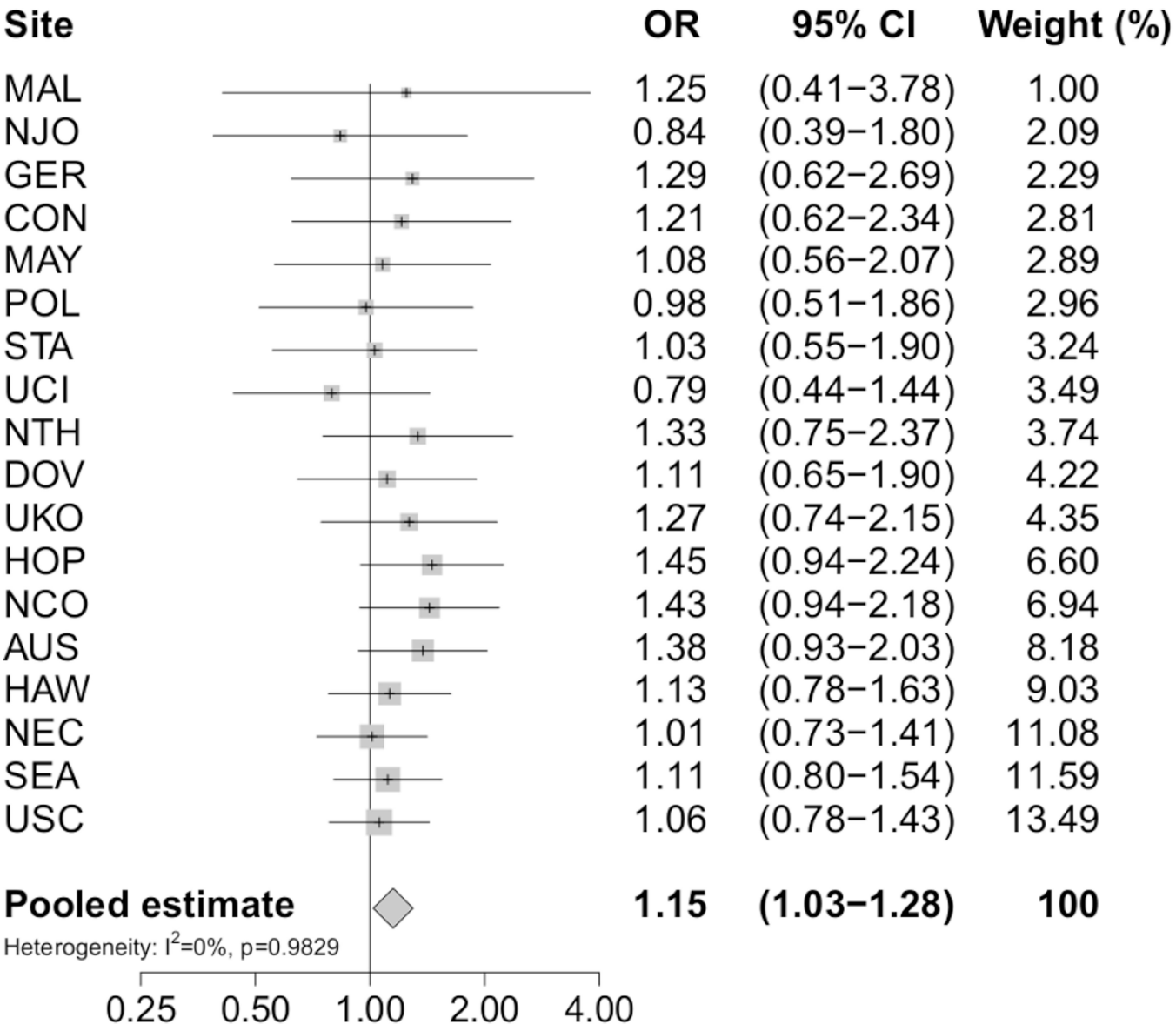

Fig. 1.

Risk of advanced tumour stage at diagnosis of ovarian cancer associated with level of education by study site and overall. Study-specific odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression models adjusted for age and race/ethnicity. The pooled odds ratio (pOR) with corresponding 95% CI was estimated using a random effects model. Level of education was parameterized as women who completed high school or less versus women who completed more than high school

Table 1

Characteristics of the 18 case-control studies included in the pooled analysis of level of education and stage at diagnosis of ovarian cancer.

Region	Study	Study acronym	Study period	Cases N	Women diagnosed at advanced tumour stage[a] (%)	Study type	Age range
Australia	Australian Ovarian Cancer Study and Australian Cancer Study (Ovarian Cancer)	AUS	2002–2006	1,073	950 (88.5)	Population-based	20–80
Europe	German Ovarian Cancer Study	GER	1993–1996	219	178 (81.3)	Population-based	21–75
	The Danish Malignant Ovarian Tumor Study	MAL	1994–1999	551	478 (86.8)	Population-based	32–80
	Nijmegen Ovarian Cancer Study	NTH	1989–2006	254	172 (67.7)	Hospital-based	23–83
	Polish Ovarian Cancer Case-Control Study	POL	2000–2003	183	112 (61.2)	Population-based	27–74
	Study of Epidemiology and Risk Factors in Cancer Heredity	SEA	1998–2010	917	522 (56.9)	Population-based	22–74
	UK Ovarian Cancer Population Study	UKO	2006–2010	524	443 (84.5)	Hospital-based	19–89
United States (US)	Connecticut Ovarian Cancer Study	CON	1998–2003	296	248 (83.8)	Population-based	36–81
	Diseases of the Ovary and their evaluation	DOV	2002–2005	592	504 (85.1)	Population-based	35–74
	Hawaii Ovarian Cancer Case-Control Study	HAW	1993–2008	681	486 (71.4)	Population-based	24–87
	Novel Risk Factors and Potential Early Detection Markers for Ovarian Cancer	HOP	2003–2009	663	552 (83.3)	Population-based	25–91
	Mayo Clinic Ovarian Cancer Case-Control Control Study	MAY	2000–2009	493	450 (91.3)	Clinic-based	21–91
	North Carolina Ovarian Cancer study	NCO	1999–2008	849	723 (85.2)	Population-based	22–74
	New England Case-Control Study	NEC	1992–2003	827	570 (68.9)	Population-based	21–77
	New Jersey Ovarian Cancer Study	NJO	2002–2008	230	184 (80.0)	Population-based	30–81
	Family Registry for Ovarian Cancer and Genetic Epidemiology of Ovarian Cancer	STA	1997–2001	488	376 (77.0)	Population-based	21–64
	University California Irvine Ovarian Study	UCI	1993–2005	384	310 (80.7)	Population-based	21–86
	Los Angeles County Case-Control Studies of Ovarian Cancer	USC	1993–2005	1,377	1,073 (77.9)	Population-based	20–84
TOTAL				**10,601**	**8,331 (78,6)**		**19–91**

[a]Women diagnosed with regional or distant stage

Table 2

Characteristics of women diagnosed with epithelial ovarian cancer, according to tumour stage at diagnosis.

	All (n = 10,601)	Localized stage (n = 2,270)	Advanced stage[b] (n = 8,331)	P-value
Age at diagnosis (years)				
Median	57.0	53.0	58.0	<0.001[c]
Interquartile range	49.0–65.0	45.7–62.0	50.0–66.0	
Histology				
Serous	6,066 (57.2)	501 (22.1)	5,565 (66.8)	<0.001[d]
Serous low-grade	479 (4.5)	98 (4.3)	381 (4.6)	
Serous high-grade	5,030 (47.4)	339 (14.9)	4,691 (56.3)	
Endometrioid	1,664 (15.7)	665 (29.3)	999 (12.0)	
Mucinous	780 (7.4)	480 (21.1)	300 (3.6)	
Clear cell	875 (8.3)	412 (18.1)	463 (5.6)	
Other[a]	1,216 (11.5)	212 (9.3)	1,004 (12.1)	
Level of education				
≤High school	5,190 (49.0)	1,054 (46.4)	4,136 (49.6)	0.008[d]
>High school	5,411 (51.0)	1,216 (53.6)	4,195 (50.4)	
BMI				
Median	24.0	23.6	24.1	<0.001[c]
Interquartile range	21.4–28.2	20.9–28.0	21.5–28.2	
Smoking status				0.02[d]
Never	5,770 (54.4)	1,227 (54.1)	4,543 (54.5)	
Former	3,391 (32.0)	694 (30.6)	2,697 (32.4)	
Current	1,440 (13.6)	349 (15.4)	1,091 (13.1)	
Race/ethnicity				<0.001[d]
Non-Hispanic White	9,129 (86.1)	1,878 (82.7)	7,251 (87.0)	
Hispanic White	306 (2.9)	62 (2.7)	244 (2.9)	
Black	265 (2.5)	53 (2.3)	212 (2.5)	
Asian	565 (5.3)	190 (8.4)	375 (4.5)	
Other	331 (3.1)	87 (3.8)	244 (2.9)	

[a] Includes mixed cell, undifferentiated and tumours of unknown histology

[b] Includes regional or distant stage

[c] The P-value was calculated using the Wilcoxon rank sum statistical test as the data were not normally distributed

[d] The P-value was calculated using the Pearson's chi square statistical test at the data were normally distributed

Numbers may not sum up to total because of missing data

Table 3

Adjusted pooled odds ratios (pORs) and 95% confidence intervals (95% CI) for the association between level of education and advanced stage at diagnosis of ovarian cancer, overall and by histotype.

	Model 1[a]		Model 2[b]	
	Cases (n = 10,601)	pOR (95% CI)	Cases (n = 10,457)	pOR (95% CI)
Overall				
>high school	5,411	1.00	5,362	1.00
≤high school	5,190	1.15 (1.03–1.28)	5,095	1.18 (1.05–1.32)
Serous				
>high school	3,003	1.00	2,973	1.00
≤high school	3,063	1.08 (0.87–1.34)	3,009	1.13 (0.90–1.41)
Serous low-grade				
>high school	143	1.00	142	1.00
≤high school	228	1.10 (0.51–2.35)	228	1.23 (0.49–3.12)
Serous high-grade				
>high school	2,568	1.00	2,541	1.00
≤high school	2,462	1.02 (0.78–1.32)	2,413	1.09 (0.83–1.43)
Endometrioid				
>high school	908	1.00	901	1.00
≤high school	756	1.10 (0.86–1.42)	749	1.17 (0.90–1.53)
Mucinous				
>high school	349	1.00	349	1.00
≤high school	271	0.97 (0.63–1.48)	266	1.09 (0.68–1.76)
Clear cell				
>high school	436	1.00	431	1.00
≤high school	390	1.19 (0.84–1.71)	376	1.21 (0.83–1.77)

[a] Adjusted for age (continuous variable) and race/ethnicity (Non-Hispanic White, Hispanic White, Black, Asian and other).

[b] Adjusted for the two factors in Model 1 plus adjustment for BMI (continuous variable) and cigarette smoking status (never, former or current).