Supplemental Appendix

Supplemental Tables

Table S1: Published findings of association between menopausal hormone therapy use and ovarian cancer survival (Online only).

Author, Year	HR (95% CI) overall survival for any HT use	Type	Study design	N, population	Notes
Pre-diagnosis					
Mascarenhas, 2006[5]	0.83 (0.65, 1.08)	Any	Cohort, follow-up on population-based cases	649, Sweden	Examination of different HRT preparations did not give different HRs
Wernli, 2008[6]	1.1 (0.85, 1.43)	Any	Case-control, population based	751, United States	
Nagle, 2008[7]	0.83 (0.64, 1.08)	Any	Cohort, population-based	676, Australia	
Zhang, 2012[8]	0.23 (0.03, 1.73)	Any	Cohort	195, China	
Hein, 2013[9]	75% (65, 86) 5-yr survival for HRT users; 43% (36, 52) for non-users	Any	Cohort	244, Bavaria	Women who had used HRT: younger, lower stage, more optimal debulking
Shafrir, 2016[10]	0.70 (0.55, 0.9)	Any	Cohort	1649, United States	
Kim, 2017[11]	0.79 (0.62, 1.01)	Any	Cohort, registry-based	1421, Canada	
Besevic, 2015[12]	0.80 (0.55, 1.16)	EPT	Cohort	1025, Europe	
	0.86 (0.54, 1.35)	ET			
Felix, 2015[13]	0.97 (0.68, 1.38)	EPT	Cohort, population-based	396, United States	Noted interaction between HRT type and histology
	1.09 (0.7, 1.68)	ET			
Post-diagnosis					
Eeles, 1991[14]	0.73 (0.44, 1.2)	Any	Cohort, retrospective	373, United Kingdom	No difference in disease-free interval
Ursic-Vrscaj,	0.67 (0.27, 1.62) (relapse)	Any	Case-control	72, Slovenia	

2001[15]	0.90 (0.24, 5.08) (survival)	Any			
Mascarenhas, 2006[5]	0.57 (0.42, 0.78)	Any	Cohort, follow-up on population-based cases	649, Sweden	Examination of different HRT preparations did not give different HRs
Wen, 2013[16]	0.82 (0.48, 1.4) (relapse)	Any	Cohort, retrospective	144, China	
	0.67 (0.18, 2.5) (survival)	Any			
Eeles, 2015[17]	0.63 (0.44, 0.90)	Any	RCT	150, United Kingdom, Spain, and Hungary	Greater relapse-free survival, HR=0.67 (0.47, 0.97)
Power, 2016[18]	0.50 (0.23, 1.09) (<55yrs old)	Any	Cohort, retrospective	357, Manitoba, Canada	
	0.85 (0.43, 1.68) (≥55yrs old)	Any			
Li, 2012[19]	0.88 (0.35, 2.32)	EPT	Cohort, prospective	75, China	
Guidozzi, 1999[20]	0.97 (0.65, 1.18) (relapse)	ET	RCT	125, South Africa	Non-significantly better overall survival as well

Table S2: Ovarian Cancer Association Consortium (OCAC) study sites with women included in the analysis (Online only).

Site code	N (%)	Full study name	Country	Study design	Data collection	Diagnosis years	Residual Disease information
AUS	558 (8.7)	Australian Ovarian Cancer Study	Australia	Population-based	Self-completed questionnaire	2002-2006	Yes
CON	241 (3.8)	Connecticut Ovary Study	United States	Population-based	In-person interview	2002-2009	No
DOV	569 (8.9)	Diseases of the Ovary and their Evaluation	United States	Population-based	In-person interview	2002-2009	No
GER	97 (1.5)	Germany Ovarian Cancer Study	Germany	Population-based	Self-completed questionnaire	1992-1998	No
HAW	265 (4.1)	Hawaii Ovarian Cancer Study	United States	Population-based	In-person interview	1994-2007	Yes
HOP	407 (6.3)	Hormones and Ovarian Cancer Prediction	United States	Population-based	In-person interview	2003-2008	Yes
MAL	377 (5.9)	Danish Malignant Ovarian Tumor Study	Denmark	Population-based	In-person or telephone interview	1994-1999	No
MAY	638 (9.9)	Mayo Clinic Ovarian Cancer Case Control Study	United States	Clinic-based	In-person interview	1999-2008	Yes
NEC	879 (13.7)	New England Case-Control Study	United States	Population-based	In-person interview	1992-2008	Yes
NJO	118 (1.8)	New Jersey Ovarian Cancer Study	United States	Population-based	Telephone interview	2004-2008	No
OPL	478 (7.4)	Ovarian Cancer Prognosis and Lifestyle Study	Australia	Population-based	Self-completed questionnaire	2012-2015	Yes
POL	109 (1.7)	Polish Ovarian Cancer Case-Control Study	Poland	Population-based	In-person interview	2001-2003	No
UCI	221 (3.4)	UC Irvine Ovarian Cancer Study	United States	Population-based	Self-completed questionnaire	1995-2005	No
UKO	352 (5.5)	UK Ovarian Cancer Population Study	United Kingdom	Population-based	Self-completed questionnaire	2006-2007	No
USC	1110 (17.3)	Study of Lifestyle and Women's Health	United States	Population-based	In-person interview	1993-2005	No

Table S3a: Hazards ratios, by histotype, for menopausal hormone therapy (MHT) use before diagnosis of ovarian cancer among women with invasive epithelial ovarian cancer in the Ovarian Cancer Association Consortium (OCAC) (Online only).

	Overall	High-grade serous	Mucinous	Endometrioid	Clear cell	Low-grade serous
N	6,419	4,393	373	925	483	245
MHT use	HR (95% CI)[a]					
None (ref)	1.0	1.0	1.0	1.0	1.0	1.0
<5 years	0.97 (0.88, 1.06)	0.94 (0.85, 1.04)	1.77 (1.04, 3.02)	0.99 (0.71, 1.37)	0.97 (0.62, 1.51)	0.98 (0.58, 1.66)
5+ years	0.80 (0.74, 0.87)	0.78 (0.71, 0.86)	0.66 (0.34, 1.26)	1.08 (0.81, 1.43)	0.83 (0.47, 1.48)	0.76 (0.47, 1.23)

[a] Hazard ratios (HRs) are adjusted for age at diagnosis and race/ethnicity, and stratified by histotype (overall analysis only), stage at diagnosis, and OCAC site.

Table S3b: Hazard ratios (95% CIs) for MHT use and overall survival, for high-grade serous histology by stage of disease at diagnosis (Online only).

	High-grade serous HR (95% CI)
MHT use[a]	
Stage I (local)	N=205
<5 years	0.69 (0.32, 1.46)
5+ years	0.62 (0.28, 1.35)
Stage II (regional)	N=469
<5 years	0.83 (0.54, 1.30)
5+ years	0.72 (0.48, 1.08)
Stage III and IV (advanced/distant)	N=3719
<5 years	0.96 (0.86, 1.06)
5+ years	0.79 (0.71, 0.86)*

[a] Reference category of no use for all analyses.
[b] Hazard ratios (HRs) are adjusted for age at diagnosis and race/ethnicity, and stratified by OCAC site.
* Significant at a level of $p<0.001$.

Table S4: HR for MHT use and progression-free survival of ovarian cancer (Online only).

	Progression-free survival
N[a]	2,150
MHT use	HR (95% CI)[b]
None (ref)	1.0
<5 years	0.94 (0.81, 1.09)
5+ years	0.94 (0.82, 1.09)

[a] Data on presence of progression and time to progression was only available for a subset of the women.
[b] Hazard ratios (HRs) were adjusted for age at diagnosis and race/ethnicity, and stratified by histotype, stage at diagnosis, and OCAC site.

Table S5: Hazards ratios for MHT use and overall survival in a fully adjusted model (Online only).

	Among women with complete information for all variables, N=4,044			
	Unadjusted	**Age and stage[1]**	**Primary model**	**Fully adjusted[2] model**
Variable included	--	Age at diagnosis, stage at diagnosis	Age, stage, race/ethnicity, histotype, OCAC site	
MHT use			HR (95% CI)[a]	
None (ref)	1.0	1.0	1.0	1.0
<5 years	0.96 (0.87, 1.07)	0.96 (0.86, 1.06)	0.96 (0.87, 1.07)	0.96 (0.87, 1.07)
5+ years	0.98 (0.89, 1.08)	0.80 (0.73, 0.88)	0.79 (0.71, 0.87)	0.79 (0.71, 0.88)

[1] Change in HR estimates was primarily driven by accounting for stage, though age confounded the relationship as well.
[2] Stratified by stage at diagnosis, OCAC site, histotype, and adjusted for age at diagnosis, race/ethnicity, BMI, education level, tubal ligation, endometriosis, hysterectomy, combined oral contraceptive use duration (never, <1 year, 1 to <5 years, 5 to <10 years, 10+ years), parity, family history of breast cancer, family history of ovarian cancer, smoking status (never, former, current).

Table S6: Hazard ratios (HRs) for MHT use and overall survival, among advanced stage, high-grade serous carcinoma, stratified by macroscopic residual disease (Online only).

	HR (95% CI)	
MHT use	Residual disease N=891	No residual disease N=497
None (ref)	1.0	1.0
<5 years	1.08 (0.86, 1.35)	1.07 (0.74, 1.53)
5+ years	0.89 (0.68, 1.17)	0.81 (0.54, 1.22)

Supplemental Figures

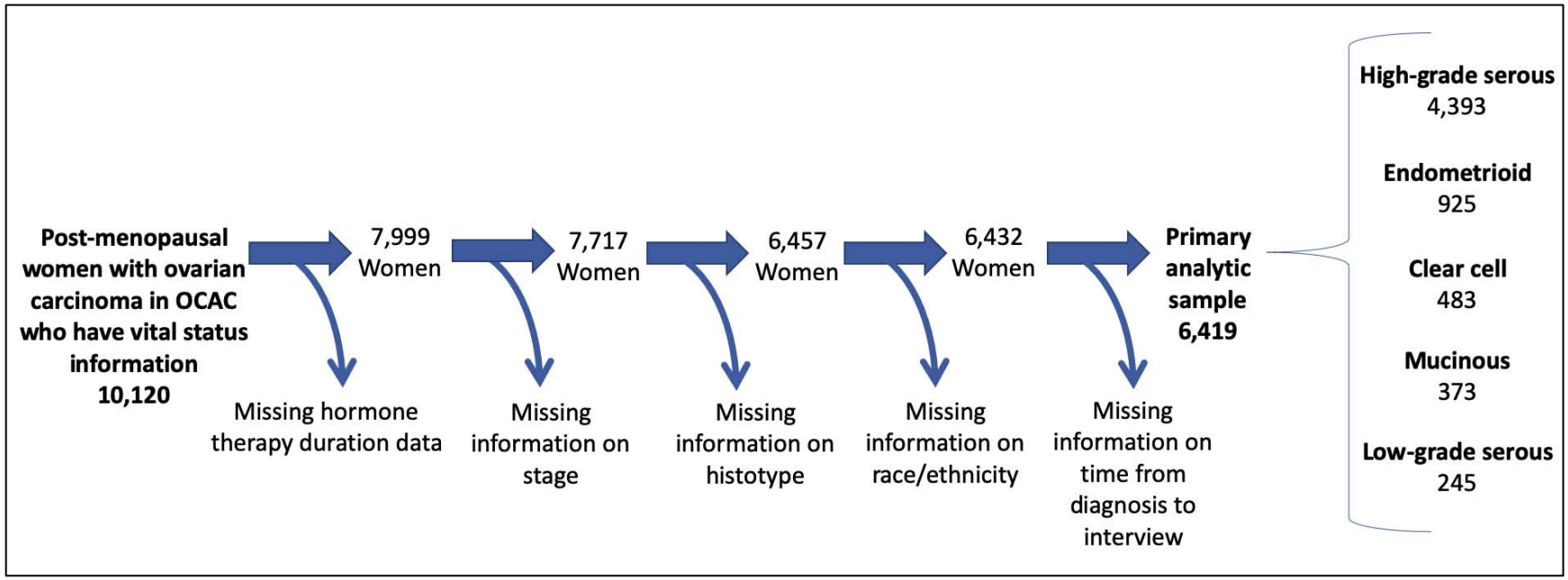

Figure S1: Study participants. All women were from the Ovarian Cancer Association Consortium (OCAC). The population-based and clinic-based studies included were done in the United States (n=9), Europe (n=4), and Australia (n=2). Only post-menopausal women with ovarian carcinoma for whom survival time data was available were considered for this analysis. The exclusion stage "missing histotype" included exclude of those with mixed cell and undifferentiated tumors. Of the five histotypes high-grade serous was the most common (68% of cases) among these women, followed by endometrioid (14%), clear cell (7.5%), mucinous (5.8%), and low-grade serous (3.8%). Of the 6,419 women in our analytic sample, subsets with complete information were analyzed for progression-free survival (n=2,239) and for the association between hormone therapy and residual disease (n=2,056). Time of interview refers to time of study enrollment; for some studies this was an in-person interview and for some it was a self-administered questionnaire.

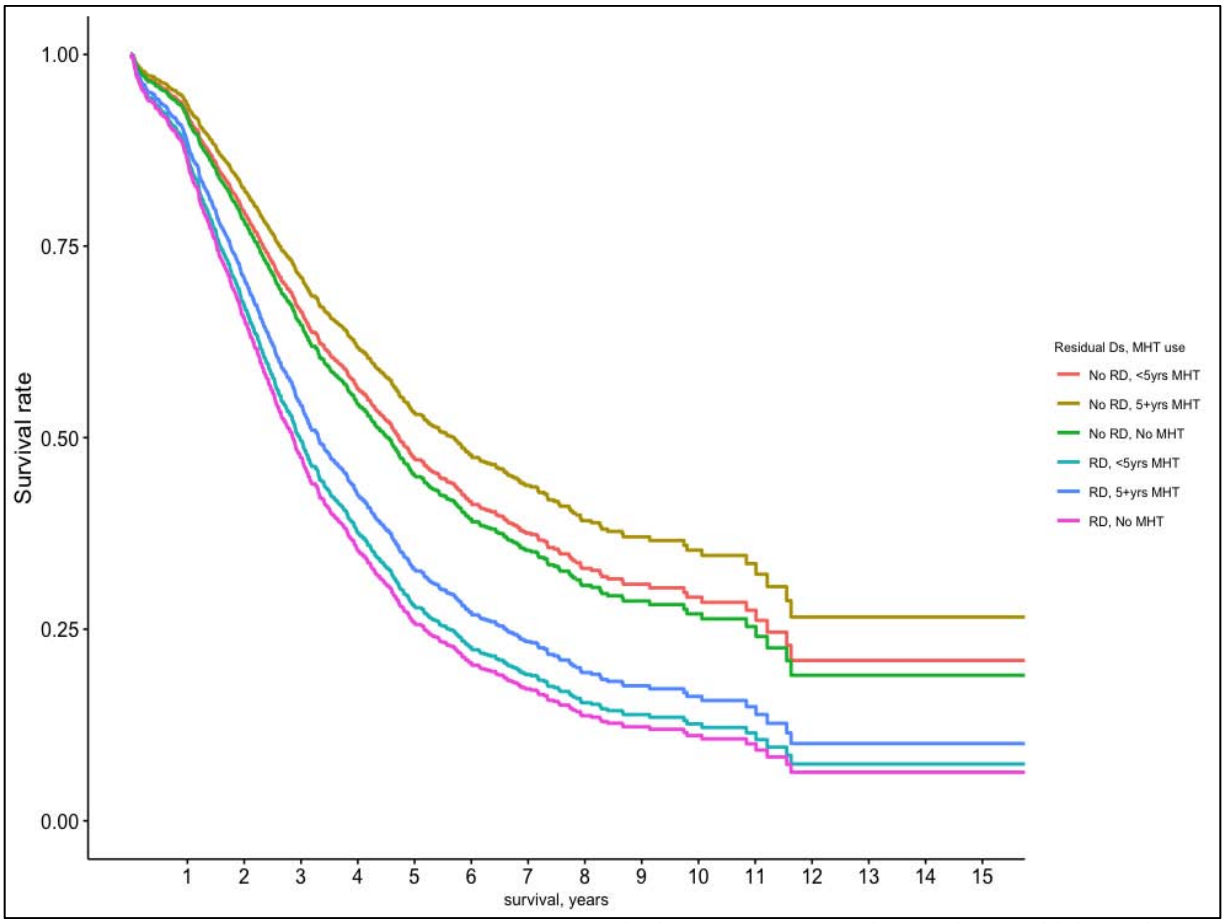

Figure S2: Adjusted overall survival curves. Survival curves, among advanced stage, high-grade serous carcinoma. Adjusted for age, race/ethnicity, and OCAC site.