

Long-term survival of non-localized epithelial ovarian cancer among women using menopausal hormone therapy prior to diagnosis - the Extreme study

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Supplementary Table S1. Classification of epithelial ovarian and fallopian tube cancer cases occurring in the Danish Cancer Registry and/or the Danish Pathology Registry 1978–2014

Histologic type	Morphology codes (ICD-O-3 and SNOMED)
Serous including papillary adenocarcinomas	80503; 82603; 84413; 84503; 84603; 84613; 90143
Mucinous	84703; 84713; 84803; 84813; 84903; 90153
Endometrioid	83803; 83813; 85703
Clear cell	83103; 83133
Other adenocarcinomas	81403; 81413; 81433; 81443; 83233; 83843; 84403; 84743; 85713; 91103
Others	80103; 80123; 80203; 80213; 80223; 80313; 80333; 80413; 80423; 80463; 80703; 80713; 80763; 80833; 80903; 81203; 81303; 82003; 82303; 82463; 82473; 82493; 83203; 85103; 85603; 85753; 89333; 89343; 89503; 89513; 89803; 89903; 90003

Abbreviations: ICD-O-3, the 3rd revision of the International Classification of Diseases for Oncology; SNOMED, the Systematized Nomenclature of Medicine.

Supplementary Table S2. Classification of menopausal hormone therapy in the Danish Prescription Registry

Regimen	Chemical content	ATC
I. Systemic estrogen	Estradiol	G03C A03
	Estriol	G03C A04
		G03C A53
	Conjugated estrogen	G03C A57
II. Systemic progestagen	Norethisterone	G03D C02
	Medroxyprogesterone acetate	G03D A02
		G03D A04
	Lynestrenol	G03D C03
III. Systemic, combined cyclic	Norethisterone acetate-estradiol	G03F B05
	Medroxyprogesterone acetate-estradiol valerat	G03F B06
	Levonorgestrel-estradiol valerat	G03F B01
		G03F B09
IV. Systemic, combined continuous	Norethisterone acetate-estradiol	G03F A01
	Medroxyprogesterone acetate-estradiol valerat	G03F A12
	Tibolone	G03D C05 (before 2008)
		G03C X01 (2008 and after)
	Raloxifene	G03X C01
V. Local, estrogen	Estradiol	G03C A03
	Estriol	G03C A04
	Conjugated estrogen	G03C A57
	Dienestrol	G03C B01
VI. Intrauterine devices, progestagen	Levonorgestrel	G02B A03

Supplementary Table S3. Codes defining comorbidity

	ICD-8 (1977–1993)	ICD-10 (since 1994)
Diabetes mellitus*	249; 250	DE10–DE14
Chronic obstructive pulmonary disease	491–492	DJ41–DJ44
Ischemic heart disease	410–414	DI20–I25
Congestive heart disease	427.09; 427.10; 427.11; 427.19; 428.99; 782.49	DI50; DI11.0; DI13.0; DI13.2
Cerebrovascular disease	430–438	DI60–DI69; DG45; DG46
Atrial fibrillation	427.93; 427.94	DI48

*Diabetes mellitus was a composite measure of diagnosis and prescription for anti-diabetics drugs (ATC A10A; A10BB; A10BC; A10BD04; A10BD09; A10BF; A10BG; A10BH; A10BX).

Supplementary Table S4. Characteristics of the study cohort of women 2005–2014 with non-localized epithelial ovarian cancer (N=2,207)

	N	%
Calendar year		
2005–2009	1,129	(51.2)
2010–2014	1,078	(48.8)
Age at diagnosis (years)		
50–59	416	(18.8)
60–69	764	(34.6)
70–79	676	(30.6)
≥80	351	(15.9)
Histology		
Serous	1,510	(68.4)
Mucinous	47	(2.1)
Endometrioid	73	(3.3)
Clear cell	43	(1.9)
Other adenocarcinomas	383	(17.4)
Others	151	(6.9)
Use of MHT prior to diagnosis		
Non-use of MHT	1,172	(53.1)
Systemic ET	415	(18.8)
EPT	553	(25.1)
Other MHT	67	(3.0)
Comorbidity		
COPD	131	(5.9)
Diabetes mellitus type I and II	176	(8.0)
Cerebrovascular disease	162	(7.3)
Congestive heart disease	81	(3.7)
Atrial fibrillation	138	(6.3)
Ischemic heart disease	219	(9.9)
Income		
Low	462	(20.9)
Medium	770	(34.9)
High	975	(44.2)
Residual disease		
Yes	931	(42.2)
No	530	(24.0)
Missing	746	(33.8)
Smoking		
Previous smoker	453	(20.5)
Current smoker	315	(14.3)

Never smoker	968	(43.9)
Missing	467	(21.2)
BMI		
BMI registered	1,847	(83.7)
Missing	360	(16.3)

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; EPT, estrogen plus progestin therapy; ET, estrogen therapy; MHT, menopausal hormone therapy.

Supplementary Table S5. Ever use of prediagnostic menopausal hormone therapy (MHT) prior to diagnosis of non-localized epithelial ovarian and fallopian tube cancer and 5- and 10-year relative survival probabilities. The analysis is stratified by postdiagnostic menopausal hormone therapy use during the first year after diagnosis and restricted to women surviving minimum one year.

	Use of postdiagnostic MHT				Non-use of postdiagnostic MHT			
	N	Crude absolute survival probability (95% CI)	Adj. relative survival probability* (95% CI)	Adj. absolute survival difference* (95% CI)	N	Crude absolute survival probability (95% CI)	Adj. relative survival probability* (95% CI)	Adj. absolute survival difference* (95% CI)
Pre-diagnostic use								
5-year survival								
Non-use of MHT	67	0.37 (0.25–0.49)	Ref.	Ref.	1,257	0.24 (0.22–0.27)	Ref.	Ref.
Ever use of MHT	349	0.31 (0.26–0.36)	0.96 (0.68–1.36)	-0.02 (-0.15–0.11)	822	0.24 (0.21–0.26)	0.96 (0.82–1.13)	-0.01 (-0.05–0.03)
Non-use of MHT	67	0.37 (0.25–0.49)	Ref.	Ref.	1,257	0.24 (0.22–0.27)	Ref.	Ref.
Ever use of systemic ET	132	0.30 (0.22–0.37)	0.95 (0.62–1.46)	-0.01 (-0.15–0.14)	303	0.25 (0.20–0.30)	1.13 (0.90–1.41)	0.02 (-0.03–0.08)
Ever use of EPT	210	0.32 (0.26–0.39)	0.98 (0.69–1.39)	-0.02 (-0.16–0.11)	452	0.23 (0.19–0.27)	0.89 (0.73–1.09)	-0.02 (-0.07–0.02)
Ever use of other MHT	7	0.13 (-0.19–0.44)	0.17 (0.00–6.38)	-0.23 (-0.60–0.14)	67	0.22 (0.12–0.32)	0.86 (0.54–1.38)	-0.03 (-0.13–0.07)
10-year survival								
Non-use of MHT	67	0.18 (0.07–0.30)	Ref.	Ref.	1,257	0.16 (0.13–0.18)	Ref.	Ref.
Ever use of MHT	349	0.21 (0.16–0.26)	1.14 (0.64–2.05)	0.07 (-0.05–0.19)	822	0.13 (0.10–0.15)	0.86 (0.68–1.09)	-0.03 (-0.06–0.01)
Non-use of MHT	67	0.18 (0.07–0.30)	Ref.	Ref.	1,257	0.16 (0.13–0.18)	Ref.	Ref.
Ever use of systemic ET	132	0.20 (0.12–0.27)	1.09 (0.57–2.09)	0.08 (-0.05–0.22)	303	0.14 (0.10–0.19)	1.05 (0.77–1.45)	0.00 (-0.04–0.05)
Ever use of EPT	210	0.22 (0.16–0.29)	1.12 (0.62–2.03)	0.07 (-0.06–0.19)	452	0.12 (0.09–0.15)	0.77 (0.57–1.04)	-0.04 (-0.08–0.01)
Ever use of other MHT	7	0.15 (-0.19–0.48)	0.35 (0.01–8.90)	-0.02 (-0.40–0.36)	67	0.12 (0.04–0.19)	0.81 (0.45–1.48)	-0.04 (-0.12–0.03)

Abbreviations: EPT, estrogen plus progestin therapy; ET, estrogen therapy; MHT, menopausal hormone therapy.

* Adjusted for age, year, histology, comorbidities, and income.

Supplementary Table S6. Ever use of prediagnostic menopausal hormone therapy (MHT) prior to diagnosis of non-localized epithelial ovarian and fallopian tube cancer and 5- and 10-year relative survival probabilities. The analysis is restricted to the study population 2005–2014 and with additional adjustment for smoking and body mass index (BMI).

	N	Crude relative survival probability (95% CI)	Adj. relative survival probability* (95% CI)	Relative survival probability with additional adjustment for smoking and BMI (95% CI)
Pre-diagnostic use				
5-year survival				
Non-use of MHT	704	Ref.	Ref.	Ref.
Ever use of MHT	592	1.13 (0.94–1.37)	1.12 (0.93–1.35)	1.12 (0.93–1.35)
Non-use of MHT	704	Ref.	Ref.	Ref.
Ever use of systemic ET	238	1.07 (0.83–1.37)	1.13 (0.87–1.46)	1.12 (0.86–1.46)
Ever use of EPT	318	1.17 (0.94–1.46)	1.09 (0.87–1.36)	1.09 (0.87–1.36)
Ever use of other MHT	36	1.25 (0.74–2.11)	1.32 (0.84–2.10)	1.33 (0.84–2.09)
10-year survival				
Non-use of MHT	704	Ref.	Ref.	Ref.
Ever use of MHT	592	0.95 (0.72–1.25)	0.91 (0.70–1.18)	0.92 (0.71–1.19)
Non-use of MHT	704	Ref.	Ref.	Ref.
Ever use of systemic ET	238	0.86 (0.59–1.26)	0.93 (0.65–1.34)	0.94 (0.65–1.35)
Ever use of EPT	318	1.02 (0.74–1.42)	0.89 (0.65–1.23)	0.90 (0.66–1.24)
Ever use of other MHT	36	0.82 (0.36–1.86)	0.93 (0.48–1.80)	0.94 (0.49–1.80)

Abbreviations: BMI, body mass index; EPT, estrogen plus progestin therapy; ET, estrogen therapy; MHT, menopausal hormone therapy.

* Adjusted for age, year, histology, comorbidities, and income.