

**Supplementary appendix: Employment disruption among women with gynecologic cancers**

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### Appendix 1. International Classification of Diseases (ICD)-9, ICD-10, and Current Procedural Terminology (CPT) codes

Endometrial cancer:

Procedure	ICD-9	CPT	ICD-10
Abdominal hysterectomy	68.0, 68.3, 68.39, 68.4, 68.49, 68.6, 68.69, 68.9	58150, 58180, 58200, 58210, 58953, 58954, 58956, 59100	0UB90ZX 0UB90ZZ
Laparoscopic hysterectomy (including LAVH)	68.31, 68.41, 68.51, 68.61, 68.71	58541, 58542, 58543, 58544, 58548, 58550, 58552, 58553, 58554, 58570, 58571, 58572, 58573	0UB93ZX 0UB93ZZ 0UB94ZZ 0UB94ZX
Robotic-assisted hysterectomy	Hysterectomy code + 17.4, 17.41, 17.42, 17.43, 17.44, 17.49	Hysterectomy code + S2900	8E0W3CZ 8E0WXCZ 8E0W4CZ
Vaginal hysterectomy	68.5, 68.59, 68.7, 68.79	58260, 58262, 58263, 58270, 58275, 58280, 58285, 58290, 58291, 58292, 58294	0UB97ZX 0UB97ZZ

Cervical cancer:

Procedure	ICD-9	CPT	ICD-10
Radical hysterectomy	68.6, 68.7	58285, 58210, 58240, 58548	
Radiation		77401-77425	DWY3, DWY6
Other hysterectomy types as above			0UT4, 0UT9
Trachelectomy, radical trachelectomy	67.4	57530, 57531	0UTC
<b>Diagnosis</b>	<b>ICD-9</b>		<b>ICD-10</b>
	180, 180.0, 180.1, 180.8, 180.9		c53, c53.0, c53.1, c53.8, c53.9

Ovarian cancer:

Procedure	ICD-9	CPT	ICD-10
Oophorectomy	65.3, 65.39, 65.4, 65.49, 65.5, 65.51, 65.52, 65.6, 65.61, 65.62	58720, 58940, 58661	0UT0, 0UT1, 0UT2, 0UT5, 0UT6, 0UT7, 0UB0, 0UB1, 0UB2, 0UB5

Removal ovary with or without multiple procedures for malignancy (hysterectomy as above)		58940-58960	
Chemo (IP)		96446	
<b>Diagnosis</b>	<b>ICD-9</b>		<b>ICD-10</b>
Ovarian cancer	183,183.x, 158.8, 158.9		C56
Fallopian tube cancer	183.2		C57
Primary peritoneal cancer	183.8, 183.9		C48.1, C48.2, C48.8

## Vulvar cancer

<b>Procedure</b>	<b>ICD-9</b>	<b>CPT</b>	<b>ICD-10</b>
Radical vulvectomy		56633, 56630	0UBM, 0UTM
Vulvectomy	71.6	56620, 56625	
Radical vulvectomy + lymph node dissection		56634, 56637, 56632, 56631, 56640	07BC, 07BF, 07BG, 07BH, 07BJ
<b>Diagnosis</b>	<b>ICD-9</b>		<b>ICD-10</b>
Vulvar cancer	184.4		c51

Applicable to all gynecologic cancer types:

<b>Procedure</b>	<b>ICD-9</b>	<b>CPT</b>	<b>ICD-10</b>
Lymphadenectomy	40.0, 40.1, 40.11, 40.3, 40.5, 40.52, 40.53, 40.59	38589, 38562, 38564, 38570, 38571, 38572, 38770, 38780, 38792, 38900, 58200, 58210, 58548, 58954	07BC0ZZ 07BC3ZZ 07BD0ZZ 07BD3ZZ
Brachytherapy	92.27	57156, 55920, 77326, 77327, 77328, 77750, 77761-77789	D717, DU12, D7179, D71797, D71797Z, D71798, D71798Z, D71799, D71799Z, D7179B, D7179BZ, D7179C, D7179CZ, D7179Y, D7179YZ, D717B, D717B7, D717B7Z, D717B8, D717B8Z, D717B9, D717B9Z, D717BB, D717BB1, D717BBZ, D717BC, D717BCZ, D717BY, D717BYZ, DU1297Z, DU1298Z, DU1299Z, DU129BZ, DU129CZ, DU129YZ, DU12B7Z, DU12B8Z, DU12B9Z, DU12BB1, DU12BBZ, DU12BCZ, DU12BYZ
External beam radiation	92.2, 92.20-92.27, 92.29, 92.3, 92.30-92.39, 92.4, 92.41	77371-77373, 77401-77416, 77418, 77422-77425, 77520-77525, 77761-77789, G0174, G0251, G0339, G0340, 0182T	DU020ZZ, DU021ZZ, DU022ZZ, DU023Z0, DU023ZZ, DU024ZZ, DU025ZZ, DU026ZZ, DWY6

Chemotherapy	V581, V5811, V5812, V662, V672, 9925, 9928	J9045, J9060, J9062, C9418, J9000, J9001, J9002, Q2048, Q2049, Q2050, J9190, J9201, C9127, C9431, J9264, J9265, J9267, 96400, 96401, 96402, 96405, 96406, 96408, 96409, 96410, 96411, 96412, 96413, 96414, 96415, 96416, 96417, 96420, 96422, 96423, 96425, 96440, 96445, 96446, 96450, 96500, 96501, 96504, 96505, 96508, 96509, 96510, 96511, 96512, 96520, 96521, 96522, 96523, 96524, 96526, 96530, 96535, 96538, 96540, 96542, 96545, 96549, C8953, C8954, C8955, G0355, G0356, G0357, G0358, G0359, G0360, G0361, G0362, Q0083, Q0084, Q0085, S9329, S9330, S9331, S9338, 99555, J8999, J9999	Z51.11, 3E00X05, 3E03305, 0JH63VZ
Secondary malignant neoplasm	197-199		C78, C79, C80

## Appendix 2. Analysis of sensitivity to unmeasured confounders

Sensitivity analysis can be used to assess the robustness of associations against potential unmeasured or uncontrolled confounders. The E-value is defined as the minimum strength of association, on the risk-ratio (RR) scale, that an unmeasured confounder would need to have with both the treatment and outcome, conditional on the measured covariates, to explain away a treatment-outcome association.<sup>1</sup> When the outcome is uncommon, such as in our study (< 15%), the hazard ratio can substitute for the RR in the following formula described by VanderWeele and Ding<sup>1</sup>:

$$\text{E-value} = \text{RR} + \sqrt{[\text{RR} \times (\text{RR} - 1)]}$$

To calculate the E-value required to include 1.0 (the null) in the CI, we used the following formula<sup>1</sup>:

$$\text{E-value} = \text{LL} + \sqrt{[\text{LL} \times (\text{LL} - 1)]}$$

where LL = the lower confidence level derived from the study.

**Appendix 3. Adjusted hazard ratios for employment change in patients with vulvar, cervical, ovarian, and endometrial cancer reported to MarketScan (2009-2018)**

Characteristic	Vulvar cancer		Cervical cancer		Ovarian cancer		Endometrial cancer	
	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value
<b>Age at diagnosis, n (%)</b>								
44 or less	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
45 to 49	1.06 (0.26-4.30)	.9	1.04 (0.68-1.57)	.9	1.09 (0.77-1.53)	.6	0.88 (0.68-1.15)	.3
50 to 53	0.47 (0.10-2.29)	.3	1.17 (0.71-1.94)	.5	0.91 (0.64-1.29)	.6	0.76 (0.59-0.98)	.03
54 to 57	1.36 (0.38-4.95)	.6	1.46 (0.88-2.42)	.1	1.09 (0.79-1.51)	.6	1.04 (0.84-1.29)	.7
58 to 63	1.37 (0.40-4.72)	.6	1.17 (0.74-1.86)	.5	1.41 (1.05-1.90)	.02	1.23 (1.00-1.51)	.05
<b>Health insurance plan type, n (%)</b>								
HMO	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
PPO	0.38 (0.11-1.25)	.1	1.16 (0.74-1.83)	.5	0.98 (0.73-1.31)	.9	1.17 (0.96-1.42)	.1
Other*	0.62 (0.17-2.27)	.5	1.24 (0.76-2.01)	.4	1.04 (0.75-1.44)	.8	1.64 (1.33-2.03)	<.0001
<b>Region, n (%)</b>								
Northeast	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
North Central	2.24 (0.72-6.92)	.2	0.99 (0.63-1.56)	.1	1.18 (0.84-1.67)	.3	1.17 (0.97-1.41)	.09
South	0.36 (0.10-1.26)	.1	0.85 (0.56-1.28)	.4	0.97 (0.71-1.31)	.8	0.69 (0.57-0.83)	<.0001
West	0.39 (0.08-1.97)	.2	0.90 (0.56-1.46)	.7	1.81 (1.31-2.50)	.0003	1.18 (0.96-1.44)	.1
<b>Charlson Comorbidity Index score, n (%)</b>								
0	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
1+	1.69 (0.50-5.69)	.4	2.18 (1.34-3.55)	.002	1.16 (0.81-1.66)	.4	1.18 (0.99-1.41)	.06
<b>Treatment group, n (%)</b>								
Surgery only	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Surgery with adjuvant treatment	0.53 (0.15-1.92)	.3	1.23 (0.86-1.75)	.2	1.90 (1.49-2.43)	<.0001	1.36 (1.02-1.80)	.03
Chemotherapy, radiation, or chemoradiation only			1.05 (0.66-1.66)	.8	2.52 (1.71-3.70)	<.0001	1.05 (0.62-1.75)	.9

<b>Adverse events, n (%)</b>							
None		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
1		0.63 (0.36-1.10)	.1	1.22 (0.97-1.55)	.09	1.04 (0.87-1.24)	.7
2+		0.98 (0.31-3.16)	.9	0.99 (0.56-1.73)	.9	1.03 (0.64-1.65)	.9
<b>Year of diagnosis, n (%)</b>							
2009		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
2010		0.92 (0.44-1.96)	.8	1.25 (0.73-2.16)	.4	0.81 (0.60-1.10)	.2
2011		1.29 (0.61-2.69)	.5	1.19 (0.70-2.04)	.5	0.91 (0.69-1.21)	.5
2012		1.42 (0.72-2.83)	.3	0.95 (0.55-1.65)	.8	0.74 (0.55-0.99)	.04
2013		1.21 (0.59-2.47)	.6	1.57 (0.90-2.71)	.1	0.85 (0.64-1.14)	.3
2014		1.13 (0.55-2.31)	.7	0.85 (0.45-1.60)	.6	0.72 (0.53-0.98)	.03
2015		1.38 (0.73-2.60)	.3	1.28 (0.76-2.17)	.3	0.86 (0.65-1.13)	.3
2016		1.24 (0.66-2.36)	.5	1.57 (0.97-2.54)	.06	0.93 (0.71-1.21)	.6
2017		1.15 (0.59-2.25)	.7	1.45 (0.89-2.35)	.1	0.90 (0.68-1.18)	.4

\*Other health insurance plans include comprehensive, point-of-service, point-of-service with capitation, high-deductible, and exclusive-provider-organization health plans.

Abbreviations: HMO, health maintenance organization; HR, hazard ratio; PPO, preferred provider organization.



**Appendix 4. Characteristics of patients with gynecologic cancer diagnosed between 2009 and 2017 and male and female controls, before and after propensity-score matching**

Characteristic	Before matching			Propensity score-matched cohort*		
	Patients with gynecologic cancer (n = 7446)	Controls (n = 6 746 428)	P <sup>‡</sup>	Patients with gynecologic cancer (n = 7391)	Controls (n = 29 078)	P
<b>Age at cohort entry, median (IQR)†</b>	53 (46,58)	46 (36,54)	<.0001	53 (46,58)	53 (46,58)	.6
<b>Age at cohort entry by group, n (%)†</b>			<.001			.9
44 or less	1613 (21.7)	3 176 568 (47.1)		1604 (21.7)	6369 (21.9)	
45 to 49	1038 (13.9)	988 626 (14.7)		1032 (14.0)	4072 (14.0)	
50 to 53	1176 (15.8)	807 257 (12.0)		1166 (15.8)	4598 (15.8)	
54 to 57	1611 (21.6)	805 891 (11.9)		1595 (21.6)	6244 (21.5)	
58 to 63	2008 (27.0)	968 086 (14.3)		1994 (27.0)	7795 (26.8)	
<b>Health insurance plan type, n (%)</b>			<.001			.6
HMO	1130 (15.2)	915 712 (13.6)		1103 (14.9)	4205 (14.5)	
PPO	4158 (55.8)	3 746 416 (55.5)		4152 (56.2)	16443 (56.5)	
Other <sup>§</sup>	2158 (29.0)	2 084 300 (30.9)		2136 (28.9)	8430 (29.0)	
<b>Region, n (%)</b>			.002			.7
Northeast	1290 (17.3)	1 100 983 (16.3)		1273 (17.2)	4981 (17.1)	
North Central	1660 (22.3)	1 476 271 (21.9)		1646 (22.3)	6448 (22.2)	
South	3056 (41.0)	2 758 635 (40.9)		3050 (41.3)	12117 (41.7)	
West	1432 (19.2)	1 396 385 (20.7)		1416 (19.2)	5520 (19.0)	
Unknown	8 (0.1)	14 154 (0.2)		6 (0.1)	12 (0.0)	
<b>Charlson Comorbidity Index score, n (%)</b>			<.001			.003
0	6512 (87.5)	6 299 548 (93.4)		6506 (88.0)	25947 (89.2)	
1+	934 (12.5)	446 880 (6.6)		885 (12.0)	3131 (10.8)	
<b>Index date year, n (%)</b>			<.001			<.001
2009	629 (8.4)	660 345 (9.8)		625 (8.5)	2110 (7.3)	
2010	681 (9.1)	657 453 (9.7)		679 (9.2)	2580 (8.9)	
2011	729 (9.8)	700 784 (10.4)		725 (9.8)	2857 (9.8)	

2012	762 (10.2)	731 804 (10.8)	754 (10.2)	2956 (10.2)
2013	705 (9.5)	582 355 (8.6)	696 (9.4)	2738 (9.4)
2014	689 (9.3)	597 982 (8.9)	683 (9.2)	2639 (9.1)
2015	899 (12.1)	736 675 (10.9)	884 (12.0)	3187 (11.0)
2016	1216 (16.3)	983 603 (14.6)	1212 (16.4)	4781 (16.4)
2017	1136 (15.3)	1 095 427 (16.2)	1133 (15.3)	5230 (18.0)

\*Propensity-score matching based on all tabulated characteristics.

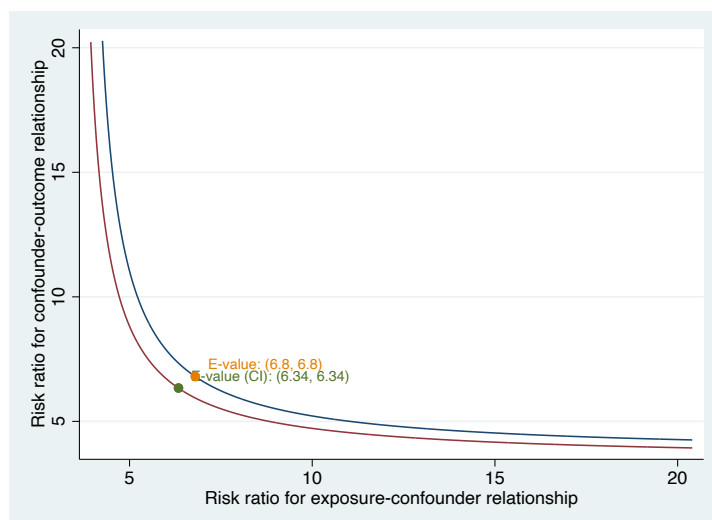
†Age at diagnosis for cancer cohort and age at index date (date of billable encounter with provider) for control cohort.

‡*P*-values were derived using the Pearson chi-square test or Wilcoxon rank-sum test.

§Other health insurance plans include comprehensive, point-of-service, point-of-service with capitation, high-deductible, and exclusive-provider-organization health plans.

Abbreviations: HMO, health maintenance organization; IQR, interquartile range; PPO, preferred provider organization.

**Appendix 5. The value of the joint minimum strength of association on the risk-ratio scale that an unmeasured confounder must have with both gynecologic cancer and employment disruption to explain away the observed hazard ratio of 3.67.**



The orange E-value demonstrates that an unmeasured confounder associated with gynecologic cancer and employment disruption by a HR of 6.8-fold each could explain away the association between gynecologic cancer and employment disruption, but a weaker confounder could not.

The green E-value demonstrates that an unmeasured confounder associated with both gynecologic cancer and employment disruption by a HR of 6.3 could explain away the lower CI, but weaker confounding could not.