

Supplemental Figure 1. Selection of cases and controls from the Surveillance, Epidemiology and End Results (SEER)-Medicare linked data

Case Selection

Women diagnosed with malignant ovarian or fallopian tube cancer as a their first cancer between 1994–2013
 N=54 338

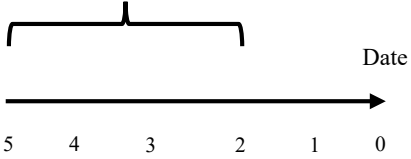
Control Selection

5% sample of women who are Medicare beneficiaries residing in SEER registry areas and do not have ovarian or fallopian tube cancer
 N=648 379

- Unknown month of diagnosis
n=365
- Unknown diagnostic confirmation/confirmation only from death certificate
n=1 730
- Enrolled in Medicare for any reason other than age
n=10 158
- Age at Diagnosis <68 or ≥90
n=14 854
- Excluded due to histology (e.g., non-epithelial or non-carcinoma)
n=2 580
- Not continuously enrolled in Medicare parts A and B in the 1 year period 2–3 years before cancer diagnosis
n=1 834
- Enrolled in an HMO any time in the 1 year period 2–3 years before cancer diagnosis
n=5 967

Cases
 N=16 850

Medicare records searched for codes related to metabolic syndrome between 2 and 5 years before the diagnosis date (cases) or index date (controls)



Three options for length of continuous Medicare enrollment (mutually exclusive, all women analyzed together, with adjustment for length of enrollment)

Enrolled in Medicare parts A and B, but not an HMO for the entire 3 year period 2-5 years before diagnosis/index date
 Cases n=13 391; Controls n=178 780

Only enrolled for the 2 year period 2-4 years before diagnosis/index date
 Cases n=1 739; Controls n=41 539

Only enrolled for the 1 year period 2-3 years before diagnosis/index date
 Cases n=1 720; Controls n=61 559

Controls
 N=281 878

- Died before 1994 or age 68, or were aged ≥90
n=38 711
- Enrolled in Medicare for any reason other than age
n=97 484
- Ever had oophorectomy in Medicare claims
n=10 374
- Not in SEER registry area by index date
n=14 703
- Not continuously enrolled in Medicare parts A and B in the 1 year period 2–3 years before index date
n=105 266
- Enrolled in an HMO any time in the 1 year period 2–3 years before index date
n=99 963

Supplemental Table 1. Morphology codes included in the histotype classifications for this analysis (cancer site: ovarian or fallopian tube)

Histotype	ICD-O-3 codes
Serous (n=7,543)	8441, 8442, 8460, 8461, 8462, 9014
Endometrioid (n=1,114)	8380, 8381, 8382, 8383, 8560, 8570
Clear Cell (n=386)	8310, 8313
Mucinous (n=797)	8470, 8471, 8480, 8481, 8482, 8490, 9015
Other Epithelial (n=7,010)	8005, 8010, 8012, 8013, 8015, 8020, 8021, 8022, 8031, 8032, 8033, 8040, 8041, 8043, 8046, 8050, 8052, 8070, 8074, 8120, 8140, 8141, 8230, 8240, 8246, 8250, 8255, 8260, 8263, 8290, 8323, 8340, 8440, 8443, 8444, 8450, 8503, 8550, 8562, 8574, 8576, 8650, 8806, 9110

Supplemental Table 2. Codes used to identify metabolic syndrome and its components, between 1994 and 2013 in SEER-Medicare linked data

We used the following ICD-9-CM diagnosis codes, where x indicates that any value (or blank) is allowed in that digit:

Condition	Codes
Overweight, obesity	A diagnosis of unspecified or overweight/obesity/morbid obesity or central adiposity (278, 278.0, 278.0x, 278.1, V77.8 ^a)
Impaired fasting glucose	A diagnosis of type 2 diabetes or impaired fasting glucose (250.x0, 250.x2, 790.2x) ^b
Hypertension	A diagnosis of hypertensive disease (401.xx through 405.xx)
High triglycerides	A diagnosis of pure hyperglycemia, mixed hyperlipidemia, hyperchylomicronemia, or other unspecified hyperlipidemia (272.1x through 272.4x) ^c
Low HDL cholesterol	A diagnosis of lipoprotein deficiency (272.5x)
Dysmetabolic syndrome	A diagnosis of metabolic syndrome (277.7) ^d

^aCode for central adiposity (V77.8) only available from 2001-2007

^bCodes 250, 250.x were not included because they generically reference both type 1 and 2 diabetes, and codes 250.x1 and 250.x3 were not included because they also include type 1 diabetes

^c272, 272.0, 272.0x are not included

^dStarted use in 2001. Our primary definition of metabolic syndrome required this diagnosis or a diagnosis of 3 or more metabolic syndrome components

Supplemental Table 3. Characteristics of the analytic population: patients with ovarian or fallopian tube cancer and controls identified between 1994 and 2013 in the SEER-Medicare linked data.

	Cases		Controls	
	n	%	n	%
Mean age in years (SD)	16 850	77.1 (5.8)	281 878	76.4 (6.5)
Race/Ethnicity				
Non-Hispanic White	14 918	88.5	238 174	84.5
Non-Hispanic Black	1 056	6.3	21 991	7.8
Hispanic	201	1.2	5 303	1.9
Asian	385	2.3	9 041	3.2
Other / unknown	290	1.7	7 369	2.6
Registry at diagnosis				
San Francisco	688	4.1	11 433	4.1
Connecticut	1 241	7.4	18 770	6.7
Detroit	1 484	8.8	20 774	7.4
Hawaii	182	1.1	3 936	1.4
Iowa	1 341	8.0	18 574	6.6
New Mexico	427	2.5	7 782	2.8
Seattle	1 214	7.2	15 892	5.6
Utah	542	3.2	7 158	2.5
Atlanta	656	3.9	9 476	3.4
San Jose	397	2.4	6 766	2.4
Los Angeles	1 386	8.2	21 980	7.8
Rural Georgia	63	0.4	701	0.2
Greater California	2 287	13.6	44 217	15.7
Kentucky	910	5.4	18 413	6.5
Louisiana	829	4.9	16 633	5.9
New Jersey	1 971	11.7	37 286	13.2
Greater Georgia	1 232	7.3	22 087	7.8
Year of diagnosis				
1994	568	3.4	21 588	7.7
1995	581	3.4	16 213	5.8
1996	612	3.6	14 387	5.1
1997	547	3.2	13 138	4.7
1998	545	3.2	12 132	4.3
1999	525	3.1	11 774	4.2
2000	1 035	6.1	11 265	4.0
2001	1 057	6.3	10 310	3.7
2002	1 046	6.2	10 103	3.6
2003	984	5.8	9 788	3.5
2004	979	5.8	10 392	3.7
2005	1 002	5.9	11 076	3.9
2006	1 096	6.5	11 768	4.2
2007	936	5.6	12 217	4.3
2008	1 047	6.2	12 894	4.6
2009	946	5.6	13 085	4.6
2010	876	5.2	14 137	5.0
2011	853	5.1	16 370	5.8
2012	810	4.8	19 530	6.9
2013	805	4.8	29 711	10.5
State buy-in at any time during claims search period				
Yes	1 892	11.2	41 957	14.9
History of smoking or tobacco use				
	1 055	6.3	20 318	7.2
Metabolic syndrome^a				
	3 751	22.3	65 041	23.1
Number of metabolic syndrome components				
0	3 085	18.3	65 943	23.4
1	4 517	26.8	72 573	25.7
2	5 524	32.8	78 822	28.0
≥3	3 724	22.1	64 540	22.9

Central adiposity	14	0.1	362	0.1
Overweight / obesity	1 328	7.9	24 997	8.9
Impaired fasting glucose	4 770	28.3	82 922	29.4
Hypertension	12 168	72.2	191 822	68.1
High triglycerides	8 958	53.2	135 329	48.0
Low HDL cholesterol	104	0.6	1 870	0.7
Cancer characteristics				
Histology				
Serous	7 543	44.8	--	--
Endometrioid	1 114	6.6	--	--
Mucinous	386	2.3	--	--
Clear Cell	797	4.7	--	--
Other Epithelial	7 010	41.6	--	--
Grade				
Low	2 491	14.8	--	--
High	7 369	43.7	--	--
Missing	6 990	41.5	--	--

n=number SD=standard deviation

^aThe primary definition of metabolic syndrome presented in our analyses was: 3 or more signs for metabolic syndrome (central adiposity or overweight/obesity, impaired fasting glucose [including type II diabetes], high blood pressure, high triglycerides, low HDL cholesterol) and/or a diagnosis of ‘dysmetabolic syndrome.’

Supplemental Table 4. Associations between metabolic syndrome, its components, and ovarian or fallopian tube cancer by race/ethnicity, SEER-Medicare linked data (1994–2013)

	Non-Hispanic White		Non-Hispanic Black		Hispanic		Asian		P ^b
	OR ^a	95% CI	OR ^a	95% CI	OR ^a	95% CI	OR ^a	95% CI	
Metabolic syndrome (≥3 vs.<3)	0.86	0.82–0.89	0.89	0.77–1.03	0.73	0.53–1.01	0.99	0.78–1.25	0.27
Number of metabolic syndrome components									
0	--	Reference	--	Reference	--	Reference	--	Reference	0.16
1	1.22	1.16–1.28	1.68	1.34–2.10	1.15	0.69–1.80	1.08	0.75–1.56	
2	1.21	1.15–1.28	1.57	1.26–1.95	1.10	0.70–1.74	1.20	0.86–1.68	
≥3	1.00	0.95–1.06	1.32	1.05–1.67	0.80	0.50–1.27	1.13	0.79–1.61	
Overweight/obesity	0.82	0.77–0.88	0.93	0.77–1.12	0.77	0.50–1.20	0.90	0.54–1.50	0.44
Impaired fasting glucose	0.89	0.85–0.92	1.01	0.89–1.16	0.87	0.64–1.17	1.07	0.86–1.33	0.06
Hypertension	1.07	1.03–1.12	1.34	1.11–1.60	0.84	0.60–1.19	1.14	0.87–1.48	0.12
High triglycerides	1.06	1.02–1.10	0.91	0.79–1.05	0.91	0.66–1.25	1.07	0.85–1.35	0.27

n=number, OR= odds ratio, CI=confidence interval

^aLogistic regression models were run separately for each exposure. Models were adjusted for diagnosis date, age, race, geographic location, state Medicare buy-in, history of smoking or tobacco use, and length of Medicare enrollment. Models for women in the “other race” group are suppressed due to model instability, but these women were included when assessing effect modification (see below).

^bTo assess effect modification across race groups, we used likelihood ratio tests comparing nested models with and without an interaction term between race and each of the metabolic syndrome exposures.

Supplemental Table 5. Prevalence estimates for metabolic syndrome components, by metabolic syndrome status and number of documented components

		Metabolic syndrome ^a				Number of metabolic syndrome signs ^b					
		No		Yes		1		2		3+	
		n	%	n	%	n	%	n	%	n	%
Cases	Central adiposity	-- ^c	--	--	--	--	--	--	--	--	--
	Overweight / obesity	287	2.2	1 041	27.8	39	0.9	249	4.5	1 040	27.9
	Impaired fasting glucose	1 424	10.9	3 346	89.2	213	4.7	1 218	22.0	3 339	89.7
	Hypertension	8 444	64.5	3 724	99.3	3 204	70.9	5 260	95.2	3 704	99.5
	High triglycerides	5 351	40.9	3 607	96.2	1 057	23.4	4 313	78.1	3 588	96.3
	Low HDL cholesterol	--	--	--	--	--	--	--	--	--	--
	Controls	Central adiposity	74	<0.1	288	0.4	15	<0.1	60	0.1	287
Overweight / obesity	4 434	2.0	20 563	31.6	691	1.0	3 763	4.8	20 543	31.8	
Impaired fasting glucose	24 508	11.3	58 414	89.8	3 942	5.4	20 667	26.2	58 313	90.4	
Hypertension	127 196	58.7	64 626	99.4	53 033	73.1	74 537	94.6	64 252	99.6	
High triglycerides	72 976	33.7	62 353	95.9	14 869	20.5	58 467	74.2	61 993	96.1	
Low HDL cholesterol	247	0.1	1 623	2.5	38	0.1	210	0.3	1 622	2.5	

n=number

^aThe primary definition of metabolic syndrome presented in our analyses was: 3 or more metabolic syndrome components (shown above) and/or a diagnosis of 'dysmetabolic syndrome.' Women meeting this definition were compared to a referent group of those not meeting it (i.e., including those with only one or two signs). When comparing the number of metabolic syndrome signs with which women were diagnosed, those without signs are the reference group.

^bNumbers for women without any metabolic syndrome components not shown.

^cNumbers suppressed due to small cell size.