

Supplemental Material

No	6,876	(38.1)	9,279	(27.8)	3,876	(25.3)	1,539	(29.1)	<0.001
Yes	11,154	(61.9)	24,128	(72.2)	11,465	(74.7)	3,746	(70.9)	
Trastuzumab									
No	14,543	(80.7)	30,957	(92.7)	13,687	(89.2)	4,827	(91.3)	<0.001
Yes	3,487	(19.3)	2,450	(7.3)	1,654	(10.8)	458	(8.7)	
Hypertension									
No	15,385	(85.3)	30,679	(91.8)	11,576	(75.5)	4,533	(85.8)	<0.001
Yes	2,645	(14.7)	2,728	(8.2)	3,765	(24.5)	752	(14.2)	
Dyslipidemia									
No	15,914	(88.3)	31,059	(93.0)	12,615	(82.2)	4,762	(90.1)	<0.001
Yes	2,116	(11.7)	2,348	(7.0)	2,726	(17.8)	523	(9.9)	
Osteoporosis									
No	16,304	(90.4)	31,364	(93.9)	13,335	(86.9)	4,739	(89.7)	<0.001
Yes	1,726	(9.6)	2,043	(6.1)	2,006	(13.1)	546	(10.3)	
Body mass index (kg/m ²)									
<23	8,681	(48.2)	19,041	(57.0)	5,715	(37.3)	2,534	(48.0)	<0.001
≥23	9,349	(51.9)	14,366	(43.0)	9,626	(62.8)	2,751	(52.1)	
Smoking									
Never	17,005	(94.3)	31,312	(93.7)	14,557	(94.9)	5,027	(95.1)	<0.001
Ever	1,025	(5.7)	2,095	(6.3)	784	(5.1)	258	(4.9)	
Alcohol consumption									
Never	13,859	(76.9)	23,786	(71.2)	12,645	(82.4)	4,083	(77.3)	<0.001
Ever	4,171	(23.1)	9,621	(28.8)	2,696	(17.6)	1,202	(22.7)	
Physical activity									
No	5,151	(28.6)	8,771	(26.3)	4,363	(28.4)	1,754	(33.2)	<0.001
Yes	12,879	(71.4)	24,636	(73.8)	10,978	(71.6)	3,531	(66.8)	
Menopausal status									
Pre-menopausal	9,324	(51.7)	27,801	(83.2)	3,107	(20.3)	3,240	(61.3)	<0.001
Post-menopausal	8,706	(48.3)	5,606	(16.8)	12,234	(79.8)	2,045	(38.7)	

AIs, aromatase inhibitors; SERMs, selective estrogen receptors modulators. *P-value by chi-square test for categorical variables and ANOVA for continuous variable.

Table S2. The subgroup analyses by age at diagnosis (<55 vs. ≥55 years)

	Age <55 years						Age ≥55 years						P-value	I ²
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*				
Composite of CVD														
Non-users	25,233	600	(2.38)	136.0	1.00	(Reference)	11,466	739	(6.45)	53.9	1.00	(Reference)		
SERMs	55,457	1,113	(2.01)	290.1	1.16	(1.05-1.28)	5,738	413	(7.20)	27.9	1.15	(1.02-1.29)	0.90	0.0%
AIs	9,018	288	(3.19)	49.3	1.21	(1.05-1.39)	15,615	871	(5.58)	70.9	1.07	(0.97-1.18)	0.17	47.0%
Both	7,750	203	(2.62)	56.4	1.36	(1.15-1.60)	2,894	174	(6.01)	17.0	1.13	(0.96-1.34)	0.12	58.0%
Stroke														
Non-users	25,233	100	(0.40)	136.0	1.00	(Reference)	13,671	235	(1.72)	53.9	1.00	(Reference)		
SERMs	55,457	215	(0.39)	290.1	1.46	(1.15-1.85)	7,009	141	(2.01)	27.9	1.11	(0.90-1.36)	0.09	65.0%
AIs	9,018	69	(0.77)	49.3	1.43	(1.05-1.96)	19,093	268	(1.40)	70.9	1.04	(0.87-1.24)	0.08	68.0%
Both	7,750	38	(0.49)	56.4	1.42	(0.96-2.08)	3,618	50	(1.38)	17.0	0.99	(0.73-1.35)	0.15	51.0%
CHD														
Non-users	25,233	191	(0.76)	136.0	1.00	(Reference)	13,671	223	(1.63)	53.9	1.00	(Reference)		
SERMs	55,457	336	(0.61)	290.1	1.11	(0.93-1.34)	7,009	129	(1.84)	27.9	1.13	(0.91-1.40)	0.91	0.0%
AIs	9,018	106	(1.18)	49.3	1.22	(0.96-1.54)	19,093	283	(1.48)	70.9	1.13	(0.94-1.35)	0.62	0.0%
Both	7,750	61	(0.79)	56.4	1.14	(0.85-1.53)	3,618	49	(1.35)	17.0	1.06	(0.78-1.45)	0.75	0.0%
VTE														
Non-users	25,233	45	(0.18)	136.0	1.00	(Reference)	13,671	51	(0.37)	53.9	1.00	(Reference)		
SERMs	55,457	127	(0.23)	290.1	1.65	(1.17-2.32)	7,009	27	(0.39)	27.9	1.31	(0.84-2.05)	0.43	0.0%
AIs	9,018	15	(0.17)	49.3	1.07	(0.61-1.89)	19,093	59	(0.31)	70.9	1.11	(0.76-1.63)	0.91	0.0%
Both	7,750	18	(0.23)	56.4	1.90	(1.08-3.36)	3,618	17	(0.47)	17.0	1.66	(0.95-2.90)	0.73	0.0%
HF														
Non-users	25,233	129	(0.51)	136.0	1.00	(Reference)	13,671	102	(0.75)	53.9	1.00	(Reference)		
SERMs	55,457	156	(0.28)	290.1	0.84	(0.66-1.05)	7,009	50	(0.71)	27.9	1.18	(0.85-1.65)	0.09	65.0%
AIs	9,018	43	(0.48)	49.3	1.13	(0.81-1.58)	19,093	113	(0.59)	70.9	1.09	(0.83-1.44)	0.88	0.0%
Both	7,750	39	(0.50)	56.4	1.69	(1.16-2.46)	3,618	21	(0.58)	17.0	1.15	(0.71-1.85)	0.22	35.0%
Arrhythmia														
Non-users	25,233	135	(0.54)	136.0	1.00	(Reference)	13,671	128	(0.94)	53.9	1.00	(Reference)		
SERMs	55,457	279	(0.50)	290.1	1.17	(0.95-1.44)	7,009	67	(0.96)	27.9	1.20	(0.90-1.60)	0.90	0.0%
AIs	9,018	55	(0.61)	49.3	1.08	(0.79-1.48)	19,093	150	(0.79)	70.9	1.03	(0.81-1.30)	0.80	0.0%
Both	7,750	47	(0.61)	56.4	1.33	(0.94-1.87)	3,618	37	(1.02)	17.0	1.28	(0.88-1.86)	0.90	0.0%

T2DM														
Non-users	25,233	808	(3.20)	136.0	1.00	(Reference)	12,648	773	(6.11)	53.9	1.00	(Reference)		
SERMs	55,457	1,630	(2.94)	290.1	1.24	(1.14-1.35)	6,368	506	(7.95)	27.9	1.41	(1.26-1.58)	0.06	71.0%
AIs	9,018	440	(4.88)	49.3	1.13	(1.01-1.27)	17,184	1,050	(6.11)	70.9	1.19	(1.08-1.30)	0.56	0.0%
Both	7,750	273	(3.52)	56.4	1.19	(1.03-1.37)	3,282	204	(6.22)	17.0	1.21	(1.04-1.42)	0.83	0.0%

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs). If the P-value was <0.1 or I²>50% in the heterogeneity test, then we hypothesized a significant difference by the stratified factor.

Table S3. The subgroup analyses by age at diagnosis (<60 vs. ≥60 years)

	Age <60years						Age ≥60 years						P-value	I ²
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*		No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*			
Composite of CVD														
Non-users	30,348	808	(2.66)	160.7	1.00	(Reference)	6,351	531	(8.36)	29.3	1.00	(Reference)		
SERMs	57,618	1,214	(2.11)	300.7	1.19	(1.08-1.30)	3,577	312	(8.72)	17.4	1.08	(0.94-1.24)	0.25	24.0%
AIs	15,386	510	(3.31)	78.5	1.17	(1.05-1.31)	9,247	649	(7.02)	41.7	1.04	(0.92-1.17)	0.15	53.0%
Both	9,009	260	(2.89)	64.0	1.37	(1.19-1.59)	1,635	117	(7.16)	9.5	1.03	(0.84-1.26)	0.02	81.0%
Stroke														
Non-users	30,348	150	(0.49)	160.7	1.00	(Reference)	6,351	185	(2.91)	29.3	1.00	(Reference)		
SERMs	57,618	245	(0.43)	300.7	1.41	(1.14-1.74)	3,577	111	(3.10)	17.4	1.05	(0.83-1.32)	0.06	71.0%
AIs	15,386	113	(0.73)	78.5	1.21	(0.95-1.55)	9,247	224	(2.42)	41.7	1.05	(0.86-1.28)	0.37	0.0%
Both	9,009	48	(0.53)	64.0	1.29	(0.92-1.79)	1,635	40	(2.45)	9.5	0.99	(0.70-1.40)	0.28	14.0%
CHD														
Non-users	30,348	256	(0.84)	160.7	1.00	(Reference)	6,351	158	(2.49)	29.3	1.00	(Reference)		
SERMs	57,618	369	(0.64)	300.7	1.17	(0.99-1.38)	3,577	96	(2.68)	17.4	1.07	(0.83-1.37)	0.54	0.0%
AIs	15,386	187	(1.22)	78.5	1.24	(1.02-1.50)	9,247	202	(2.18)	41.7	1.02	(0.82-1.26)	0.19	42.0%
Both	9,009	78	(0.87)	64.0	1.24	(0.96-1.61)	1,635	32	(1.96)	9.5	0.93	(0.63-1.36)	0.22	34.0%
VTE														
Non-users	30,348	67	(0.22)	160.7	1.00	(Reference)	6,351	29	(0.46)	29.3	1.00	(Reference)		
SERMs	57,618	137	(0.24)	300.7	1.49	(1.11-2.02)	3,577	17	(0.48)	17.4	1.40	(0.79-2.48)	0.85	0.0%
AIs	15,386	30	(0.19)	78.5	0.98	(0.64-1.49)	9,247	44	(0.48)	41.7	1.38	(0.86-2.22)	0.28	14.0%
Both	9,009	25	(0.28)	64.0	1.75	(1.09-2.81)	1,635	10	(0.61)	9.5	1.76	(0.85-3.65)	0.99	0.0%
HF														
Non-users	30,348	159	(0.52)	160.7	1.00	(Reference)	6,351	72	(1.13)	29.3	1.00	(Reference)		
SERMs	57,618	168	(0.29)	300.7	0.90	(0.72-1.11)	3,577	38	(1.06)	17.4	1.07	(0.72-1.58)	0.44	0.0%
AIs	15,386	73	(0.47)	78.5	1.11	(0.85-1.47)	9,247	83	(0.90)	41.7	1.05	(0.76-1.46)	0.80	0.0%
Both	9,009	47	(0.52)	64.0	1.67	(1.19-2.35)	1,635	13	(0.80)	9.5	0.97	(0.54-1.77)	0.12	58.0%
Arrhythmia														
Non-users	30,348	176	(0.58)	160.7	1.00	(Reference)	6,351	87	(1.37)	29.3	1.00	(Reference)		
SERMs	57,618	296	(0.51)	300.7	1.19	(0.99-1.44)	3,577	50	(1.40)	17.4	1.08	(0.77-1.53)	0.63	0.0%
AIs	15,386	109	(0.71)	78.5	1.15	(0.90-1.47)	9,247	96	(1.04)	41.7	0.93	(0.69-1.25)	0.27	19.0%
Both	9,009	62	(0.69)	64.0	1.38	(1.02-1.85)	1,635	22	(1.35)	9.5	1.09	(0.68-1.75)	0.41	0.0%

T2DM														
Non-users	30,348	1,063	(3.50)	160.7	1.00	(Reference)	6,351	518	(8.16)	29.3	1.00	(Reference)		
SERMs	57,618	1,782	(3.09)	300.7	1.30	(1.20-1.41)	3,577	354	(9.90)	17.4	1.32	(1.15-1.50)	0.89	0.0%
AIs	15,386	772	(5.02)	78.5	1.17	(1.07-1.29)	9,247	718	(7.76)	41.7	1.11	(0.99-1.25)	0.47	0.0%
Both	9,009	339	(3.76)	64.0	1.23	(1.08-1.39)	1,635	138	(8.44)	9.5	1.19	(0.98-1.43)	0.77	0.0%

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs). If the P-value was <0.1 or I²>50% in the heterogeneity test, then we hypothesized a significant difference by the stratified factor.

Table S4. The subgroup analyses by age at diagnosis (<55 year; 40-54 and 45-54 years)

	Age 40-54 years					Age 45-54 years				
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*
Composite of CVD										
Non-users	19,175	515	(2.69)	101.8	1.00 (Reference)	14,022	414	(2.95)	74.5	1.00 (Reference)
SERMs	43,755	938	(2.14)	223.1	1.18 (1.05-1.31)	26,938	665	(2.47)	133.2	1.24 (1.09-1.40)
AIs	8,928	288	(3.23)	48.8	1.19 (1.03-1.37)	8,671	279	(3.22)	47.1	1.20 (1.04-1.40)
Both	7,143	192	(2.69)	52.2	1.33 (1.12-1.57)	5,877	163	(2.77)	42.6	1.31 (1.09-1.58)
Stroke										
Non-users	19,175	90	(0.47)	101.8	1.00 (Reference)	14,022	75	(0.53)	74.5	1.00 (Reference)
SERMs	43,755	186	(0.43)	223.1	1.48 (1.14-1.91)	26,938	140	(0.52)	133.2	1.60 (1.20-2.13)
AIs	8,928	69	(0.77)	48.8	1.39 (1.01-1.91)	8,671	66	(0.76)	47.1	1.40 (1.00-1.96)
Both	7,143	36	(0.50)	52.2	1.37 (0.92-2.04)	5,877	33	(0.56)	42.6	1.44 (0.94-2.19)
CHD										
Non-users	19,175	178	(0.93)	101.8	1.00 (Reference)	14,022	156	(1.11)	74.5	1.00 (Reference)
SERMs	43,755	303	(0.69)	223.1	1.08 (0.89-1.31)	26,938	220	(0.82)	133.2	1.02 (0.82-1.26)
AIs	8,928	106	(1.19)	48.8	1.21 (0.95-1.54)	8,671	104	(1.20)	47.1	1.19 (0.93-1.52)
Both	7,143	60	(0.84)	52.2	1.13 (0.84-1.53)	5,877	55	(0.94)	42.6	1.12 (0.82-1.54)
VTE										
Non-users	19,175	35	(0.18)	101.8	1.00 (Reference)	14,022	25	(0.18)	74.5	1.00 (Reference)
SERMs	43,755	101	(0.23)	223.1	1.76 (1.18-2.62)	26,938	71	(0.26)	133.2	2.05 (1.28-3.29)
AIs	8,928	15	(0.17)	48.8	1.05 (0.58-1.89)	8,671	15	(0.17)	47.1	1.27 (0.68-2.38)
Both	7,143	15	(0.21)	52.2	1.69 (0.91-3.16)	5,877	13	(0.22)	42.6	2.05 (1.02-4.11)
HF										
Non-users	19,175	102	(0.53)	101.8	1.00 (Reference)	14,022	80	(0.57)	74.5	1.00 (Reference)
SERMs	43,755	119	(0.27)	223.1	0.83 (0.64-1.08)	26,938	78	(0.29)	133.2	0.89 (0.65-1.22)
AIs	8,928	43	(0.48)	48.8	1.10 (0.78-1.56)	8,671	40	(0.46)	47.1	1.01 (0.70-1.45)
Both	7,143	36	(0.50)	52.2	1.63 (1.10-2.43)	5,877	24	(0.41)	42.6	1.31 (0.81-2.11)
Arrhythmia										
Non-users	19,175	110	(0.57)	101.8	1.00 (Reference)	14,022	78	(0.56)	74.5	1.00 (Reference)
SERMs	43,755	229	(0.52)	223.1	1.20 (0.95-1.52)	26,938	156	(0.58)	133.2	1.40 (1.06-1.84)
AIs	8,928	55	(0.62)	48.8	1.08 (0.78-1.50)	8,671	54	(0.62)	47.1	1.21 (0.85-1.72)

Both	7,143	45	(0.63)	52.2	1.34 (0.94-1.91)	5,877	38	(0.65)	42.6	1.42 (0.96-2.12)
T2DM										
Non-users	19,175	726	(3.79)	101.8	1.00 (Reference)	14,022	589	(4.20)	74.5	1.00 (Reference)
SERMs	43,755	1,429	(3.27)	223.1	1.22 (1.12-1.34)	26,938	1,022	(3.79)	133.2	1.28 (1.16-1.42)
AIs	8,928	439	(4.92)	48.8	1.14 (1.01-1.28)	8,671	425	(4.90)	47.1	1.14 (1.00-1.29)
Both	7,143	264	(3.70)	52.2	1.18 (1.02-1.36)	5,877	232	(3.95)	42.6	1.19 (1.02-1.39)

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs).

Table S5. The subgroup analyses by age at diagnosis (<60 years;40-59 and 45-59 years)

	Age 40-59 years						Age 45-59 years					
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*		No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*	
Composite of CVD												
Non-users	24,290	723	(2.98)	126.5	1.00	(Reference)	19,137	622	(3.25)	74.5	1.00	(Reference)
SERMs	45,916	1,039	(2.26)	233.6	1.21	(1.09-1.33)	29,099	766	(2.63)	133.2	1.26	(1.13-1.41)
AIs	15,296	510	(3.33)	78.0	1.16	(1.04-1.30)	15,039	501	(3.33)	47.1	1.17	(1.04-1.32)
Both	8,402	249	(2.96)	59.8	1.35	(1.17-1.57)	7,136	220	(3.08)	42.6	1.34	(1.15-1.57)
Stroke												
Non-users	24,290	140	(0.58)	126.5	1.00	(Reference)	19,137	125	(0.65)	74.5	1.00	(Reference)
SERMs	45,916	216	(0.47)	233.6	1.41	(1.13-1.76)	29,099	170	(0.58)	133.2	1.48	(1.16-1.88)
AIs	15,296	113	(0.74)	78.0	1.19	(0.93-1.53)	15,039	110	(0.73)	47.1	1.20	(0.93-1.55)
Both	8,402	46	(0.55)	59.8	1.25	(0.89-1.76)	7,136	43	(0.60)	42.6	1.27	(0.89-1.81)
CHD												
Non-users	24,290	243	(1.00)	126.5	1.00	(Reference)	19,137	221	(1.15)	74.5	1.00	(Reference)
SERMs	45,916	336	(0.73)	233.6	1.13	(0.95-1.34)	29,099	253	(0.87)	133.2	1.08	(0.90-1.31)
AIs	15,296	187	(1.22)	78.0	1.24	(1.02-1.51)	15,039	185	(1.23)	47.1	1.23	(1.01-1.50)
Both	8,402	77	(0.92)	59.8	1.22	(0.94-1.59)	7,136	72	(1.01)	42.6	1.21	(0.92-1.59)
VTE												
Non-users	24,290	57	(0.23)	126.5	1.00	(Reference)	19,137	47	(0.25)	74.5	1.00	(Reference)
SERMs	45,916	111	(0.24)	233.6	1.60	(1.14-2.24)	29,099	81	(0.28)	133.2	1.75	(1.20-2.55)
AIs	15,296	30	(0.20)	78.0	0.94	(0.61-1.45)	15,039	30	(0.20)	47.1	1.02	(0.65-1.60)
Both	8,402	22	(0.26)	59.8	1.63	(0.98-2.71)	7,136	20	(0.28)	42.6	1.82	(1.06-3.13)
HF												
Non-users	24,290	132	(0.54)	126.5	1.00	(Reference)	19,137	110	(0.57)	74.5	1.00	(Reference)
SERMs	45,916	131	(0.29)	233.6	0.91	(0.71-1.17)	29,099	90	(0.31)	133.2	1.00	(0.75-1.33)
AIs	15,296	73	(0.48)	78.0	1.10	(0.83-1.46)	15,039	70	(0.47)	47.1	1.05	(0.78-1.42)
Both	8,402	44	(0.52)	59.8	1.64	(1.15-2.33)	7,136	32	(0.45)	42.6	1.39	(0.92-2.10)
Arrhythmia												
Non-users	24,290	151	(0.62)	126.5	1.00	(Reference)	19,137	119	(0.62)	74.5	1.00	(Reference)
SERMs	45,916	246	(0.54)	233.6	1.24	(1.01-1.53)	29,099	173	(0.59)	133.2	1.43	(1.12-1.81)
AIs	15,296	109	(0.71)	78.0	1.15	(0.90-1.48)	15,039	108	(0.72)	47.1	1.23	(0.94-1.60)
Both	8,402	60	(0.71)	59.8	1.41	(1.04-1.91)	7,136	53	(0.74)	42.6	1.49	(1.07-2.08)
T2DM												

Non-users	24,290	981	(4.04)	126.5	1.00	(Reference)	19,137	844	(4.41)	74.5	1.00	(Reference)
SERMs	45,916	1,581	(3.44)	233.6	1.28	(1.18-1.39)	29,099	1,174	(4.03)	133.2	1.34	(1.22-1.47)
AIs	15,296	771	(5.04)	78.0	1.18	(1.08-1.30)	15,039	757	(5.03)	47.1	1.19	(1.08-1.32)
Both	8,402	330	(3.93)	59.8	1.21	(1.06-1.37)	7,136	298	(4.18)	42.6	1.21	(1.06-1.39)

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs).

Table S6. The subgroup analysis by histological types

	Invasive						<i>In situ</i>						P-value	I ²
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*		No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*			
Composite of CVD														
Non-users	33,252	1,251	(3.76)	173.1	1.00	(Reference)	3,447	88	(2.55)	16.9	1.00	(Reference)		
SERMs	52,004	1,324	(2.55)	275.2	1.12	(1.04-1.22)	9,191	202	(2.20)	42.8	1.09	(0.84-1.41)	0.82	0.0%
AIs	24,530	1,156	(4.71)	119.7	1.14	(1.05-1.23)	103	3	(2.91)	0.5	2.93	(1.51-5.68)	<0.01	87.0%
Both	10,459	369	(3.53)	72.2	1.25	(1.11-1.40)	185	8	(4.32)	1.2	1.08	(0.52-2.26)	0.71	0.0%
Stroke														
Non-users	33,252	311	(0.94)	173.1	1.00	(Reference)	3,447	24	(0.70)	16.9	1.00	(Reference)		
SERMs	52,004	309	(0.59)	275.2	1.21	(1.04-1.42)	9,191	47	(0.51)	42.8	1.07	(0.64-1.78)	0.64	0.0%
AIs	24,530	336	(1.37)	119.7	1.17	(1.00-1.37)	103	1	(0.97)	0.5	1.82	(0.43-7.75)	0.55	0.0%
Both	10,459	86	(0.82)	72.2	1.14	(0.90-1.46)	185	2	(1.08)	1.2	0.79	(0.18-3.41)	0.62	0.0%
CHD														
Non-users	33,252	377	(1.13)	173.1	1.00	(Reference)	3,447	37	(1.07)	16.9	1.00	(Reference)		
SERMs	52,004	397	(0.76)	275.2	1.05	(0.91-1.21)	9,191	68	(0.74)	42.8	0.84	(0.55-1.27)	0.32	0.0%
AIs	24,530	388	(1.58)	119.7	1.24	(1.07-1.43)	103	1	(0.97)	0.5	2.02	(0.61-6.68)	0.43	0.0%
Both	10,459	108	(1.03)	72.2	1.18	(0.95-1.47)	185	2	(1.08)	1.2	0.63	(0.15-2.65)	0.40	0.0%
VTE														
Non-users	33,252	90	(0.27)	173.1	1.00	(Reference)	3,447	6	(0.17)	16.9	1.00	(Reference)		
SERMs	52,004	137	(0.26)	275.2	1.47	(1.12-1.93)	9,191	17	(0.18)	42.8	1.35	(0.51-3.56)	0.86	0.0%
AIs	24,530	74	(0.30)	119.7	1.16	(0.85-1.58)	103	0	0.00	0.5	4.47	(0.49-40.62)	0.23	29.0%
Both	10,459	34	(0.33)	72.2	1.70	(1.13-2.54)	185	1	(0.54)	1.2	2.78	(0.31-24.83)	0.66	0.0%
HF														
Non-users	33,252	225	(0.68)	173.1	1.00	(Reference)	3,447	6	(0.17)	16.9	1.00	(Reference)		
SERMs	52,004	191	(0.37)	275.2	0.95	(0.78-1.16)	9,191	15	(0.16)	42.8	1.37	(0.52-3.62)	0.48	0.0%
AIs	24,530	155	(0.63)	119.7	1.03	(0.84-1.27)	103	1	(0.97)	0.5	11.86	(2.89-48.67)	<0.01	91.0%
Both	10,459	58	(0.55)	72.2	1.38	(1.02-1.85)	185	2	(1.08)	1.2	4.19	(0.81-21.78)	0.19	41.0%
Arrhythmia														
Non-users	33,252	248	(0.75)	173.1	1.00	(Reference)	3,447	15	(0.44)	16.9	1.00	(Reference)		
SERMs	52,004	291	(0.56)	275.2	1.11	(0.93-1.31)	9,191	55	(0.60)	42.8	1.54	(0.86-2.77)	0.29	12.0%
AIs	24,530	205	(0.84)	119.7	1.06	(0.88-1.27)	103	0	0.00	0.5	2.40	(0.31-18.38)	0.43	0.0%
Both	10,459	83	(0.79)	72.2	1.26	(0.98-1.62)	185	1	(0.54)	1.2	1.12	(0.15-8.65)	0.91	0.0%

T2DM														
Non-users	33,252	1,469	(4.42)	173.1	1.00	(Reference)	3,447	112	(3.25)	16.9	1.00	(Reference)		
SERMs	52,004	1,857	(3.57)	275.2	1.22	(1.14-1.31)	9,191	279	(3.04)	42.8	1.14	(0.91-1.43)	0.57	0.0%
AIs	24,530	1,484	(6.05)	119.7	1.22	(1.14-1.32)	103	6	(5.83)	0.5	3.03	(1.62-5.66)	<0.01	87.0%
Both	10,459	468	(4.47)	72.2	1.25	(1.12-1.39)	185	9	(4.86)	1.2	1.03	(0.52-2.06)	0.60	0.0%

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs). If the P-value was <0.1 or I²>50% in the heterogeneity test, then we hypothesized a significant difference by the stratified factor.

Table S7. The subgroup analysis by surgery

	No surgery						Surgery						P-value	I ²
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*				
Composite of CVD														
Non-users	7,004	405	(5.78)	38.1	1.00	(Reference)	29,695	934	(3.15)	151.8	1.00	(Reference)		
SERMs	7,087	274	(3.87)	41.2	1.03	(0.88-1.20)	54,108	1,252	(2.31)	276.8	1.19	(1.09-1.29)	0.12	59.0%
AIs	2,587	161	(6.22)	13.9	1.10	(0.92-1.31)	22,046	998	(4.53)	106.3	1.16	(1.06-1.27)	0.58	0.0%
Both	1,613	88	(5.46)	11.2	1.26	(0.99-1.59)	9,031	289	(3.20)	62.2	1.25	(1.09-1.43)	0.97	0.0%
Stroke														
Non-users	7,004	129	(1.84)	38.1	1.00	(Reference)	29,695	206	(0.69)	151.8	1.00	(Reference)		
SERMs	7,087	74	(1.04)	41.2	0.92	(0.69-1.22)	54,108	282	(0.52)	276.8	1.40	(1.17-1.68)	0.02	83.0%
AIs	2,587	48	(1.86)	13.9	0.87	(0.62-1.20)	22,046	289	(1.31)	106.3	1.30	(1.08-1.55)	0.03	78.0%
Both	1,613	21	(1.30)	11.2	0.96	(0.60-1.53)	9,031	67	(0.74)	62.2	1.25	(0.95-1.66)	0.33	0.0%
CHD														
Non-users	7,004	127	(1.81)	38.1	1.00	(Reference)	29,695	287	(0.97)	151.8	1.00	(Reference)		
SERMs	7,087	97	(1.37)	41.2	1.12	(0.86-1.46)	54,108	368	(0.68)	276.8	1.03	(0.88-1.21)	0.61	0.0%
AIs	2,587	61	(2.36)	13.9	1.37	(1.01-1.86)	22,046	328	(1.49)	106.3	1.20	(1.03-1.42)	0.47	0.0%
Both	1,613	25	(1.55)	11.2	1.12	(0.73-1.74)	9,031	85	(0.94)	62.2	1.16	(0.91-1.49)	0.90	0.0%
VTE														
Non-users	7,004	33	(0.47)	38.1	1.00	(Reference)	29,695	63	(0.21)	151.8	1.00	(Reference)		
SERMs	7,087	20	(0.28)	41.2	0.96	(0.56-1.64)	54,108	134	(0.25)	276.8	1.70	(1.25-2.32)	0.07	70.0%
AIs	2,587	10	(0.39)	13.9	1.12	(0.59-2.12)	22,046	64	(0.29)	106.3	1.22	(0.86-1.74)	0.82	0.0%
Both	1,613	11	(0.68)	11.2	1.98	(0.98-4.03)	9,031	24	(0.27)	62.2	1.65	(1.02-2.67)	0.67	0.0%
HF														
Non-users	7,004	51	(0.73)	38.1	1.00	(Reference)	29,695	180	(0.61)	151.8	1.00	(Reference)		
SERMs	7,087	29	(0.41)	41.2	0.86	(0.55-1.34)	54,108	177	(0.33)	276.8	1.00	(0.81-1.23)	0.56	0.0%
AIs	2,587	22	(0.85)	13.9	1.22	(0.75-1.99)	22,046	134	(0.61)	106.3	1.03	(0.82-1.28)	0.52	0.0%
Both	1,613	12	(0.74)	11.2	1.38	(0.72-2.64)	9,031	48	(0.53)	62.2	1.41	(1.02-1.96)	0.95	0.0%
Arrhythmia														
Non-users	7,004	65	(0.93)	38.1	1.00	(Reference)	29,695	198	(0.67)	151.8	1.00	(Reference)		
SERMs	7,087	54	(0.76)	41.2	1.22	(0.85-1.74)	54,108	292	(0.54)	276.8	1.15	(0.96-1.39)	0.80	0.0%
AIs	2,587	20	(0.77)	13.9	1.02	(0.63-1.63)	22,046	185	(0.84)	106.3	1.10	(0.90-1.35)	0.76	0.0%
Both	1,613	19	(1.18)	11.2	1.70	(1.00-2.87)	9,031	65	(0.72)	62.2	1.21	(0.91-1.61)	0.27	19.0%

T2DM														
Non-users	7,004	423	(6.04)	38.1	1.00	(Reference)	29,695	1,158	(3.90)	151.8	1.00	(Reference)		
SERMs	7,087	377	(5.32)	41.2	1.21	(1.05-1.39)	54,108	1,759	(3.25)	276.8	1.25	(1.16-1.35)	0.64	0.0%
AIs	2,587	213	(8.23)	13.9	1.31	(1.11-1.55)	22,046	1,277	(5.79)	106.3	1.21	(1.12-1.31)	0.42	0.0%
Both	1,613	85	(5.27)	11.2	1.07	(0.85-1.36)	9,031	392	(4.34)	62.2	1.30	(1.16-1.46)	0.16	50.0%

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs). If the P-value was <0.1 or I²>50% in the heterogeneity test, then we hypothesized a significant difference by the stratified factor.

Table S8. The subgroup analysis by chemotherapy

	No chemotherapy						Chemotherapy						P-value	I ²
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*				
Composite of CVD														
Non-users	11,404	539	(4.73)	61.2	1.00 (Reference)	25,295	800	(3.16)	128.8	1.00 (Reference)				
SERMs	27,663	701	(2.53)	137.9	1.07 (0.96-1.21)	33,532	825	(2.46)	180.1	1.17 (1.06-1.29)	0.29	11.0%		
AIs	8,575	433	(5.05)	39.5	1.06 (0.92-1.21)	16,058	726	(4.52)	80.6	1.19 (1.08-1.32)	0.16	50.0%		
Both	2,748	143	(5.20)	18.1	1.28 (1.06-1.55)	7,896	234	(2.96)	55.4	1.23 (1.06-1.43)	0.76	0.0%		
Stroke														
Non-users	11,404	169	(1.48)	61.2	1.00 (Reference)	25,295	166	(0.66)	128.8	1.00 (Reference)				
SERMs	27,663	170	(0.61)	137.9	0.94 (0.76-1.17)	33,532	186	(0.55)	180.1	1.50 (1.21-1.85)	<0.01	89.0%		
AIs	8,575	151	(1.76)	39.5	1.03 (0.81-1.29)	16,058	186	(1.16)	80.6	1.27 (1.03-1.56)	0.18	45.0%		
Both	2,748	35	(1.27)	18.1	0.96 (0.67-1.40)	7,896	53	(0.67)	55.4	1.29 (0.94-1.77)	0.24	28.0%		
CHD														
Non-users	11,404	183	(1.60)	61.2	1.00 (Reference)	25,295	231	(0.91)	128.8	1.00 (Reference)				
SERMs	27,663	237	(0.86)	137.9	0.99 (0.81-1.21)	33,532	228	(0.68)	180.1	1.11 (0.92-1.34)	0.41	0.0%		
AIs	8,575	155	(1.81)	39.5	1.16 (0.92-1.47)	16,058	234	(1.46)	80.6	1.25 (1.04-1.50)	0.63	0.0%		
Both	2,748	47	(1.71)	18.1	1.27 (0.92-1.77)	7,896	63	(0.80)	55.4	1.09 (0.82-1.45)	0.49	0.0%		
VTE														
Non-users	11,404	38	(0.33)	61.2	1.00 (Reference)	25,295	58	(0.23)	128.8	1.00 (Reference)				
SERMs	27,663	66	(0.24)	137.9	1.08 (0.74-1.56)	33,532	88	(0.26)	180.1	1.59 (1.13-2.23)	0.13	57.0%		
AIs	8,575	22	(0.26)	39.5	0.84 (0.55-1.29)	16,058	52	(0.32)	80.6	1.28 (0.88-1.86)	0.15	52.0%		
Both	2,748	12	(0.44)	18.1	1.02 (0.55-1.89)	7,896	23	(0.29)	55.4	1.73 (1.06-2.84)	0.19	42.0%		
HF														
Non-users	11,404	56	(0.49)	61.2	1.00 (Reference)	25,295	175	(0.69)	128.8	1.00 (Reference)				
SERMs	27,663	67	(0.24)	137.9	1.08 (0.74-1.56)	33,532	139	(0.41)	180.1	0.87 (0.70-1.09)	0.34	0.0%		
AIs	8,575	37	(0.43)	39.5	0.84 (0.55-1.29)	16,058	119	(0.74)	80.6	1.18 (0.93-1.49)	0.18	44.0%		
Both	2,748	13	(0.47)	18.1	1.02 (0.55-1.89)	7,896	47	(0.60)	55.4	1.60 (1.14-2.23)	0.21	36.0%		
Arrhythmia														
Non-users	11,404	93	(0.82)	61.2	1.00 (Reference)	25,295	170	(0.67)	128.8	1.00 (Reference)				
SERMs	27,663	161	(0.58)	137.9	1.30 (1.00-1.70)	33,532	185	(0.55)	180.1	1.09 (0.88-1.34)	0.30	7.0%		
AIs	8,575	69	(0.80)	39.5	1.15 (0.83-1.60)	16,058	136	(0.85)	80.6	1.07 (0.85-1.34)	0.70	0.0%		
Both	2,748	36	(1.31)	18.1	1.95 (1.31-2.90)	7,896	48	(0.61)	55.4	1.03 (0.74-1.42)	0.01	83.0%		

T2DM														
Non-users	11,404	563	(4.94)	61.2	1.00	(Reference)	25,295	1,018	(4.02)	128.8	1.00	(Reference)		
SERMs	27,663	919	(3.32)	137.9	1.14	(1.02-1.27)	33,532	1,217	(3.63)	180.1	1.27	(1.17-1.38)	0.12	59.0%
AIs	8,575	496	(5.78)	39.5	1.12	(0.99-1.28)	16,058	994	(6.19)	80.6	1.26	(1.15-1.37)	0.15	52.0%
Both	2,748	145	(5.28)	18.1	1.18	(0.98-1.42)	7,896	332	(4.20)	55.4	1.28	(1.13-1.45)	0.48	0.0%

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs). If the P-value was <0.1 or $I^2 > 50\%$ in the heterogeneity test, then we hypothesized a significant difference by the stratified factor.

Table S9. The subgroup analysis by radiotherapy

	No radiotherapy						Radiotherapy						P-value	I ²
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*				
Composite of CVD														
Non-users	15,348	712	(4.64)	81.5	1.00 (Reference)	21,351	627	(2.94)	108.5	1.00 (Reference)				
SERMs	18,670	626	(3.35)	101.9	1.18 (1.06-1.31)	42,525	900	(2.12)	216.1	1.11 (1.00-1.23)	0.41	0.0%		
AIs	7,292	436	(5.98)	36.9	1.11 (0.98-1.25)	17,341	723	(4.17)	83.3	1.17 (1.05-1.30)	0.52	0.0%		
Both	3,579	161	(4.50)	24.9	1.25 (1.05-1.49)	7,065	216	(3.06)	48.6	1.24 (1.06-1.46)	0.97	0.0%		
Stroke														
Non-users	15,348	202	(1.32)	81.5	1.00 (Reference)	21,351	133	(0.62)	108.5	1.00 (Reference)				
SERMs	18,670	182	(0.97)	101.9	1.25 (1.02-1.52)	42,525	174	(0.41)	216.1	1.18 (0.93-1.49)	0.71	0.0%		
AIs	7,292	146	(2.00)	36.9	1.09 (0.88-1.35)	17,341	191	(1.10)	83.3	1.25 (1.00-1.57)	0.39	0.0%		
Both	3,579	37	(1.03)	24.9	0.97 (0.68-1.38)	7,065	51	(0.72)	48.6	1.31 (0.94-1.83)	0.21	35.0%		
CHD														
Non-users	15,348	217	(1.41)	81.5	1.00 (Reference)	21,351	197	(0.92)	108.5	1.00 (Reference)				
SERMs	18,670	180	(0.96)	101.9	1.10 (0.90-1.34)	42,525	285	(0.67)	216.1	1.01 (0.84-1.23)	0.57	0.0%		
AIs	7,292	143	(1.96)	36.9	1.28 (1.03-1.59)	17,341	246	(1.42)	83.3	1.16 (0.96-1.41)	0.49	0.0%		
Both	3,579	46	(1.29)	24.9	1.21 (0.87-1.67)	7,065	64	(0.91)	48.6	1.09 (0.82-1.45)	0.64	0.0%		
VTE														
Non-users	15,348	51	(0.33)	81.5	1.00 (Reference)	21,351	45	(0.21)	108.5	1.00 (Reference)				
SERMs	18,670	54	(0.29)	101.9	1.32 (0.90-1.94)	42,525	100	(0.24)	216.1	1.69 (1.17-2.44)	0.37	0.0%		
AIs	7,292	29	(0.40)	36.9	1.27 (0.80-2.01)	17,341	45	(0.26)	83.3	1.14 (0.75-1.73)	0.74	0.0%		
Both	3,579	13	(0.36)	24.9	1.54 (0.82-2.86)	7,065	22	(0.31)	48.6	1.94 (1.15-3.27)	0.58	0.0%		
HF														
Non-users	15,348	114	(0.74)	81.5	1.00 (Reference)	21,351	117	(0.55)	108.5	1.00 (Reference)				
SERMs	18,670	86	(0.46)	101.9	1.07 (0.81-1.42)	42,525	120	(0.28)	216.1	0.91 (0.70-1.18)	0.40	0.0%		
AIs	7,292	51	(0.70)	36.9	0.89 (0.65-1.23)	17,341	105	(0.61)	83.3	1.19 (0.91-1.56)	0.18	45.0%		
Both	3,579	26	(0.73)	24.9	1.42 (0.92-2.20)	7,065	34	(0.48)	48.6	1.40 (0.95-2.08)	0.96	0.0%		
Arrhythmia														
Non-users	15,348	128	(0.83)	81.5	1.00 (Reference)	21,351	135	(0.63)	108.5	1.00 (Reference)				
SERMs	18,670	125	(0.67)	101.9	1.20 (0.94-1.53)	42,525	221	(0.52)	216.1	1.11 (0.89-1.38)	0.64	0.0%		
AIs	7,292	69	(0.95)	36.9	1.07 (0.80-1.43)	17,341	136	(0.78)	83.3	1.12 (0.87-1.42)	0.82	0.0%		
Both	3,579	39	(1.09)	24.9	1.55 (1.08-2.24)	7,065	45	(0.64)	48.6	1.12 (0.79-1.58)	0.20	38.0%		

T2DM														
Non-users	15,348	781	(5.09)	81.5	1.00	(Reference)	21,351	800	(3.75)	108.5	1.00	(Reference)		
SERMs	18,670	766	(4.10)	101.9	1.18	(1.07-1.31)	42,525	1,370	(3.22)	216.1	1.28	(1.16-1.40)	0.28	15.0%
AIs	7,292	511	(7.01)	36.9	1.23	(1.09-1.37)	17,341	979	(5.65)	83.3	1.21	(1.10-1.33)	0.88	0.0%
Both	3,579	176	(4.92)	24.9	1.14	(0.97-1.35)	7,065	301	(4.26)	48.6	1.32	(1.15-1.51)	0.20	39.0%

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs). If the P-value was <0.1 or $I^2 > 50\%$ in the heterogeneity test, then we hypothesized a significant difference by the stratified factor.

Table S10. The subgroup analysis by trastuzumab

	No trastuzumab						Trastuzumab						P-value	I ²
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*				
Composite of CVD														
Non-users	30,794	1,146	(3.72)	165.8	1.00	(Reference)	5,905	193	(3.27)	24.2	1.00	(Reference)		
SERMs	56,672	1,410	(2.49)	298.8	1.13	(1.04-1.22)	4,523	116	(2.56)	19.2	0.98	(0.77-1.25)	0.30	7.0%
AIs	22,283	1,055	(4.73)	110.5	1.12	(1.03-1.22)	2,350	104	(4.43)	9.7	1.31	(1.03-1.66)	0.21	35.0%
Both	9,867	358	(3.63)	69.1	1.23	(1.09-1.39)	777	19	(2.45)	4.3	1.33	(0.82-2.15)	0.75	0.0%
Stroke														
Non-users	30,794	306	(0.99)	165.8	1.00	(Reference)	5,905	29	(0.49)	24.2	1.00	(Reference)		
SERMs	56,672	335	(0.59)	298.8	1.16	(0.99-1.35)	4,523	21	(0.46)	19.2	1.67	(0.93-3.02)	0.24	28.0%
AIs	22,283	313	(1.40)	110.5	1.11	(0.95-1.30)	2,350	24	(1.02)	9.7	1.77	(1.03-3.06)	0.11	62.0%
Both	9,867	84	(0.85)	69.1	1.10	(0.86-1.41)	777	4	(0.51)	4.3	1.38	(0.48-3.97)	0.69	0.0%
CHD														
Non-users	30,794	375	(1.22)	165.8	1.00	(Reference)	5,905	39	(0.66)	24.2	1.00	(Reference)		
SERMs	56,672	438	(0.77)	298.8	1.01	(0.88-1.16)	4,523	27	(0.60)	19.2	1.28	(0.76-2.17)	0.39	0.0%
AIs	22,283	368	(1.65)	110.5	1.21	(1.04-1.40)	2,350	21	(0.89)	9.7	1.32	(0.79-2.20)	0.75	0.0%
Both	9,867	104	(1.05)	69.1	1.11	(0.89-1.38)	777	6	(0.77)	4.3	1.91	(0.80-4.61)	0.24	29.0%
VTE														
Non-users	30,794	77	(0.25)	165.8	1.00	(Reference)	5,905	19	(0.32)	24.2	1.00	(Reference)		
SERMs	56,672	149	(0.26)	298.8	1.62	(1.22-2.14)	4,523	5	(0.11)	19.2	0.51	(0.19-1.36)	0.03	80.0%
AIs	22,283	65	(0.29)	110.5	1.20	(0.86-1.67)	2,350	9	(0.38)	9.7	1.16	(0.53-2.55)	0.94	0.0%
Both	9,867	33	(0.33)	69.1	1.80	(1.18-2.73)	777	2	(0.26)	4.3	1.49	(0.34-6.59)	0.81	0.0%
HF														
Non-users	30,794	154	(0.50)	165.8	1.00	(Reference)	5,905	77	(1.30)	24.2	1.00	(Reference)		
SERMs	56,672	158	(0.28)	298.8	0.99	(0.79-1.23)	4,523	48	(1.06)	19.2	0.82	(0.56-1.20)	0.41	0.0%
AIs	22,283	125	(0.56)	110.5	1.03	(0.81-1.30)	2,350	31	(1.32)	9.7	1.16	(0.76-1.75)	0.62	0.0%
Both	9,867	54	(0.55)	69.1	1.35	(0.99-1.86)	777	6	(0.77)	4.3	1.79	(0.77-4.20)	0.54	0.0%
Arrhythmia														
Non-users	30,794	234	(0.76)	165.8	1.00	(Reference)	5,905	29	(0.49)	24.2	1.00	(Reference)		
SERMs	56,672	331	(0.58)	298.8	1.16	(0.98-1.38)	4,523	15	(0.33)	19.2	0.77	(0.40-1.48)	0.23	30.0%
AIs	22,283	186	(0.83)	110.5	1.07	(0.88-1.30)	2,350	19	(0.81)	9.7	1.38	(0.76-2.51)	0.42	0.0%
Both	9,867	83	(0.84)	69.1	1.33	(1.03-1.72)	777	1	(0.13)	4.3	0.31	(0.04-2.31)	0.16	50.0%

T2DM														
Non-users	30,794	1,390	(4.51)	165.8	1.00	(Reference)	5,905	191	(3.23)	24.2	1.00	(Reference)		
SERMs	56,672	2,038	(3.60)	298.8	1.23	(1.15-1.32)	4,523	98	(2.17)	19.2	1.04	(0.80-1.34)	0.20	39.0%
AIs	22,283	1,392	(6.25)	110.5	1.23	(1.14-1.33)	2,350	98	(4.17)	9.7	1.12	(0.88-1.43)	0.47	0.0%
Both	9,867	457	(4.63)	69.1	1.25	(1.13-1.40)	777	20	(2.57)	4.3	1.12	(0.70-1.78)	0.64	0.0%

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. ¹Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs). If the P-value was <0.1 or I²>50% in the heterogeneity test, then we hypothesized a significant difference by the stratified factor.

Table S11. The subgroup analysis by regimen types

	No. of total	No. of events	(%)	1,000 PY	Age-adjusted HR (95% CI)	Adjusted HR (95% CI)*
Composite of CVD						
Non-users	36,699	1,399	(3.81)	190.0	1.00 (Reference)	1.00 (Reference)
Tamoxifen	58,809	1,341	(2.28)	299.0	0.96 (0.89-1.04)	1.04 (0.96-1.13)
Toremifene	1,502	138	(9.19)	11.7	1.22 (1.02-1.46)	1.20 (1.00-1.43)
Anastrozole	9,173	475	(5.18)	47.2	0.99 (0.89-1.10)	1.04 (0.93-1.15)
Letrozole	14,495	642	(4.43)	68.1	0.98 (0.89-1.08)	1.04 (0.94-1.15)
Stroke						
Non-users	36,699	335	(0.91)	190.0	1.00 (Reference)	1.00 (Reference)
Tamoxifen	58,809	307	(0.52)	299.0	1.07 (0.91-1.25)	1.14 (0.97-1.34)
Toremifene	1,502	42	(2.80)	11.7	1.28 (0.93-1.77)	1.19 (0.86-1.65)
Anastrozole	9,173	142	(1.55)	47.2	1.04 (0.85-1.26)	1.11 (0.91-1.35)
Letrozole	14,495	186	(1.28)	68.1	1.02 (0.85-1.22)	1.10 (0.91-1.32)
CHD						
Non-users	36,699	414	(1.13)	190.0	1.00 (Reference)	1.00 (Reference)
Tamoxifen	58,809	400	(0.68)	299.0	0.92 (0.79-1.05)	0.93 (0.80-1.08)
Toremifene	1,502	46	(3.06)	11.7	1.32 (0.97-1.79)	1.24 (0.91-1.69)
Anastrozole	9,173	156	(1.70)	47.2	1.06 (0.88-1.27)	1.09 (0.90-1.32)
Letrozole	14,495	225	(1.55)	68.1	1.13 (0.96-1.33)	1.18 (1.00-1.40)
VTE						
Non-users	36,699	96	(0.26)	190.0	1.00 (Reference)	1.00 (Reference)
Tamoxifen	58,809	140	(0.24)	299.0	1.24 (0.95-1.62)	1.36 (1.03-1.79)
Toremifene	1,502	11	(0.73)	11.7	1.51 (0.81-2.83)	1.51 (0.80-2.83)
Anastrozole	9,173	31	(0.34)	47.2	1.00 (0.66-1.50)	1.05 (0.69-1.59)
Letrozole	14,495	37	(0.26)	68.1	0.86 (0.59-1.26)	0.90 (0.61-1.33)
HF						
Non-users	36,699	231	(0.63)	190.0	1.00 (Reference)	1.00 (Reference)
Tamoxifen	58,809	191	(0.32)	299.0	0.71 (0.59-0.87)	0.94 (0.77-1.16)
Toremifene	1,502	12	(0.80)	11.7	0.71 (0.39-1.26)	0.83 (0.46-1.49)
Anastrozole	9,173	67	(0.73)	47.2	0.90 (0.68-1.18)	1.02 (0.77-1.35)
Letrozole	14,495	74	(0.51)	68.1	0.71 (0.55-0.93)	0.78 (0.60-1.03)
Arrhythmia						
Non-users	36,699	263	(0.72)	190.0	1.00 (Reference)	1.00 (Reference)
Tamoxifen	58,809	304	(0.52)	299.0	0.99 (0.83-1.17)	0.99 (0.83-1.17)
Toremifene	1,502	27	(1.80)	11.7	1.28 (0.86-1.90)	1.28 (0.86-1.90)
Anastrozole	9,173	80	(0.87)	47.2	0.93 (0.72-1.20)	0.93 (0.72-1.20)
Letrozole	14,495	121	(0.83)	68.1	1.04 (0.84-1.30)	1.04 (0.84-1.30)
T2DM						
Non-users	36,699	1,581	(4.31)	190.0	1.00 (Reference)	1.00 (Reference)
Tamoxifen	58,809	1,910	(3.25)	299.0	1.08 (1.01-1.16)	1.14 (1.07-1.23)
Toremifene	1,502	157	(10.45)	11.7	1.22 (1.04-1.44)	1.15 (0.97-1.35)
Anastrozole	9,173	591	(6.44)	47.2	1.10 (1.00-1.21)	1.10 (1.00-1.21)
Letrozole	14,495	834	(5.75)	68.1	1.14 (1.05-1.24)	1.14 (1.05-1.25)

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs).

Table S12. The subgroup analysis by menopausal status in the health screening subjects

	Pre-menopausal						Post-menopausal						P-value	I ²
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*		No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*			
Composite of CVD														
Non-users	9,324	218	(2.34)	45.5	1.00	(Reference)	8,706	322	(3.70)	35.6	1.00	(Reference)		
SERMs	27,801	478	(1.72)	127.8	1.11	(0.94-1.31)	5,606	194	(3.46)	24.1	1.05	(0.88-1.26)	0.66	0.0%
AIs	3,107	126	(4.06)	17.5	1.31	(1.05-1.63)	12,234	435	(3.56)	48.8	1.02	(0.88-1.18)	0.06	72.0%
Both	3,240	78	(2.41)	22.7	1.26	(0.97-1.64)	2,045	68	(3.33)	11.0	1.00	(0.76-1.30)	0.22	33.0%
Stroke														
Non-users	9,324	41	(0.44)	45.5	1.00	(Reference)	8,706	88	(1.01)	35.6	1.00	(Reference)		
SERMs	27,801	94	(0.34)	127.8	1.28	(0.88-1.87)	5,606	45	(0.80)	24.1	0.82	(0.58-1.18)	0.09	64.0%
AIs	3,107	30	(0.97)	17.5	1.35	(0.84-2.16)	12,234	122	(1.00)	48.8	1.07	(0.81-1.42)	0.42	0.0%
Both	3,240	14	(0.43)	22.7	1.15	(0.62-2.15)	2,045	19	(0.93)	11.0	0.97	(0.59-1.61)	0.67	0.0%
CHD														
Non-users	9,324	68	(0.73)	45.5	1.00	(Reference)	8,706	108	(1.24)	35.6	1.00	(Reference)		
SERMs	27,801	141	(0.51)	127.8	1.03	(0.77-1.39)	5,606	74	(1.32)	24.1	1.02	(0.75-1.37)	0.93	0.0%
AIs	3,107	44	(1.42)	17.5	1.49	(1.03-2.16)	12,234	135	(1.10)	48.8	0.91	(0.70-1.18)	0.03	78.0%
Both	3,240	26	(0.80)	22.7	1.33	(0.83-2.11)	2,045	22	(1.08)	11.0	0.91	(0.57-1.46)	0.27	19.0%
VTE														
Non-users	9,324	12	(0.13)	45.5	1.00	(Reference)	8,706	24	(0.28)	35.6	1.00	(Reference)		
SERMs	27,801	58	(0.21)	127.8	2.59	(1.36-4.90)	5,606	12	(0.21)	24.1	1.04	(0.53-2.06)	0.06	72.0%
AIs	3,107	6	(0.19)	17.5	1.22	(0.47-3.18)	12,234	30	(0.25)	48.8	0.93	(0.54-1.61)	0.63	0.0%
Both	3,240	8	(0.25)	22.7	2.58	(1.03-6.48)	2,045	6	(0.29)	11.0	1.24	(0.50-3.09)	0.27	19.0%
HF														
Non-users	9,324	43	(0.46)	45.5	1.00	(Reference)	8,706	47	(0.54)	35.6	1.00	(Reference)		
SERMs	27,801	56	(0.20)	127.8	0.75	(0.51-1.12)	5,606	24	(0.43)	24.1	1.40	(0.86-2.29)	0.05	73.0%
AIs	3,107	21	(0.68)	17.5	1.51	(0.90-2.53)	12,234	64	(0.52)	48.8	1.11	(0.76-1.64)	0.35	0.0%
Both	3,240	13	(0.40)	22.7	1.43	(0.75-2.74)	2,045	7	(0.34)	11.0	0.97	(0.43-2.19)	0.47	0.0%
Arrhythmia														
Non-users	9,324	54	(0.58)	45.5	1.00	(Reference)	8,706	55	(0.63)	35.6	1.00	(Reference)		
SERMs	27,801	129	(0.46)	127.8	1.02	(0.74-1.41)	5,606	39	(0.70)	24.1	1.26	(0.84-1.90)	0.43	0.0%
AIs	3,107	25	(0.80)	17.5	1.01	(0.62-1.63)	12,234	85	(0.69)	48.8	1.14	(0.81-1.62)	0.67	0.0%
Both	3,240	17	(0.52)	22.7	0.96	(0.55-1.68)	2,045	14	(0.68)	11.0	1.08	(0.60-1.96)	0.78	0.0%

T2DM														
Non-users	9,324	284	(3.05)	45.5	1.00	(Reference)	8,706	375	(4.31)	35.6	1.00	(Reference)		
SERMs	27,801	720	(2.59)	127.8	1.24	(1.08-1.43)	5,606	267	(4.76)	24.1	1.27	(1.08-1.48)	0.87	0.0%
AIs	3,107	162	(5.21)	17.5	1.12	(0.92-1.36)	12,234	590	(4.82)	48.8	1.24	(1.09-1.42)	0.38	0.0%
Both	3,240	99	(3.06)	22.7	1.14	(0.90-1.43)	2,045	107	(5.23)	11.0	1.39	(1.11-1.73)	0.22	33.0%

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, T2DM (or CVDs), BMI, smoking, alcohol consumption, and physical activity. If the P-value was <0.1 or I²>50% in the heterogeneity test, then we hypothesized a significant difference by the stratified factor.

Table S13. The sensitivity analysis after excluding short-term users; ≥ 6 or ≥ 12 month use)

	≥ 6 months use (N=130,696)					≥ 12 months use (N=125,555)				
	No. of total	No. of events	(%)	Adjusted HR (95% CI)*		No. of total	No. of events	(%)	Adjusted HR (95% CI)*	
Composite of CVD										
Non-users	36,699	1,339	(3.65)	1.00	(Reference)	36,699	1,339	(3.65)	1.00	(Reference)
SERMs	59,417	1,475	(2.48)	1.12	(1.04-1.21)	55,949	1,405	(2.51)	1.10	(1.02-1.18)
AIs	24,044	1,140	(4.74)	1.13	(1.04-1.22)	22,692	1,109	(4.89)	1.11	(1.02-1.20)
Both	10,536	373	(3.54)	1.23	(1.09-1.38)	10,215	365	(3.57)	1.21	(1.08-1.36)
Stroke										
Non-users	36,699	335	(0.91)	1.00	(Reference)	36,699	335	(0.91)	1.00	(Reference)
SERMs	59,417	336	(0.57)	1.18	(1.01-1.37)	55,949	312	(0.56)	1.13	(0.97-1.32)
AIs	24,044	330	(1.37)	1.14	(0.98-1.33)	22,692	326	(1.44)	1.15	(0.99-1.34)
Both	10,536	87	(0.83)	1.12	(0.88-1.42)	10,215	85	(0.83)	1.10	(0.87-1.41)
CHD										
Non-users	36,699	414	(1.13)	1.00	(Reference)	36,699	414	(1.13)	1.00	(Reference)
SERMs	59,417	447	(0.75)	1.01	(0.88-1.16)	55,949	431	(0.77)	1.01	(0.88-1.16)
AIs	24,044	384	(1.60)	1.21	(1.05-1.40)	22,692	376	(1.66)	1.20	(1.04-1.38)
Both	10,536	108	(1.03)	1.13	(0.91-1.40)	10,215	106	(1.04)	1.12	(0.90-1.39)
VTE										
Non-users	36,699	96	(0.26)	1.00	(Reference)	36,699	96	(0.26)	1.00	(Reference)
SERMs	59,417	152	(0.26)	1.49	(1.15-1.94)	55,949	143	(0.26)	1.43	(1.10-1.87)
AIs	24,044	72	(0.30)	1.15	(0.85-1.57)	22,692	66	(0.29)	1.08	(0.79-1.47)
Both	10,536	35	(0.33)	1.72	(1.16-2.55)	10,215	34	(0.33)	1.66	(1.11-2.48)
HF										
Non-users	36,699	231	(0.63)	1.00	(Reference)	36,699	231	(0.63)	1.00	(Reference)
SERMs	59,417	202	(0.34)	0.99	(0.81-1.20)	55,949	189	(0.34)	0.95	(0.78-1.15)
AIs	24,044	154	(0.64)	1.04	(0.85-1.28)	22,692	146	(0.64)	1.01	(0.82-1.24)
Both	10,536	60	(0.57)	1.41	(1.05-1.89)	10,215	59	(0.58)	1.39	(1.04-1.87)
Arrhythmia										
Non-users	36,699	263	(0.72)	1.00	(Reference)	36,699	263	(0.72)	1.00	(Reference)
SERMs	59,417	339	(0.57)	1.14	(0.97-1.34)	55,949	331	(0.59)	1.14	(0.97-1.34)
AIs	24,044	202	(0.84)	1.08	(0.89-1.30)	22,692	197	(0.87)	1.06	(0.88-1.28)
Both	10,536	83	(0.79)	1.26	(0.98-1.62)	10,215	81	(0.79)	1.24	(0.96-1.60)

T2DM										
Non-users	36,699	1,581	(4.31)	1.00	(Reference)	36,699	1,581	(4.31)	1.00	(Reference)
SERMs	59,417	2,076	(3.49)	1.22	(1.14-1.30)	55,949	2,007	(3.59)	1.21	(1.14-1.30)
AIs	24,044	1,478	(6.15)	1.22	(1.14-1.31)	22,692	1,445	(6.37)	1.21	(1.13-1.30)
Both	10,536	476	(4.52)	1.24	(1.12-1.38)	10,215	469	(4.59)	1.24	(1.12-1.38)

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs).

Table S14. The sensitivity analysis in patients with a followed-up duration ≥ 5 years

	No. of total	No. of events	(%)	1,000 PY	Age adjusted HR (95% CI)	Adjusted HR (95% CI)*
Composite of CVD						
Non-users	16,678	399	(2.39)	135.5	1.00 (Reference)	1.00 (Reference)
SERMs	28,314	501	(1.77)	224.7	1.39 (1.23-1.58)	1.44 (1.26-1.63)
AIs	10,375	318	(3.07)	80.7	1.17 (1.02-1.35)	1.21 (1.04-1.40)
Both	7,566	210	(2.78)	63.2	1.33 (1.12-1.57)	1.36 (1.15-1.61)
Stroke						
Non-users	16,678	97	(0.58)	135.5	1.00 (Reference)	1.00 (Reference)
SERMs	28,314	110	(0.39)	224.7	1.42 (1.09-1.85)	1.48 (1.13-1.94)
AIs	10,375	105	(1.01)	80.7	1.36 (1.03-1.78)	1.42 (1.07-1.87)
Both	7,566	44	(0.58)	63.2	1.18 (0.83-1.69)	1.23 (0.86-1.76)
CHD						
Non-users	16,678	122	(0.73)	135.5	1.00 (Reference)	1.00 (Reference)
SERMs	28,314	173	(0.61)	224.7	1.45 (1.15-1.82)	1.45 (1.15-1.83)
AIs	10,375	106	(1.02)	80.7	1.34 (1.04-1.73)	1.42 (1.10-1.84)
Both	7,566	60	(0.79)	63.2	1.24 (0.91-1.70)	1.30 (0.95-1.78)
VTE						
Non-users	16,678	28	(0.17)	135.5	1.00 (Reference)	1.00 (Reference)
SERMs	28,314	40	(0.14)	224.7	1.41 (0.88-2.26)	1.50 (0.93-2.41)
AIs	10,375	21	(0.20)	80.7	1.29 (0.75-2.21)	1.39 (0.80-2.40)
Both	7,566	18	(0.24)	63.2	1.59 (0.88-2.88)	1.66 (0.91-3.02)
HF						
Non-users	16,678	45	(0.27)	135.5	1.00 (Reference)	1.00 (Reference)
SERMs	28,314	56	(0.20)	224.7	1.44 (1.00-2.09)	1.55 (1.06-2.25)
AIs	10,375	37	(0.36)	80.7	1.35 (0.89-2.05)	1.41 (0.92-2.16)
Both	7,566	36	(0.48)	63.2	1.98 (1.28-3.08)	2.09 (1.34-3.26)
Arrhythmia						
Non-users	16,678	107	(0.64)	135.5	1.00 (Reference)	1.00 (Reference)
SERMs	28,314	122	(0.43)	224.7	1.25 (0.97-1.61)	1.28 (0.99-1.65)
AIs	10,375	49	(0.47)	80.7	0.72 (0.52-0.99)	0.68 (0.49-0.95)
Both	7,566	52	(0.69)	63.2	1.21 (0.87-1.69)	1.17 (0.84-1.64)
T2DM						
Non-users	16,678	548	(3.29)	135.5	1.00 (Reference)	1.00 (Reference)
SERMs	28,314	626	(2.21)	224.7	1.18 (1.05-1.31)	1.22 (1.09-1.37)
AIs	10,375	480	(4.63)	80.7	1.30 (1.16-1.47)	1.30 (1.15-1.47)
Both	7,566	268	(3.54)	63.2	1.20 (1.03-1.39)	1.20 (1.03-1.39)

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs).

Table S15. The sensitivity analysis; the users having at least two prescriptions

	No. of total	No. of events	(%)	1,000 PY	Age-adjusted HR (95% CI)	Adjusted HR (95% CI)*
Composite of CVD						
Non-users	38,519	1,399	(3.63)	198.6	1.00 (Reference)	1.00 (Reference)
SERMs	61,457	1,612	(2.62)	320.5	1.07 (0.99-1.14)	1.14 (1.06-1.23)
AIs	24,714	1,118	(4.52)	121.9	0.99 (0.92-1.07)	1.04 (0.96-1.13)
Both	8,481	272	(3.21)	60.6	1.15 (1.01-1.32)	1.18 (1.04-1.35)
Stroke						
Non-users	38,519	352	(0.91)	198.6	1.00 (Reference)	1.00 (Reference)
SERMs	61,457	369	(0.60)	320.5	1.13 (0.98-1.31)	1.18 (1.02-1.37)
AIs	24,714	330	(1.34)	121.9	1.03 (0.89-1.20)	1.10 (0.95-1.29)
Both	8,481	65	(0.77)	60.6	1.11 (0.85-1.45)	1.12 (0.86-1.47)
CHD						
Non-users	38,519	434	(1.13)	198.6	1.00 (Reference)	1.00 (Reference)
SERMs	61,457	482	(0.78)	320.5	1.01 (0.89-1.15)	1.02 (0.89-1.16)
AIs	24,714	382	(1.55)	121.9	1.10 (0.96-1.27)	1.14 (0.99-1.31)
Both	8,481	80	(0.94)	60.6	1.08 (0.85-1.37)	1.08 (0.85-1.38)
VTE						
Non-users	38,519	99	(0.26)	198.6	1.00 (Reference)	1.00 (Reference)
SERMs	61,457	168	(0.27)	320.5	1.44 (1.12-1.85)	1.58 (1.22-2.04)
AIs	24,714	67	(0.27)	121.9	0.92 (0.68-1.25)	0.98 (0.71-1.33)
Both	8,481	25	(0.29)	60.6	1.57 (1.00-2.45)	1.62 (1.03-2.54)
HF						
Non-users	38,519	241	(0.63)	198.6	1.00 (Reference)	1.00 (Reference)
SERMs	61,457	220	(0.36)	320.5	0.79 (0.66-0.95)	1.02 (0.85-1.23)
AIs	24,714	145	(0.59)	121.9	0.85 (0.69-1.04)	0.94 (0.76-1.16)
Both	8,481	47	(0.55)	60.6	1.33 (0.97-1.83)	1.49 (1.08-2.05)
Arrhythmia						
Non-users	38,519	274	(0.71)	198.6	1.00 (Reference)	1.00 (Reference)
SERMs	61,457	373	(0.61)	320.5	1.02 (0.85-1.23)	1.16 (0.99-1.37)
AIs	24,714	196	(0.79)	121.9	0.94 (0.76-1.16)	0.96 (0.79-1.15)
Both	8,481	55	(0.65)	60.6	1.49 (1.08-2.05)	1.09 (0.81-1.46)
T2DM						
Non-users	38,519	1,659	(4.31)	198.6	1.00 (Reference)	1.00 (Reference)
SERMs	61,457	2,203	(3.58)	320.5	1.14 (0.98-1.34)	1.21 (1.13-1.29)
AIs	24,714	1,445	(5.85)	121.9	0.95 (0.79-1.14)	1.14 (1.06-1.22)
Both	8,481	377	(4.45)	60.6	1.10 (0.82-1.47)	1.31 (1.17-1.46)

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs).

Table S16. The sensitivity analysis in the health screening subjects

	No. of total	No. of events	(%)	1,000 PY	Age-adjusted HR (95% CI)	Adjusted HR (95% CI)*	Adjusted HR (95% CI)†		
Composite of CVD									
Non-users	18,030	540	(3.00)	81.0	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)		
SERMs	33,407	672	(2.01)	151.9	0.99 (0.89-1.11)	1.06 (0.94-1.19)	1.06 (0.94-1.19)		
AIs	15,341	561	(3.66)	66.3	1.08 (0.96-1.21)	1.12 (0.99-1.26)	1.12 (0.99-1.27)		
Both	5,285	146	(2.76)	33.7	1.10 (0.91-1.33)	1.12 (0.93-1.36)	1.12 (0.93-1.36)		
Stroke									
Non-users	18,030	129	(0.72)	81.0	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)		
SERMs	33,407	139	(0.42)	151.9	1.01 (0.79-1.28)	1.03 (0.81-1.32)	1.02 (0.80-1.31)		
AIs	15,341	152	(0.99)	66.3	1.09 (0.87-1.38)	1.15 (0.90-1.46)	1.16 (0.91-1.48)		
Both	5,285	33	(0.62)	33.7	1.04 (0.71-1.54)	1.04 (0.71-1.54)	1.04 (0.71-1.54)		
CHD									
Non-users	18,030	176	(0.98)	81.0	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)		
SERMs	33,407	215	(0.64)	151.9	0.96 (0.79-1.18)	0.94 (0.77-1.16)	0.96 (0.78-1.18)		
AIs	15,341	179	(1.17)	66.3	1.09 (0.89-1.34)	1.10 (0.89-1.36)	1.09 (0.88-1.35)		
Both	5,285	48	(0.91)	33.7	1.11 (0.80-1.53)	1.10 (0.79-1.52)	1.11 (0.80-1.54)		
VTE									
Non-users	18,030	36	(0.20)	81.0	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)		
SERMs	33,407	70	(0.21)	151.9	1.56 (1.04-2.34)	1.70 (1.11-2.59)	1.66 (1.09-2.54)		
AIs	15,341	36	(0.23)	66.3	1.07 (0.68-1.69)	1.11 (0.70-1.77)	1.13 (0.71-1.81)		
Both	5,285	14	(0.26)	33.7	1.67 (0.89-3.13)	1.74 (0.92-3.27)	1.73 (0.92-3.25)		
HF									
Non-users	18,030	90	(0.50)	81.0	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)		
SERMs	33,407	80	(0.24)	151.9	0.65 (0.48-0.87)	0.94 (0.69-1.28)	0.91 (0.66-1.25)		
AIs	15,341	85	(0.55)	66.3	1.04 (0.78-1.40)	1.20 (0.88-1.62)	1.22 (0.90-1.65)		
Both	5,285	20	(0.38)	33.7	1.04 (0.63-1.70)	1.22 (0.74-2.01)	1.21 (0.73-1.99)		
Arrhythmia									
Non-users	18,030	109	(0.60)	81.0	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)		
SERMs	33,407	168	(0.50)	151.9	1.10 (0.86-1.40)	1.12 (0.87-1.44)	1.12 (0.87-1.44)		
AIs	15,341	110	(0.72)	66.3	1.11 (0.85-1.45)	1.09 (0.83-1.43)	1.09 (0.83-1.43)		
Both	5,285	31	(0.59)	33.7	1.06 (0.70-1.58)	1.02 (0.68-1.53)	1.02 (0.68-1.53)		
T2DM									
Non-users	18,030	659	(3.66)	81.0	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)		

SERMs	33,407	987	(2.95)	151.9	1.16	(1.05-1.28)	1.21	(1.10-1.34)	1.22	(1.10-1.35)
AIs	15,341	752	(4.90)	66.3	1.22	(1.10-1.35)	1.21	(1.09-1.35)	1.21	(1.08-1.34)
Both	5,285	206	(3.90)	33.7	1.25	(1.07-1.47)	1.26	(1.07-1.47)	1.26	(1.07-1.48)

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and (T2DM or CVDs). †Additionally adjusted for BMI, smoking, alcohol consumption, physical activity, and menopausal status.

Table S17. The sensitivity analysis in patients with previous history of CVDs

	Overall						with previous history of CVD					
	No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*		No. of total	No. of events	(%)	1,000 PY	Adjusted HR (95% CI)*	
Composite of CVD												
Non-users	36,699	1,339	(3.65)	190.0	1.00	(Reference)	1,583	333	(21.04)	6.4	1.00	(Reference)
SERMs	61,195	1,526	(2.49)	318.0	1.13	(1.05-1.21)	1,728	356	(20.60)	7.3	1.18	(1.02-1.38)
AIs	24,633	1,159	(4.71)	120.2	1.14	(1.05-1.23)	1,858	383	(20.61)	7.5	1.06	(0.91-1.23)
Both	10,644	377	(3.54)	73.4	1.24	(1.10-1.39)	431	76	(17.63)	2.3	1.10	(0.85-1.42)
Stroke												
Non-users	36,699	335	(0.91)	190.0	1.00	(Reference)	1,583	80	(5.05)	6.4	1.00	(Reference)
SERMs	61,195	356	(0.58)	318.0	1.20	(1.04-1.40)	1,728	88	(5.09)	7.3	1.41	(1.03-1.92)
AIs	24,633	337	(1.37)	120.2	1.16	(0.99-1.35)	1,858	99	(5.33)	7.5	1.19	(0.88-1.60)
Both	10,644	88	(0.83)	73.4	1.13	(0.89-1.44)	431	21	(4.87)	2.3	1.31	(0.80-2.14)
CHD												
Non-users	36,699	414	(1.13)	190.0	1.00	(Reference)	1,583	146	(9.22)	6.4	1.00	(Reference)
SERMs	61,195	465	(0.76)	318.0	1.03	(0.90-1.18)	1,728	126	(7.29)	7.3	0.98	(0.77-1.26)
AIs	24,633	389	(1.58)	120.2	1.22	(1.06-1.41)	1,858	165	(8.88)	7.5	1.03	(0.82-1.29)
Both	10,644	110	(1.03)	73.4	1.14	(0.92-1.42)	431	32	(7.42)	2.3	1.03	(0.70-1.52)
VTE												
Non-users	36,699	96	(0.26)	190.0	1.00	(Reference)	1,583	14	(0.88)	6.4	1.00	(Reference)
SERMs	61,195	154	(0.25)	318.0	1.47	(1.13-1.90)	1,728	8	(0.46)	7.3	0.67	(0.26-1.69)
AIs	24,633	74	(0.30)	120.2	1.17	(0.86-1.58)	1,858	10	(0.54)	7.5	0.82	(0.37-1.83)
Both	10,644	35	(0.33)	73.4	1.72	(1.15-2.55)	431	2	(0.46)	2.3	0.84	(0.19-3.77)
HF												
Non-users	36,699	231	(0.63)	190.0	1.00	(Reference)	1,583	26	(1.64)	6.4	1.00	(Reference)
SERMs	61,195	206	(0.34)	318.0	0.98	(0.81-1.18)	1,728	29	(1.68)	7.3	1.78	(1.03-3.07)
AIs	24,633	156	(0.63)	120.2	1.05	(0.85-1.29)	1,858	27	(1.45)	7.5	0.90	(0.51-1.57)
Both	10,644	60	(0.56)	73.4	1.41	(1.05-1.89)	431	4	(0.93)	2.3	0.82	(0.28-2.40)

Arrhythmia

Non-users	36,699	263	(0.72)	190.0	1.00	(Reference)	1,583	68	(4.30)	6.4	1.00	(Reference)
SERMs	61,195	346	(0.57)	318.0	1.14	(0.97-1.34)	1,728	105	(6.08)	7.3	1.21	(0.88-1.67)
AIs	24,633	205	(0.83)	120.2	1.08	(0.90-1.30)	1,858	83	(4.47)	7.5	1.18	(0.85-1.64)
Both	10,644	84	(0.79)	73.4	1.28	(0.99-1.64)	431	17	(3.94)	2.3	1.18	(0.69-2.03)

AIs, aromatase inhibitors; CHD, coronary heart diseases; CI, confidence intervals; CVD, cardiovascular diseases; HF, heart failure; HR, hazard ratio; PY, person-years; SERMs, selective estrogen receptor modulators; T2DM, type 2 diabetes mellitus; VTE, venous thromboembolism. *Adjusted for age at diagnosis, income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs).

Table S18. Baseline characteristics of study population after PSM; SERMs vs. non-users

	Non-users (N=31,022, 50.0%)		SERMs (N=31,022, 50.0%)		SMD
Age at diagnosis (mean, SD)	48.0	(9.8)	47.3	(9.8)	-0.08
<40	6,038	(19.5)	5,800	(18.7)	
40-49	11,652	(37.6)	15,192	(49.0)	
50-59	9,948	(32.1)	6,789	(21.9)	
60-69	2,578	(8.3)	2,032	(6.6)	
≥70	806	(2.6)	1,209	(3.9)	
Insurance based income					
1st (lowest)	7,565	(24.4)	7,652	(24.7)	0.01
2nd	5,991	(19.3)	6,011	(19.4)	
3rd	7,358	(23.7)	7,486	(24.1)	
4rd (highest)	10,108	(32.6)	9,873	(31.8)	
Region of residence					
Metropolitan	15,387	(49.6)	15,094	(48.7)	-0.02
Urban	6,866	(22.1)	6,996	(22.6)	
Rural	8,684	(28.0)	8,842	(28.5)	
Histological type					
Invasive	27,661	(89.2)	27,367	(88.2)	-0.03
<i>In situ</i>	3,361	(10.8)	3,655	(11.8)	
Surgery					
No	5,185	(16.7)	5,180	(16.7)	0.00
Yes	25,837	(83.3)	25,842	(83.3)	
Chemotherapy					
No	10,286	(33.2)	9,626	(31.0)	0.05
Yes	20,736	(66.8)	21,396	(69.0)	
Radiotherapy					
No	12,035	(38.8)	12,491	(40.3)	-0.03
Yes	18,987	(61.2)	18,531	(59.7)	
Trastuzumab					
No	27,653	(89.1)	27,035	(87.1)	0.06
Yes	3,369	(10.9)	3,987	(12.9)	
Hypertension					
No	27,887	(89.9)	27,964	(90.1)	-0.01
Yes	3,135	(10.1)	3,058	(9.9)	
Dyslipidemia					
No	28,701	(92.5)	28,681	(92.5)	<0.01
Yes	2,321	(7.5)	2,341	(7.5)	
Osteoporosis					
No	28,964	(93.4)	28,956	(93.3)	<0.01
Yes	2,058	(6.6)	2,066	(6.7)	

PSM, propensity score matching; SERMs, selective estrogen receptor modulators; SMD, standardized mean difference. If SMD >0.1, the covariate has the poor balance.

Table S19. Baseline characteristics of study population after PSM; AIs vs. non-users

	Non-users (N=17,336, 50.0%)		AIs (N=17,336, 50.0%)		SMD
Age at diagnosis (mean, SD)	57.5	(8.8)	56.6	(7.5)	-0.06
<40	179	(1.0)	90	(0.5)	
40-49	2,605	(15.0)	2,036	(11.7)	
50-59	8,944	(51.6)	10,254	(59.1)	
60-69	3,932	(22.7)	3,797	(21.9)	
≥70	1,676	(9.7)	1,159	(6.7)	
Insurance based income					
1st (lowest)	4,565	(26.3)	4,425	(25.5)	-0.02
2nd	3,296	(19.0)	3,242	(18.7)	
3rd	3,972	(22.9)	3,988	(23.0)	
4rd (highest)	5,503	(31.7)	5,681	(32.8)	
Region of residence					
Metropolitan	8,894	(51.3)	8,898	(51.3)	<0.01
Urban	3,281	(18.9)	3,394	(19.6)	
Rural	5,128	(29.6)	5,012	(28.9)	
Histological type					
Invasive	17,236	(99.4)	17,233	(99.4)	<0.01
<i>In situ</i>	100	(0.6)	103	(0.6)	
Surgery					
No	2,493	(14.4)	2,205	(12.7)	0.05
Yes	14,843	(85.6)	15,131	(87.3)	
Chemotherapy					
No	4,430	(25.6)	4,529	(26.1)	-0.01
Yes	12,906	(74.4)	12,807	(73.9)	
Radiotherapy					
No	6,387	(36.8)	5,955	(34.4)	0.05
Yes	10,949	(63.2)	11,381	(65.6)	
Trastuzumab					
No	1,485	(8.6)	15,152	(87.4)	-0.06
Yes	2,531	(14.6)	2,184	(12.6)	
Hypertension					
No	13,768	(79.4)	13,584	(78.4)	0.03
Yes	3,568	(20.6)	3,752	(21.6)	
Dyslipidemia					
No	14,973	(86.4)	14,899	(85.9)	0.01
Yes	2,363	(13.6)	2,437	(14.1)	
Osteoporosis					
No	15,355	(88.6)	15,396	(88.8)	-0.01
Yes	1,981	(11.4)	1,940	(11.2)	

PSM, propensity score matching; AIs, aromatase inhibitors; SMD, standardized mean difference. If SMD >0.1, the covariate has the poor balance.

Table S20. Baseline characteristics of study population after PSM; AIs vs. SERMs

	SERMs		AIs		SMD
	(N=11,209, 50.0%)		(N=11,209, 50.0%)		
Age at diagnosis (mean, SD)	55.2	(8.9)	55.2	(8.4)	0.01
<40	105	(0.9)	90	(0.8)	
40-49	2,406	(21.5)	2,046	(18.3)	
50-59	6,052	(54.0)	6,519	(58.2)	
60-69	1,588	(14.2)	1,633	(14.6)	
≥70	1,058	(9.4)	921	(8.2)	
Insurance based income					
1st (lowest)	2,914	(26.0)	2,888	(25.8)	-0.01
2nd	2,223	(19.8)	2,103	(18.8)	
3rd	2,462	(22.0)	2,422	(21.6)	
4rd (highest)	3,610	(32.2)	3,796	(33.9)	
Region of residence					
Metropolitan	5,468	(48.8)	5,493	(49.0)	<0.01
Urban	2,356	(21.0)	2,388	(21.3)	
Rural	3,358	(30.0)	3,303	(29.5)	
Histological type					
Invasive	11,072	(98.8)	11,108	(99.1)	0.03
<i>In situ</i>	137	(1.2)	101	(0.9)	
Surgery					
No	1,551	(13.8)	1,451	(12.9)	0.03
Yes	9,658	(86.2)	9,758	(87.1)	
Chemotherapy					
No	3,808	(34.0)	4,120	(36.8)	-0.06
Yes	7,401	(66.0)	7,089	(63.2)	
Radiotherapy					
No	3,795	(33.9)	3,964	(35.4)	-0.03
Yes	7,414	(66.1)	7,245	(64.6)	
Trastuzumab					
No	10,148	(90.5)	10,248	(91.4)	-0.03
Yes	1,061	(9.5)	961	(8.6)	
Hypertension					
No	9,126	(81.4)	9,075	(81.0)	0.01
Yes	2,083	(18.6)	2,134	(19.0)	
Dyslipidemia					
No	9,807	(87.5)	9,946	(88.7)	-0.04
Yes	1,402	(12.5)	1,263	(11.3)	
Osteoporosis					
No	10,062	(89.8)	10,112	(90.2)	-0.01
Yes	1,147	(10.2)	1,097	(9.8)	

PSM, propensity score matching; SERMs, selective estrogen receptor modulators; AIs, aromatase inhibitors; SMD, standardized mean difference. If SMD >0.1, the covariate has the poor balance.

Table S21. The comparison of results between before and after PSM (SERMs vs. non-users)

	Before PSM (Main findings)						After PSM					
	No. of total	No. of events	(%)	1,000 PY	HR (95% CI)*	No. of total	No. of events	(%)	1,000 PY	HR (95% CI)†		
Composite of CVD												
Non-users	36,699	1,339	(3.65)	190.0	1.00 (Reference)	31,022	965	(3.11)	164.0	1.00 (Reference)		
SERMs	61,195	1,526	(2.49)	318.0	1.13 (1.05-1.21)	31,022	1,009	(3.25)	164.7	1.02 (0.91-1.15)		
Stroke												
Non-users	36,699	335	(0.91)	190.0	1.00 (Reference)	31,022	216	(0.70)	164.0	1.00 (Reference)		
SERMs	61,195	356	(0.58)	318.0	1.20 (1.04-1.40)	31,022	265	(0.85)	164.7	1.15 (0.91-1.46)		
CHD												
Non-users	36,699	414	(1.13)	190.0	1.00 (Reference)	31,022	315	(1.02)	164.0	1.00 (Reference)		
SERMs	61,195	465	(0.76)	318.0	1.03 (0.90-1.18)	31,022	303	(0.98)	164.7	0.98 (0.78-1.23)		
VTE												
Non-users	36,699	96	(0.26)	190.0	1.00 (Reference)	31,022	68	(0.22)	164.0	1.00 (Reference)		
SERMs	61,195	154	(0.25)	318.0	1.47 (1.13-1.90)	31,022	86	(0.28)	164.7	1.60 (1.05-2.44)		
HF												
Non-users	36,699	231	(0.63)	190.0	1.00 (Reference)	31,022	162	(0.52)	164.0	1.00 (Reference)		
SERMs	61,195	206	(0.34)	318.0	0.98 (0.81-1.18)	31,022	153	(0.49)	164.7	0.87 (0.66-1.14)		
Arrhythmia												
Non-users	36,699	263	(0.72)	190.0	1.00 (Reference)	31,022	204	(0.66)	164.0	1.00 (Reference)		
SERMs	61,195	346	(0.57)	318.0	1.14 (0.97-1.34)	31,022	203	(0.65)	164.7	0.93 (0.71-1.22)		
T2DM												
Non-users	36,699	1,581	(4.31)	190.0	1.00 (Reference)	31,022	1,216	(3.92)	164.0	1.00 (Reference)		
SERMs	61,195	2,136	(3.49)	318.0	1.22 (1.14-1.30)	31,022	1,397	(4.50)	164.7	1.25 (1.13-1.39)		

PSM, propensity score matching; PY, person-years; SERMs, selective estrogen receptor modulators; CVD, cardiovascular diseases; CHD, coronary heart diseases; VTE, venous thromboembolism; HF, heart failure; T2DM, type 2 diabetes mellitus; *Adjusted for age, insurance based income, region of residence, histological type, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (of CVDs). †Non-users and SERMs users were matched as the 1:1 ratio according to age, insurance based income, region of residence, histological type, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, and osteoporosis using the PSM, and T2DM (or CVDs) was added in the adjusted model

Table S22. The comparison of results between before and after PSM (AIs vs. non-users)

	Before PSM (Main findings)						After PSM					
	No. of total	No. of events	(%)	1,000 PY	HR (95% CI)*		No. of total	No. of events	(%)	1,000 PY	HR (95% CI)†	
Composite of CVD												
Non-users	36,699	1,339	(3.65)	190.0	1.00	(Reference)	17,336	870	(5.02)	87.2	1.00	(Reference)
AIs	24,633	1,159	(4.71)	120.2	1.14	(1.05-1.23)	17,336	762	(4.40)	87.0	0.92	(0.81-1.04)
Stroke												
Non-users	36,699	335	(0.91)	190.0	1.00	(Reference)	17,336	256	(1.48)	87.2	1.00	(Reference)
AIs	24,633	337	(1.37)	120.2	1.16	(0.99-1.35)	17,336	209	(1.21)	87.0	0.79	(0.61-1.01)
CHD												
Non-users	36,699	414	(1.13)	190.0	1.00	(Reference)	17,336	269	(1.55)	87.2	1.00	(Reference)
AIs	24,633	389	(1.58)	120.2	1.22	(1.06-1.41)	17,336	262	(1.51)	87.0	1.00	(0.80-1.24)
VTE												
Non-users	36,699	96	(0.26)	190.0	1.00	(Reference)	17,336	61	(0.35)	87.2	1.00	(Reference)
AIs	24,633	74	(0.30)	120.2	1.17	(0.86-1.58)	17,336	49	(0.28)	87.0	0.96	(0.58-1.59)
HF												
Non-users	36,699	231	(0.63)	190.0	1.00	(Reference)	17,336	126	(0.73)	87.2	1.00	(Reference)
AIs	24,633	156	(0.63)	120.2	1.05	(0.85-1.29)	17,336	110	(0.63)	87.0	0.90	(0.66-1.24)
Arrhythmia												
Non-users	36,699	263	(0.72)	190.0	1.00	(Reference)	17,336	158	(0.91)	87.2	1.00	(Reference)
AIs	24,633	205	(0.83)	120.2	1.08	(0.90-1.30)	17,336	133	(0.77)	87.0	1.05	(0.77-1.42)
T2DM												
Non-users	36,699	1,581	(4.31)	190.0	1.00	(Reference)	17,336	1,015	(5.85)	87.2	1.00	(Reference)
AIs	24,633	1,490	(6.05)	120.2	1.22	(1.14-1.31)	17,336	1,021	(5.89)	87.0	1.03	(0.92-1.16)

PSM, propensity score matching; PY, person-years; AIs, aromatase inhibitors; CVD, cardiovascular diseases; CHD, coronary heart diseases; VTE, venous thromboembolism; HF, heart failure; T2DM, type 2 diabetes mellitus; *Adjusted for age, insurance based income, region of residence, histological type, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs). †Non-users and AIs users were matched as the 1:1 ratio according to age, insurance based income, region of residence, histological type, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, and osteoporosis using the PSM, and T2DM (or CVDs) was added in the adjusted model

Table S23. The comparison of results between before and after PSM (AIs vs. SERMs)

	Before PSM (Main findings)						After PSM					
	No. of total	No. of events	(%)	1,000 PY	HR (95% CI)*		No. of total	No. of events	(%)	1,000 PY	HR (95% CI)†	
Composite of CVD												
SERMs	61,195	1,526	(2.49)	318.0	1.00	(Reference)	11,209	564	(5.03)	55.7	1.00	(Reference)
AIs	24,633	1,159	(4.71)	120.2	1.01	(0.93-1.09)	11,209	462	(4.12)	58.1	0.94	(0.80-1.10)
Stroke												
SERMs	61,195	356	(0.58)	318.0	1.00	(Reference)	11,209	176	(1.57)	55.7	1.00	(Reference)
AIs	24,633	337	(1.37)	120.2	0.96	(0.83-1.12)	11,209	125	(1.12)	58.1	0.77	(0.56-1.06)
CHD												
SERMs	61,195	465	(0.76)	318.0	1.00	(Reference)	11,209	176	(1.57)	55.7	1.00	(Reference)
AIs	24,633	389	(1.58)	120.2	1.19	(1.03-1.37)	11,209	164	(1.46)	58.1	1.18	(0.88-1.59)
VTE												
SERMs	61,195	154	(0.25)	318.0	1.00	(Reference)	11,209	44	(0.39)	55.7	1.00	(Reference)
AIs	24,633	74	(0.30)	120.2	0.80	(0.60-1.06)	11,209	29	(0.26)	58.1	0.74	(0.42-1.28)
HF												
SERMs	61,195	206	(0.34)	318.0	1.00	(Reference)	11,209	70	(0.62)	55.7	1.00	(Reference)
AIs	24,633	156	(0.63)	120.2	1.07	(0.87-1.33)	11,209	61	(0.54)	58.1	0.95	(0.62-1.47)
Arrhythmia												
SERMs	61,195	346	(0.57)	318.0	1.00	(Reference)	11,209	99	(0.88)	55.7	1.00	(Reference)
AIs	24,633	205	(0.83)	120.2	0.95	(0.79-1.14)	11,209	84	(0.75)	58.1	0.96	(0.65-1.43)
T2DM												
SERMs	61,195	2,136	(3.49)	318.0	1.00	(Reference)	11,209	765	(6.82)	55.7	1.00	(Reference)
AIs	24,633	1,490	(6.05)	120.2	1.00	(0.94-1.08)	11,209	618	(5.51)	58.1	0.80	(0.70-0.93)

PSM, propensity score matching; PY, person-years; AIs, aromatase inhibitors; SERMs, selective estrogen receptor modulators; CVD, cardiovascular diseases; CHD, coronary heart diseases; VTE, venous thromboembolism; HF, heart failure; T2DM, type 2 diabetes mellitus; *Adjusted for age, insurance based income, region of residence, histological type, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and T2DM (or CVDs).

†SERMs and AIs users were matched as the 1:1 ratio according to age, insurance based income, region of residence, histological type, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, and osteoporosis using the PSM, and T2DM (or CVDs) was added in the adjusted model

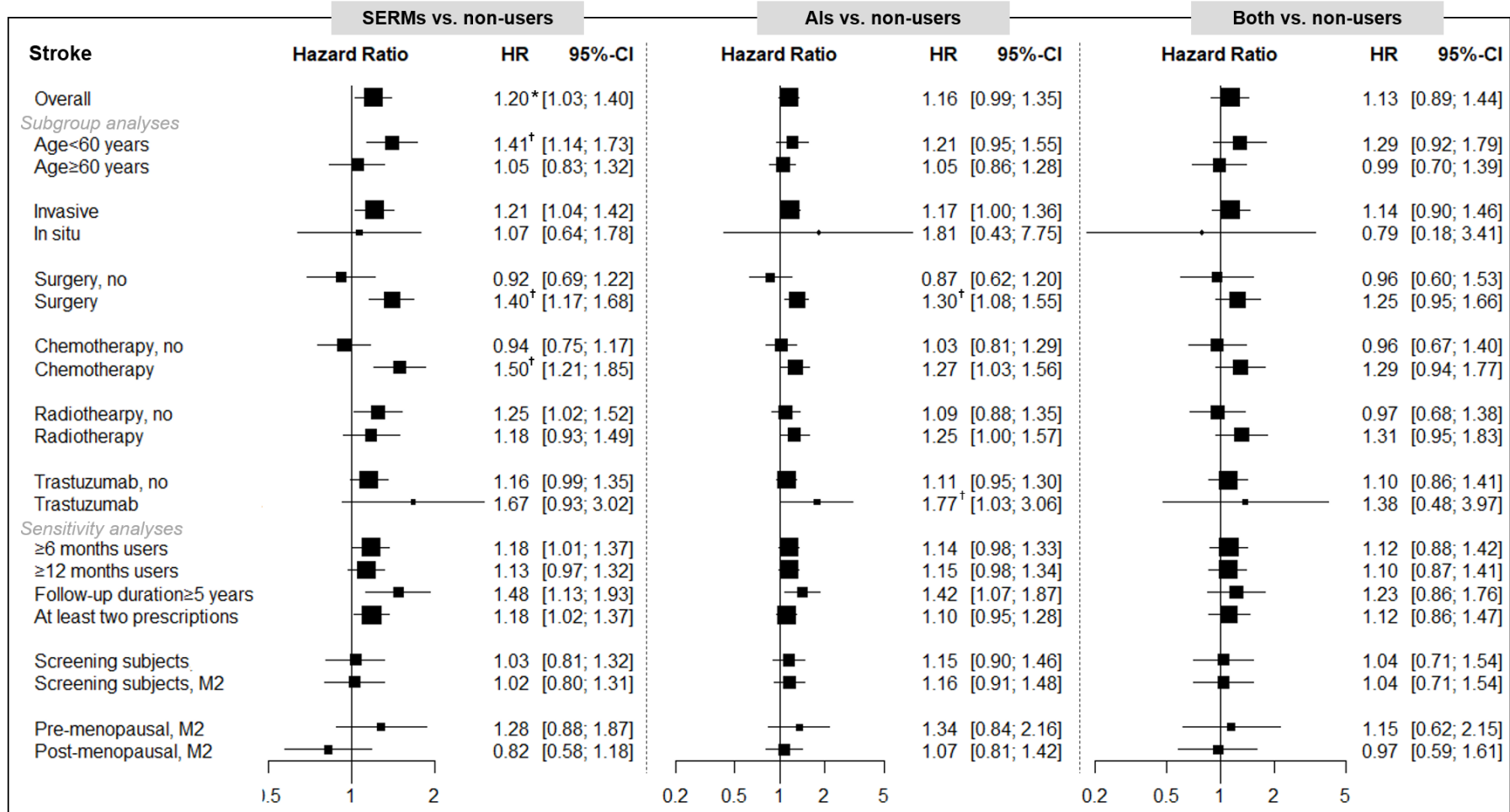


Figure S1. Summary of results for stroke (comparison with non-users)

SERMs, selective estrogen receptor modulators; AIs, aromatase inhibitors. The multivariable adjusted model included age at diagnosis (continuous), insurance-based income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and type 2 diabetes; however, model 2 (M2) additionally include body mass index, lifestyle factors, and menopausal status. The * mark indicates the significance after multiple-testing by a false discovery rate (FDR; P for FDR < 0.05) in Table 2. The † mark indicates the results of heterogeneity (P-value < 0.1 or I² > 50%) by the stratified factor in supplementary materials.

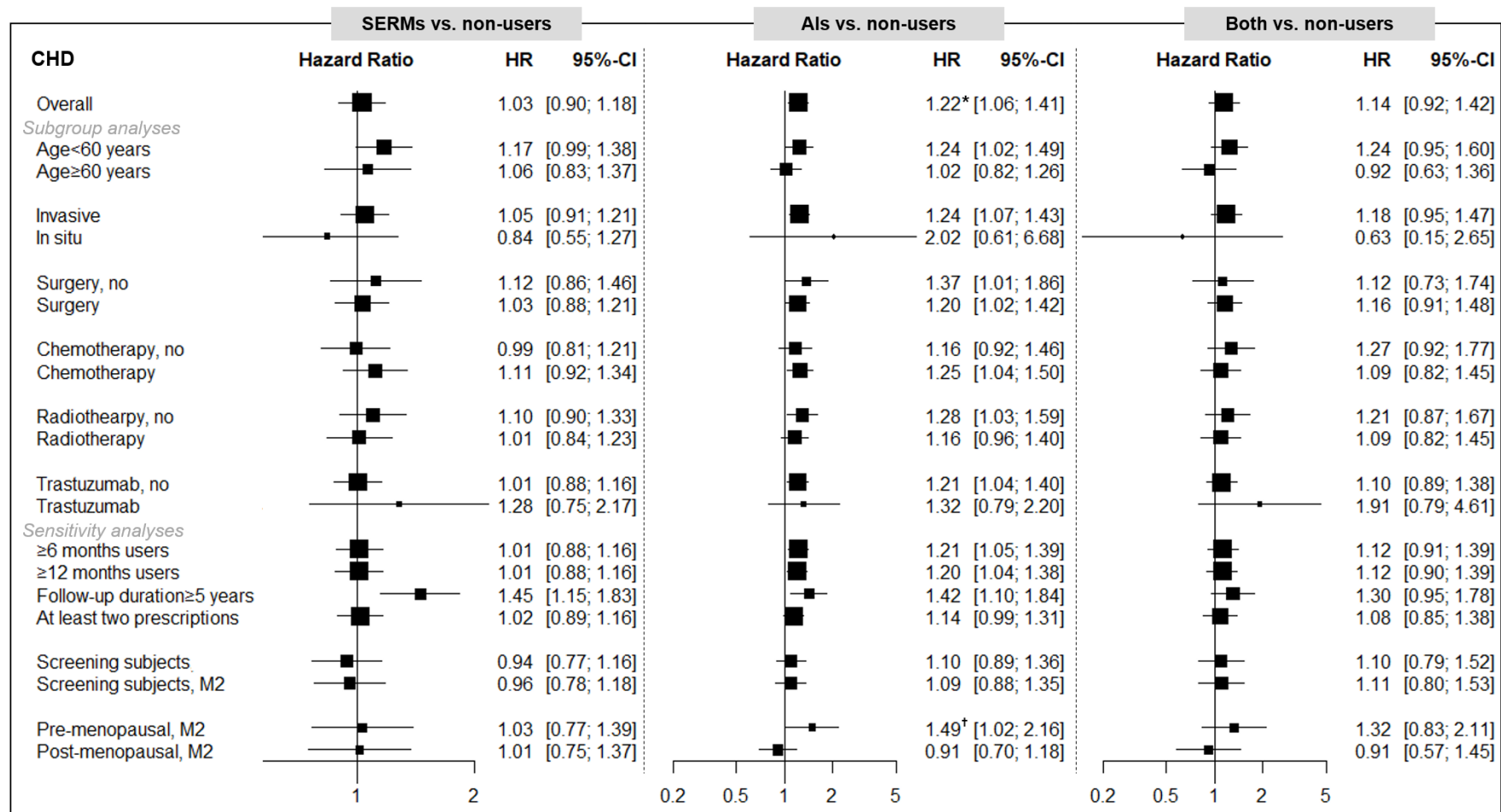


Figure S2. Summary of results for coronary heart diseases (comparison with non-users)

CHD, coronary heart diseases; SERMs, selective estrogen receptor modulators; AIs, aromatase inhibitors. The multivariable adjusted model included age at diagnosis (continuous), insurance-based income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and type 2 diabetes; however, model 2 (M2) additionally include body, mass index, lifestyle factors, and menopausal status. The * mark indicates the significance after multiple-testing by a false discovery rate (FDR; P for FDR<0.05) in Table 2. The † mark indicates the results of heterogeneity (P-value <0.1 or I²>50%) by the stratified factor in supplementary materials.

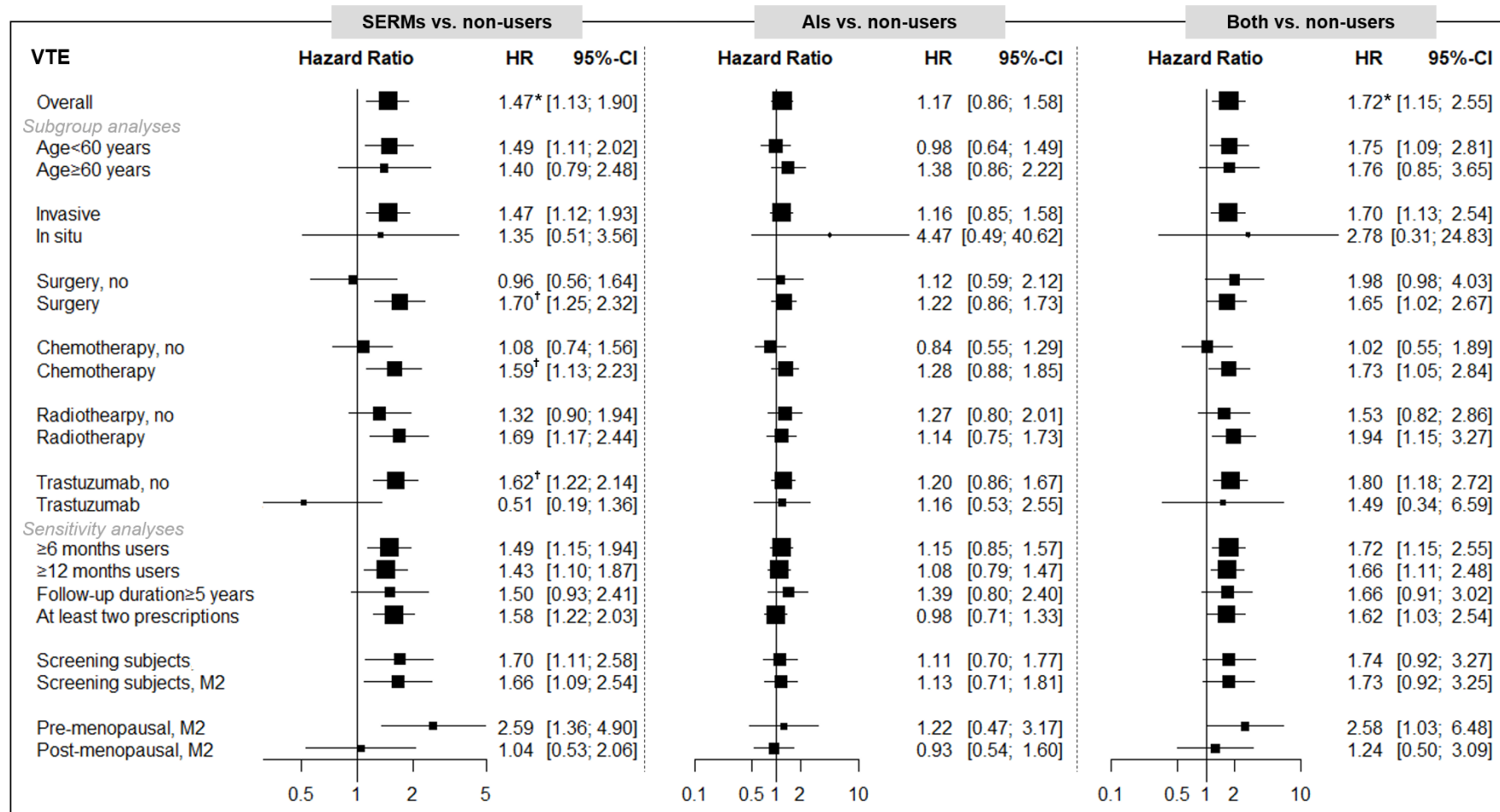


Figure S3. Summary of results for venous thromboembolism (comparison with non-users)

VTE, venous thromboembolism; SERMs, selective estrogen receptor modulators; AIs, aromatase inhibitors. The multivariable adjusted model included age at diagnosis (continuous), insurance-based income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and type 2 diabetes; however, model 2 (M2) additionally include body mass index, lifestyle factors, and menopausal status. The * mark indicates the significance after multiple-testing by a false discovery rate (FDR; P for FDR < 0.05) in Table 2. The † mark indicates the results of heterogeneity (P-value < 0.1 or I² > 50%) by the stratified factor in supplementary materials.

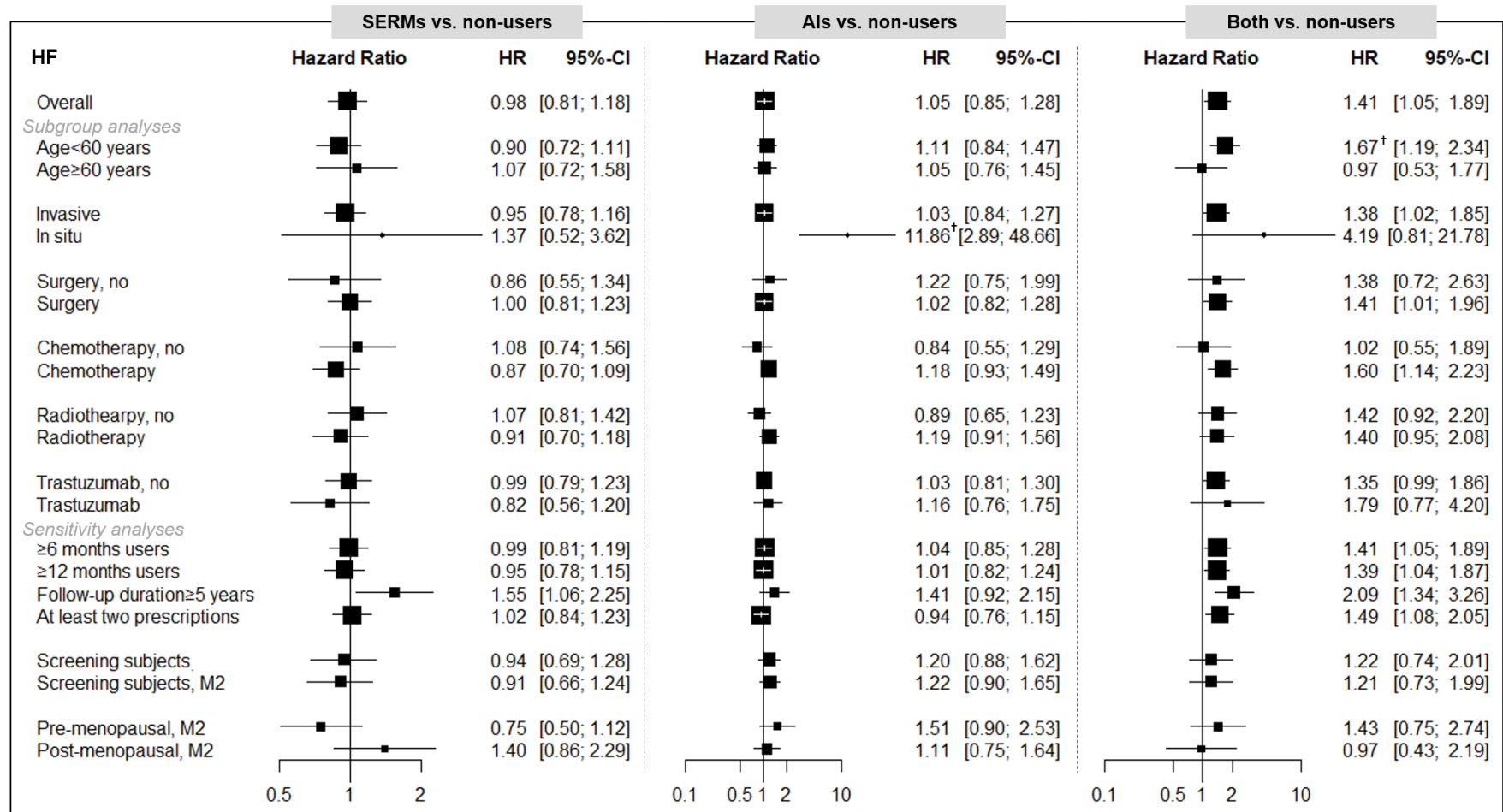


Figure S4. Summary of results for heart failure (comparison with non-users)

HF, heart failure; SERMs, selective estrogen receptor modulators; AIs, aromatase inhibitors. The multivariable adjusted model included age at diagnosis (continuous), insurance-based income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and type 2 diabetes; however, model 2 (M2) additionally include body mass index, lifestyle factors, and menopausal status. The * mark indicates the significance after multiple-testing by a false discovery rate (FDR; P for FDR < 0.05) in Table 2. The † mark indicates the results of heterogeneity (P-value < 0.1 or I² > 50%) by the stratified factor in supplementary materials.

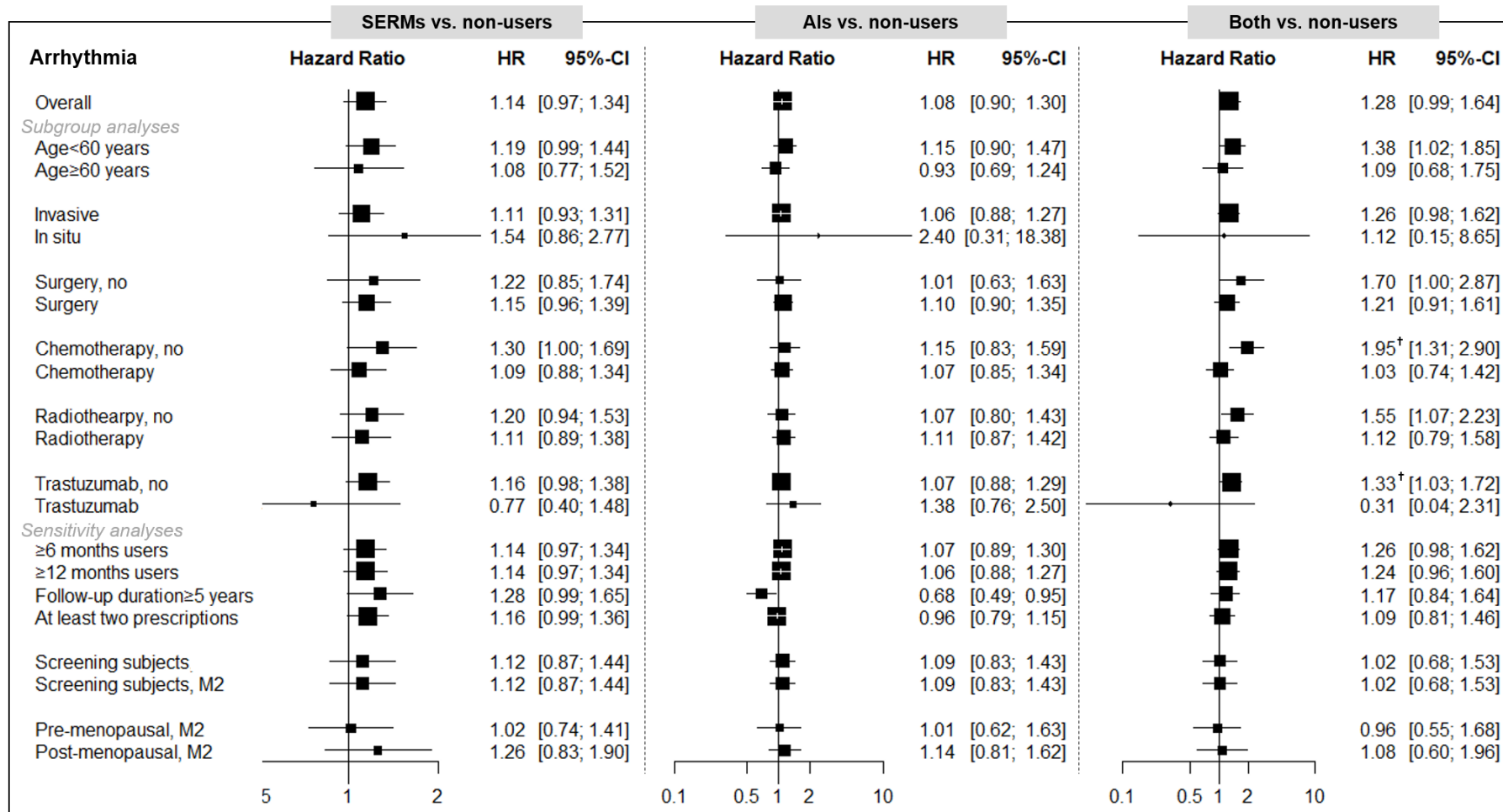


Figure S5. Summary of results for arrhythmia (comparison with non-users)

SERMs, selective estrogen receptor modulators; AIs, aromatase inhibitors. The multivariable adjusted model included age at diagnosis (continuous), insurance-based income level, region of residence, histological subtype, surgery, chemotherapy, radiotherapy, trastuzumab, hypertension, dyslipidemia, osteoporosis, and type 2 diabetes; however, model 2 (M2) additionally include body mass index, lifestyle factors, and menopausal status. The * mark indicates the significance after multiple-testing by a false discovery rate (FDR; P for FDR<0.05) in Table 2. The † mark indicates the results of heterogeneity (P-value <0.1 or I²>50%) by the stratified factor in supplementary materials.