

Additional file 1. Antiplatelet drugs and breast cancer risk in a large nationwide Danish case-control study.

Manon Cairat, Anton Pottegård, Morten Olesen, Laure Dossus, Agnès Fournier, Blánaid Hicks

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Appendix S1 – Danish Nationwide Registries

The **Danish Cancer Registry** has recorded incident cases of cancer on a nationwide basis since 1943 and provides accurate and almost complete records of cancer cases in Denmark. Cancer diagnoses are coded according to the *International Classification of Diseases, Tenth Revision* 10 (ICD-10) and the ICD for Oncology (ICD-O-1-3) for topography and morphology.

The **Danish Pathology Register** contains records of pathological specimens, which for some departments dates back as early as 1970. Since 1990, all departments of pathology have used electronic registrations and from 1997, it became a legal obligation to report the pathologies to the Danish Pathology Register. The registry contains coded diagnoses based on the Danish Systematized Nomenclature of Medicine (SNOMED).

The **Danish National Prescription Registry** contains data on all prescription drugs filled by Danish residents since 1995. The data include the type of drug, date of filling, and quantity. The dosing information and the indication for prescribing are not available and no information is available on drugs used at hospital level. Drugs are categorized according to the Anatomic Therapeutic Chemical (ATC) index, a hierarchical classification system developed by the World Health Organization, and the quantity dispensed for each prescription is described by the number and strength of the pharmaceutical entities (e.g., tablets), as well as defined daily doses (DDD).

The **Danish National Patient Registry** contains nationwide data on all non-psychiatric hospital admissions since 1977 and on ambulatory hospital contacts and psychiatric admissions since 1995. Discharge/contact diagnoses have been coded according to ICD-8 from 1977 to 1993 and ICD-10 since 1994.

Statistics Denmark is a governmental institution that collects and processes information for a variety of statistical and scientific purposes, e.g. education and income. It hosts the **Population Education Registry**, which contains information on nearly all adult Danes and provides the highest completed level of education, defined as the longest duration of schooling.

The Danish **Civil Registration System** contains data on addresses, migration, and date of death. This system allowed us to extract population controls and to keep track of all subjects during the study period.

Appendix S2– Codes and definitions of outcome, exposure and exclusion criteria

Breast cancer diagnosis, morphology and stage		
Breast cancer cases	<i>ICD-10</i>	C50.0-C50.9
Histological subtype		
Ductal adenocarcinoma	<i>Morphology code</i>	85003, 85013, 85023, 85033, 85043, 85073, 85213, 85403, 85413
Lobular adenocarcinoma	<i>Morphology code</i>	85203, 85223
Other	<i>Morphology code</i>	81403, 82003, 82013, 82113, 82303, 82463, 82603, 83103, 83153, 84013, 84413, 84503, 84803, 84813, 84903, 85103, 85303, 85503, 85603, 85703, 85723, 85733, 85753, 80103, 80123, 80133, 80203, 80213, 80223, 80413, 80463, 80503, 80703, 80743, 80003, 80013, 87203, 88003, 88103, 88303, 88903, 89343, 89403, 89803, 89823, 90103, 90203, 91203, 91303, 95903, 95913, 96703, 96733, 96803, 96903, 97023
Stage		
Localized	<i>TNM</i>	(T=11-19 & N=30 & M=40) or (T=11-13 & [N=30 or N=39] & [M=40 or M=49]) or (T=14 & N=30 & M=49) or (T=14 & N=39 & M=40)
Non localized	<i>TNM</i>	(T=11-19 & N=31-33) or M=41
Others	<i>TNM</i>	(T=19 & N=39 & M=49) or none of the above
ER status		
ER+	<i>Pathology code</i>	F29521, FYY501
ER-	<i>Pathology code</i>	F29525, FYY505
Exclusion criteria		
Any cancer (except non-melanoma skin cancer)	<i>ICD-10</i>	C00-97 (except C44)
Mastectomy	<i>NCSP-code</i>	KHAC
Antiplatelet drugs		
Clopidogrel	<i>ATC code</i>	B01AC04
Low-dose aspirin	<i>ATC code</i>	B01AC06, B01AC30, B01AC56, N02BA01 (≤ 100 mg), and N02BA51 (≤ 150 mg)
Dipyridamole	<i>ATC code</i>	B01AC07, B01AC30

Abbreviations: ATC, Anatomical Therapeutic Chemical; ER, Estrogen Receptor; ICD, International Classification of Disease; NCSP, Nordic Classification of Surgical procedures; TNM, Tumor Node Metastasis staging system.

Appendix S3– Codes and definitions of covariates

Drugs		
Antidiabetics	ATC code	A10
Statins	ATC code	C10AA
Spirolactone	ATC code	C03DA01
Loop diuretics	ATC code	C03CA
Beta-blockers	ATC code	C07AA and C07AB
Vascular calcium-channel blockers	ATC code	C08C
Selective serotonin reuptake inhibitors	ATC code	N06AB
Raloxifen		G03XC01
Hormone replacement therapy excluding vaginally administered estrogens	ATC code	G03C, G03F, G03HB01 (excluding vaginally administered estrogens)
Oral contraceptives	ATC code	G03A
Prior diagnoses (diagnostic code or drug marker)		
Alcohol-related diseases (proxy of heavy alcohol consumption)	ICD-8	291, 303, 425.5, 537.5, 571.0, 571.1, 571.2, 571.3, 577.10
	ICD-10	F10, E244, G312, G621, G721, I426, K292, K70, K852, K860, Q860, Z502 Z714, Z721
	ATC code	N07BB
Chronic obstructive pulmonary disease (proxy for heavy smoking)	ICD-8	490, 491, 492
	ICD-10	J41–J44
	ATC code	R03BB
Hypertension	ICD-8	400-404
	ICD-10	I10-I15
	ATC code	C03A, C07, C08, C09
Hypercholesterolemia	ICD-10	E78.5
	ATC code	C10
Diabetes type 1 and 2	ICD-8	249, 250
	ICD-10	E10–E14
	ATC codes	A10
Acute myocardial infarction	ICD-8	410
	ICD-10	I21-I23
Other ischemic heart disease	ICD-8	411
	ICD-10	I24
Angina pectoris	ICD-8	413
	ICD-10	I20
Heart failure	ICD-8	42709, 42710, 42711, 42719, 42899, 78249
	ICD-10	I110, I130, I132, I50
Stroke	ICD-8	430-434
	ICD-10	I61-I64
Other cerebrovascular diseases	ICD-8	435-438
	ICD-10	I65-I69
Atrial fibrillation or atrial flutter	ICD-8	42793, 42794
	ICD-10	I48
Pulmonary embolism and infarction	ICD-8	450
	ICD-10	I26
Phlebitis and thrombophlebitis	ICD-8	451
	ICD-10	I801-3, I809
Portal vein thrombosis	ICD-8	452
	ICD-10	I81
Other venous embolism and thrombosis	ICD-8	453
	ICD-10	I82
Educational level		
Basic	Duration	10 years
Medium	Duration	11–13 years
Higher	Duration	>13 years
Unknown	Duration	-

Abbreviations: ATC, Anatomical Therapeutic Chemical; ICD, International Classification of Disease.

Table S1. Associations of antiplatelet drug use with risk of invasive breast cancer by estrogen receptor status.

	ER+			ER-			<i>P</i> _{homogeneity}
	n cases	n controls	OR (95% CI) ¹	n cases	n controls	OR (95% CI) ¹	
Low-dose aspirin							
Use categories							
Never use	35,214	352,586	1.00 (ref.)	8,374	83,992	1.00 (ref.)	
Ever use	5,197	51,524	1.00 (0.96-1.03)	1,060	10,348	1.02 (0.93-1.10)	0.67
Long-term use	3,129	30,216	1.02 (0.97-1.07)	625	6,216	0.98 (0.88-1.09)	0.49
Cumulative DDDs							
Never use	35,214	352,586	1.00 (ref.)	8,374	83,992	1.00 (ref.)	
<500	1,094	11,066	0.97 (0.91-1.04)	238	2,175	1.09 (0.94-1.25)	
≥500 - <1000	974	10,242	0.94 (0.87-1.01)	197	1,957	1.00 (0.85-1.16)	
≥1000 - <2000	1,428	13,846	1.02 (0.96-1.09)	260	2,674	0.96 (0.84-1.10)	
≥2000 - <3000	894	8,585	1.04 (0.96-1.12)	180	1,705	1.04 (0.88-1.23)	
≥3000	807	7,785	1.04 (0.96-1.13)	185	1,837	0.99 (0.84-1.17)	
<i>OR per 1000 DDDs</i>	5,197	51,524	1.01 (0.99-1.03)	1,060	10,348	0.99 (0.96-1.03)	
Clopidogrel							
Use categories							
Never use	39,870	397,924	1.00 (ref.)	9,302	92,888	1.00 (ref.)	
Ever use	541	6,186	0.88 (0.80-0.97)	132	1,452	0.90 (0.73-1.10)	0.87
Long-term use	112	1,381	0.81 (0.66-0.98)	37	376	0.98 (0.69-1.39)	0.38
Cumulative DDDs							
Never use	39,870	397,924	1.00 (ref.)	9,302	92,888	1.00 (ref.)	
<500	304	3,557	0.87 (0.76-0.99)	61	757	0.78 (0.59-1.03)	
≥500 - <1000	125	1,248	1.00 (0.83-1.21)	34	319	1.06 (0.74-1.53)	
≥1000 - <2000	71	925	0.76 (0.60-0.97)	30	238	1.26 (0.85-1.86)	
≥2000 - <3000	26	281	0.92 (0.62-1.38)	6	76	0.79 (0.34-1.83)	
≥3000	15	175	0.84 (0.49-1.42)	(n<5)	62	(-)	
<i>OR per 1000 DDDs</i>	541	6,186	0.92 (0.84-1.01)	132	1,452	0.90 (0.76-1.07)	
Dipyridamole							
Use categories							
Never use	39,800	397,640	1.00 (ref.)	9,294	93,050	1.00 (ref.)	
Ever use	611	6,470	0.94 (0.85-1.04)	140	1,290	1.17 (0.95-1.45)	0.08
Long-term use	305	3,181	0.95 (0.83-1.08)	69	661	1.14 (0.86-1.52)	0.27
Cumulative DDDs							
Never use	39,800	397,640	1.00 (ref.)	9,294	93,050	1.00 (ref.)	
<500	195	2,068	0.93 (0.79-1.08)	51	411	1.33 (0.98-1.81)	
≥500 - <1000	111	1,221	0.91 (0.74-1.11)	20	218	0.99 (0.62-1.60)	
≥1000 - <2000	152	1,639	0.93 (0.78-1.11)	30	309	1.05 (0.71-1.56)	
≥2000 - <3000	90	934	0.96 (0.77-1.20)	21	199	1.15 (0.72-1.83)	
≥3000	63	608	1.05 (0.80-1.36)	18	153	1.27 (0.76-2.10)	
<i>OR per 1000 DDDs</i>	611	6,470	0.99 (0.94-1.05)	140	1,290	1.06 (0.96-1.17)	

Abbreviations: CI, confidence interval; ER, estrogen receptor; DDD, defined daily dose; OR, Odds ratio.

¹ Adjusted for age, calendar time (by risk-set matching and the conditional analysis) and other covariates listed in the appendix S3.

Table S2. Associations of antiplatelet drug use with risk of invasive breast cancer by histological type.

	Ductal adenocarcinoma			Lobular adenocarcinoma			Others			<i>P</i> _{homogeneity}
	n cases	n controls	OR (95% CI) ¹	n cases	n controls	OR (95% CI) ¹	n cases	n controls	OR (95% CI) ¹	
Low-dose aspirin										
Use categories										
Never use	45,547	456,463	1.00 (ref.)	7,685	76,004	1.00 (ref.)	7,036	70,896	1.00 (ref.)	
Ever use	6,076	59,767	1.01 (0.97-1.04)	1,136	12,206	0.94 (0.87-1.02)	1,336	12,824	0.99 (0.92-1.07)	0.31
Long-term use	3,624	35,451	1.01 (0.96-1.05)	711	7,363	1.00 (0.91-1.11)	851	8,053	1.01 (0.92-1.11)	0.99
Cumulative DDDs										
Never use	45,547	456,463	1.00 (ref.)	7,685	76,004	1.00 (ref.)	7,036	70,896	1.00 (ref.)	
<500	1,345	12,868	1.03 (0.97-1.09)	226	2,530	0.88 (0.77-1.02)	251	2,497	0.98 (0.86-1.13)	
≥500 - <1000	1,107	11,448	0.95 (0.89-1.02)	199	2,313	0.87 (0.75-1.02)	234	2,274	0.99 (0.86-1.14)	
≥1000 - <2000	1,569	15,555	1.00 (0.95-1.06)	290	3,029	0.98 (0.86-1.12)	338	3,201	1.01 (0.89-1.14)	
≥2000 - <3000	1,002	9,768	1.02 (0.95-1.10)	202	2,044	1.02 (0.87-1.19)	233	2,234	0.98 (0.85-1.14)	
≥3000	1,053	10,128	1.04 (0.97-1.12)	219	2,290	1.00 (0.86-1.17)	280	2,618	1.01 (0.87-1.16)	
OR per 1000 DDDs	6,076	59,767	1.01 (0.99-1.02)	1,136	12,206	1.00 (0.97-1.04)	1,336	12,824	1.00 (0.97-1.03)	
Clopidogrel										
Use categories										
Never use	50,870	507,989	1.00 (ref.)	8,669	86,502	1.00 (ref.)	8,198	81,906	1.00 (ref.)	
Ever use	753	8,241	0.93 (0.86-1.01)	152	1,708	0.99 (0.82-1.20)	174	1,814	0.86 (0.72-1.03)	0.56
Long-term use	198	2,039	0.98 (0.84-1.14)	39	450	0.97 (0.69-1.36)	50	492	0.89 (0.66-1.22)	0.87
Cumulative DDDs										
Never use	50,870	507,989	1.00 (ref.)	8,669	86,502	1.00 (ref.)	8,198	81,906	1.00 (ref.)	
<500	381	4,478	0.87 (0.78-0.97)	76	839	1.02 (0.79-1.32)	76	909	0.77 (0.59-0.99)	
≥500 - <1000	174	1,724	1.02 (0.87-1.20)	37	419	0.98 (0.69-1.38)	48	413	1.02 (0.75-1.40)	
≥1000 - <2000	136	1,345	1.02 (0.85-1.23)	23	288	0.88 (0.57-1.35)	37	314	1.05 (0.74-1.49)	
≥2000 - <3000	41	403	1.04 (0.75-1.44)	12	98	1.36 (0.74-2.51)	7	98	0.61 (0.28-1.33)	
≥3000	21	291	0.73 (0.47-1.14)	(n<5)	64	(-)	6	80	0.64 (0.28-1.48)	
OR per 1000 DDDs	753	8,241	0.98 (0.91-1.05)	152	1,708	1.00 (0.86-1.16)	174	1,814	0.92 (0.79-1.05)	
Dipyridamole										
Use categories										
Never use	50,913	509,099	1.00 (ref.)	8,699	86,688	1.00 (ref.)	8,180	82,159	1.00 (ref.)	
Ever use	710	7,131	1.03 (0.94-1.13)	122	1,522	0.84 (0.68-1.04)	192	1,561	1.11 (0.93-1.34)	0.10
Long-term use	358	3,617	1.02 (0.91-1.16)	66	783	0.92 (0.69-1.21)	103	805	1.15 (0.90-1.45)	0.49
Cumulative DDDs										
Never use	50,913	509,099	1.00 (ref.)	8,699	86,688	1.00 (ref.)	8,180	82,159	1.00 (ref.)	
<500	231	2,250	1.04 (0.90-1.20)	29	472	0.63 (0.43-0.93)	56	482	1.06 (0.79-1.42)	
≥500 - <1000	121	1,264	0.99 (0.82-1.21)	27	267	1.07 (0.71-1.61)	33	274	1.10 (0.75-1.60)	
≥1000 - <2000	165	1,725	0.99 (0.84-1.18)	36	372	1.03 (0.72-1.49)	49	358	1.24 (0.90-1.70)	
≥2000 - <3000	107	1,055	1.05 (0.86-1.29)	13	219	0.61 (0.35-1.09)	25	257	0.86 (0.56-1.33)	
≥3000	86	837	1.08 (0.86-1.36)	17	192	0.95 (0.57-1.59)	29	190	1.40 (0.93-2.12)	
OR per 1000 DDDs	710	7,131	1.02 (0.97-1.07)	122	1,522	0.96 (0.86-1.07)	192	1,561	1.06 (0.98-1.16)	

Abbreviations: CI, confidence interval; DDD, defined daily dose; OR, Odds ratio.

¹ Adjusted for age, calendar time (by risk-set matching and the conditional analysis) and other covariates listed in the appendix S3.

Table S3. Associations of antiplatelet drug use with risk of invasive breast cancer by tumor stage.

	Localized			Non localized			Unknown			<i>P</i> _{heterogeneity}
	n cases	n controls	OR (95% CI) ¹	n cases	n controls	OR (95% CI) ¹	n cases	n controls	OR (95% CI) ¹	
Low-dose aspirin										
Use categories										
Never use	27,195	272,862	1.00 (ref.)	21,157	211,184	1.00 (ref.)	11,916	119,317	1.00 (ref.)	
Ever use	4,271	41,798	1.01 (0.97-1.05)	3,028	30,666	0.99 (0.95-1.04)	1,249	12,333	0.96 (0.89-1.04)	0.55
Long-term use	2,643	25,902	1.01 (0.96-1.06)	1,900	18,637	1.02 (0.96-1.09)	643	6,328	0.95 (0.86-1.06)	0.50
Cumulative DDDs										
Never use	27,195	272,862	1.00 (ref.)	21,157	211,184	1.00 (ref.)	11,916	119,317	1.00 (ref.)	
<500	917	8,448	1.06 (0.99-1.14)	592	6,310	0.94 (0.86-1.03)	313	3,137	0.95 (0.84-1.08)	
≥500 - <1000	711	7,448	0.94 (0.86-1.02)	536	5,719	0.95 (0.86-1.04)	293	2,868	0.97 (0.86-1.11)	
≥1000 - <2000	1,087	10,681	1.01 (0.94-1.08)	793	7,954	1.01 (0.93-1.09)	317	3,150	0.95 (0.84-1.08)	
≥2000 - <3000	743	7,199	1.02 (0.94-1.11)	552	5,409	1.04 (0.94-1.14)	142	1,438	0.93 (0.78-1.12)	
≥3000	813	8,022	1.01 (0.93-1.10)	555	5,274	1.07 (0.97-1.18)	184	1,740	1.02 (0.86-1.21)	
OR per 1000 DDDs	4,271	41,798	1.00 (0.99-1.02)	3,028	30,666	1.02 (1.00-1.04)	1,249	12,333	0.99 (0.95-1.03)	
Clopidogrel										
Use categories										
Never use	30,874	308,219	1.00 (ref.)	23,823	237,674	1.00 (ref.)	13,040	130,504	1.00 (ref.)	
Ever use	592	6,441	0.92 (0.84-1.01)	362	4,176	0.94 (0.83-1.06)	125	1,146	1.01 (0.82-1.24)	0.74
Long-term use	164	1,623	1.02 (0.86-1.21)	90	1,039	0.90 (0.72-1.12)	33	319	0.94 (0.64-1.37)	0.64
Cumulative DDDs										
Never use	30,874	308,219	1.00 (ref.)	23,823	237,674	1.00 (ref.)	13,040	130,504	1.00 (ref.)	
<500	286	3,424	0.83 (0.73-0.95)	190	2,225	0.94 (0.80-1.11)	57	577	0.93 (0.70-1.25)	
≥500 - <1000	142	1,394	1.02 (0.85-1.22)	82	912	0.96 (0.76-1.21)	35	250	1.26 (0.87-1.83)	
≥1000 - <2000	104	1,046	1.00 (0.81-1.23)	71	698	1.07 (0.83-1.38)	21	203	0.95 (0.60-1.51)	
≥2000 - <3000	39	340	1.17 (0.83-1.63)	13	193	0.70 (0.40-1.23)	8	66	1.07 (0.51-2.26)	
≥3000	21	237	0.90 (0.57-1.41)	6	148	0.43 (0.19-0.97)	(n<5)	50	(-)	
OR per 1000 DDDs	592	6,441	1.01 (0.94-1.09)	362	4,176	0.91 (0.81-1.01)	125	1,146	0.98 (0.83-1.15)	
Dipyridamole										
Use categories										
Never use	31,000	309,665	1.00 (ref.)	23,808	237,968	1.00 (ref.)	12,984	130,313	1.00 (ref.)	
Ever use	466	4,995	0.94 (0.84-1.06)	377	3,882	1.03 (0.91-1.17)	181	1,337	1.25 (1.03-1.50)	0.06
Long-term use	265	2,712	0.99 (0.86-1.14)	199	2,006	1.07 (0.91-1.26)	63	487	1.20 (0.90-1.61)	0.49
Cumulative DDDs										
Never use	31,000	309,665	1.00 (ref.)	23,808	237,968	1.00 (ref.)	12,984	130,313	1.00 (ref.)	
<500	134	1,463	0.91 (0.76-1.09)	112	1,169	1.01 (0.82-1.24)	70	572	1.12 (0.86-1.46)	
≥500 - <1000	67	820	0.83 (0.65-1.08)	66	707	0.99 (0.77-1.29)	48	278	1.62 (1.17-2.24)	
≥1000 - <2000	122	1,257	0.99 (0.81-1.20)	96	978	1.04 (0.84-1.30)	32	220	1.32 (0.89-1.95)	
≥2000 - <3000	72	773	0.95 (0.74-1.21)	56	622	0.96 (0.73-1.28)	17	136	1.16 (0.69-1.95)	
≥3000	71	682	1.08 (0.84-1.39)	47	406	1.25 (0.91-1.71)	14	131	0.99 (0.56-1.74)	
OR per 1000 DDDs	466	4,995	1.01 (0.95-1.06)	377	3,882	1.04 (0.98-1.11)	181	1,337	1.06 (0.95-1.18)	

Abbreviations: OR, Odds ratio; CI, confidence interval; DDD, defined daily dose.

¹ Adjusted for age, calendar time (by risk-set matching and the conditional analysis) and other covariates listed in the appendix S3.

Table S4. Association between antiplatelet drug use and invasive breast cancer risk with exposure with no lag period, 1-year lag and 2-year lag.

	Lag 0 year		Lag 1 year		Lag 2 years	
	n cases/controls	OR (95% CI) ¹	n cases/controls	OR (95% CI) ¹	n cases/controls	OR (95% CI) ¹
Low-dose aspirin						
Never use	59,406/594,376	1.00 (ref.)	60,268/603,363	1.00 (ref.)	61,183/612,231	1.00 (ref.)
Ever use	9,410/93,784	0.99 (0.96-1.02)	8,548/84,797	1.00 (0.97-1.03)	7,633/75,929	0.99 (0.96-1.02)
Long-term use	5,836/57,967	0.99 (0.96-1.03)	5,186/50,867	1.00 (0.97-1.04)	4,540/44,126	1.01 (0.98-1.05)
Clopidogrel						
Never use	67,475/673,674	1.00 (ref.)	67,737/676,397	1.00 (ref.)	67,924/678,626	1.00 (ref.)
Ever use	1,341/14,486	0.93 (0.88-1.00)	1,079/11,763	0.93 (0.87-1.00)	892/9,534	0.95 (0.88-1.03)
Long-term use	397/4,080	0.97 (0.87-1.09)	287/2,981	0.96 (0.85-1.09)	207/2,112	0.94 (0.82-1.10)
Dipyridamole						
Never use	67,673/676,686	1.00 (ref.)	67,792/677,946	1.00 (ref.)	67,908/679,140	1.00 (ref.)
Ever use	1,143/11,474	1.00 (0.93-1.08)	1,024/10,214	1.02 (0.94-1.10)	908/9,020	1.02 (0.94-1.11)
Long-term use	597/6,018	1.02 (0.93-1.12)	527/5,205	1.03 (0.93-1.14)	468/4,430	1.08 (0.97-1.20)

Abbreviations: OR, Odds ratio; CI, confidence interval

¹ Adjusted for age and calendar time (by risk-set matching and the conditional analysis) and other covariates listed in the appendix S3.

Table S5. Associations between antiplatelet drug use and invasive breast cancer risk restricted to women with a diagnosis of stroke or myocardial infarction.

	n cases	n controls	OR (95% CI) ¹	OR (95% CI) ²
Low-dose aspirin				
Use categories				
Never use	715	7,004	1.00 (ref.)	1.00 (ref.)
Ever use	1,768	18,727	0.98 (0.82-1.17)	0.98 (0.80-1.19)
Long-term use	1,248	12,810	0.99 (0.80-1.21)	0.94 (0.75-1.19)
Cumulative DDDs				
Never use	715	7,004	1.00 (ref.)	1.00 (ref.)
<500	250	2,759	1.03 (0.76-1.39)	1.04 (0.77-1.42)
≥500 - <1000	270	3,158	0.91 (0.69-1.20)	0.90 (0.67-1.20)
≥1000 - <2000	454	4,911	0.98 (0.78-1.24)	0.98 (0.76-1.25)
≥2000 - <3000	351	3,611	0.96 (0.74-1.24)	0.93 (0.71-1.23)
≥3000	443	4,288	1.03 (0.82-1.29)	1.03 (0.80-1.32)
<i>OR per 1000 DDDs</i>	1,768	18,727	1.02 (0.97-1.07)	1.02 (0.97-1.08)
Clopidogrel				
Use categories				
Never use	1,841	18,652	1.00 (ref.)	1.00 (ref.)
Ever use	642	7,079	0.96 (0.80-1.16)	0.95 (0.78-1.15)
Long-term use	172	1,843	0.83 (0.58-1.19)	0.79 (0.54-1.14)
Cumulative DDDs				
Never use	1,841	18,652	1.00 (ref.)	1.00 (ref.)
<500	322	3,719	0.95 (0.75-1.19)	0.93 (0.73-1.19)
≥500 - <1000	148	1,517	0.91 (0.65-1.27)	0.88 (0.62-1.24)
≥1000 - <2000	119	1,162	1.03 (0.72-1.47)	1.03 (0.71-1.49)
≥2000 - <3000	34	387	1.12 (0.60-2.07)	1.02 (0.54-1.94)
≥ 3000	19	294	1.12 (0.49-2.58)	1.21 (0.52-2.80)
<i>OR per 1000 DDDs</i>	642	7,079	1.04 (0.90-1.20)	1.04 (0.90-1.20)
Dipyridamole				
Use categories				
Never use	1,798	18,806	1.00 (ref.)	1.00 (ref.)
Ever use	685	6,925	1.05 (0.89-1.25)	1.04 (0.86-1.27)
Long-term use	365	3,712	1.01 (0.80-1.28)	0.99 (0.77-1.29)
Cumulative DDDs				
Never use	1,798	18,806	1.00 (ref.)	1.00 (ref.)
<500	194	1,992	1.01 (0.75-1.35)	1.03 (0.76-1.40)
≥500 - <1000	126	1,221	1.09 (0.76-1.57)	1.06 (0.73-1.54)
≥1000 - <2000	170	1,698	1.04 (0.77-1.42)	1.01 (0.73-1.40)
≥2000 - <3000	97	1,125	0.96 (0.66-1.40)	0.98 (0.66-1.46)
≥3000	98	889	1.20 (0.83-1.73)	1.15 (0.78-1.67)
<i>OR per 1000 DDDs</i>	685	6,925	1.03 (0.95-1.12)	1.02 (0.94-1.11)

Abbreviations: CI, confidence interval; DDD, defined daily dose; OR, Odds ratio.

¹ Adjusted for age and calendar time (by risk-set matching and the conditional analysis).

² Adjusted for age and calendar time (by risk-set matching and the conditional analysis) and other covariates listed in the appendix S3.

Table S6. Associations between antiplatelet drug use and breast cancer risk among women who are >55 years and never users of hormone replacement therapy.

	n cases	n controls	OR (95% CI) ¹	OR (95% CI) ²
Low-dose aspirin				
Use categories				
Never use	26,792	298,408	1.00 (ref.)	1.00 (ref.)
Ever use	5,261	57,117	1.03 (1.00-1.07)	0.99 (0.95-1.03)
Long-term use	3,274	34,891	1.05 (1.01-1.09)	1.00 (0.95-1.05)
Cumulative DDDs				
Never use	26,792	298,408	1.00 (ref.)	1.00 (ref.)
<500	1,044	11,355	1.03 (0.96-1.10)	0.99 (0.93-1.06)
≥500 - <1000	943	10,871	0.98 (0.91-1.05)	0.94 (0.88-1.01)
≥1000 - <2000	1,387	14,914	1.03 (0.97-1.09)	0.99 (0.93-1.06)
≥2000 - <3000	926	9,708	1.08 (1.01-1.16)	1.04 (0.96-1.12)
≥3000	961	10,269	1.04 (0.97-1.12)	1.01 (0.93-1.09)
OR per 1000 DDDs	5,261	57,117	1.01 (1.00-1.03)	1.00 (0.99-1.02)
Clopidogrel				
Use categories				
Never use	31,409	348,006	1.00 (ref.)	1.00 (ref.)
Ever use	644	7,519	0.95 (0.87-1.03)	0.96 (0.87-1.05)
Long-term use	170	1,877	1.00 (0.85-1.18)	0.99 (0.84-1.17)
Cumulative DDDs				
Never use	31,409	348,006	1.00 (ref.)	1.00 (ref.)
<500	309	4,024	0.86 (0.76-0.96)	0.87 (0.77-0.99)
≥500 - <1000	165	1,618	1.11 (0.95-1.32)	1.10 (0.93-1.31)
≥1000 - <2000	117	1,268	1.04 (0.85-1.26)	1.02 (0.84-1.25)
≥2000 - <3000	38	343	1.21 (0.86-1.71)	1.20 (0.85-1.70)
≥ 3000	15	266	0.61 (0.36-1.04)	0.60 (0.35-1.02)
OR per 1000 DDDs	644	7,519	0.99 (0.92-1.06)	0.99 (0.92-1.07)
Dipyridamole				
Use categories				
Never use	31,433	348,606	1.00 (ref.)	1.00 (ref.)
Ever use	620	6,919	1.00 (0.92-1.09)	0.96 (0.87-1.06)
Long-term use	317	3,529	1.00 (0.89-1.13)	0.97 (0.85-1.10)
Cumulative DDDs				
Never use	31,433	348,606	1.00 (ref.)	1.00 (ref.)
<500	192	2,136	1.01 (0.87-1.18)	0.97 (0.82-1.13)
≥500 - <1000	111	1,254	0.98 (0.80-1.19)	0.94 (0.76-1.15)
≥1000 - <2000	156	1,688	1.05 (0.88-1.24)	1.01 (0.84-1.20)
≥2000 - <3000	85	1,021	0.92 (0.73-1.15)	0.88 (0.69-1.11)
≥3000	76	820	1.04 (0.81-1.32)	1.01 (0.79-1.29)
OR per 1000 DDDs	620	6,919	1.00 (0.96-1.05)	0.99 (0.94-1.04)

Abbreviations: CI, confidence interval; DDD, defined daily dose; OR, Odds ratio.dose

¹ Adjusted for age and calendar time (by risk-set matching and the conditional analysis).

² Adjusted for age and calendar time (by risk-set matching and the conditional analysis) and other covariates listed in the appendix S3.

Table S7. Association between breast cancer risk and antiplatelet drugs taken alone or in combination with low-dose aspirin.

Use categories	n cases	n controls	OR (95% CI) ¹	OR (95% CI) ²
Use of low-dose aspirin but never concomitantly with clopidogrel or dipyridamole				
Never	61,862	620,058		
Ever	6,954	68,102	1.03 (1.00-1.05)	1.00 (0.97-1.03)
Long-term	4,053	39,323	1.04 (1.00-1.07)	1.01 (0.98-1.05)
Use of clopidogrel but never concomitantly with low-dose aspirin				
Never	68,358	683,226		
Ever	458	4,934	0.93 (0.84-1.02)	0.93 (0.84-1.02)
Long-term	182	1,783	1.01 (0.87-1.18)	1.01 (0.86-1.18)
Use of dipyridamole but never concomitantly with low-dose aspirin				
Never	68,736	687,504		
Ever	80	656	1.22 (0.97-1.54)	1.20 (0.95-1.52)
Long-term	17	157	1.09 (0.66-1.80)	1.10 (0.67-1.81)
Concomitant use of low-dose aspirin and clopidogrel				
Never	68,063	680,004		
Ever	753	8,156	0.92 (0.85-0.99)	0.96 (0.88-1.04)
Long-term	618	6,482	0.95 (0.88-1.03)	0.99 (0.90-1.09)
Concomitant use of low-dose aspirin and dipyridamole				
Never	67,751	677,164		
Ever	1,065	10,996	0.97 (0.91-1.03)	0.97 (0.90-1.04)
Long-term	836	8,363	1.00 (0.93-1.07)	1.00 (0.92-1.09)

Abbreviations: OR, Odds ratio; CI, confidence interval; DDD, defined daily dose

¹ Adjusted for age and calendar time (by risk-set matching and the conditional analysis).

² Adjusted for age and calendar time (by risk-set matching and the conditional analysis) and other covariates listed in the appendix S3.

Table S8. Associations between Vitamin K antagonists use and invasive breast cancer risk.

Use categories	n cases	n controls	OR (95% CI) ¹	OR (95% CI) ²
Never use	66,987	672,591	1.00 (ref.)	1.00 (ref.)
Ever use	1,829	15,569	1.18 (1.13-1.25)	1.07 (1.00-1.14)
Long-term use	456	3,621	1.26 (1.14-1.39)	1.14 (1.02-1.28)
Cumulative DDDs				
Never use	66,987	672,591	1.00 (ref.)	1.00 (ref.)
<500	1,000	9,294	1.08 (1.02-1.16)	0.99 (0.91-1.06)
≥500 - <1000	373	2,654	1.42 (1.27-1.58)	1.26 (1.12-1.42)
≥1000 - <2000	275	2,249	1.24 (1.09-1.40)	1.10 (0.96-1.25)
≥2000 - <3000	106	806	1.33 (1.09-1.63)	1.18 (0.96-1.46)
≥3000	75	566	1.34 (1.05-1.70)	1.21 (0.95-1.55)
<i>OR per 1000 DDDs</i>	1,829	15,569	1.14 (1.10-1.19)	1.08 (1.03-1.13)

Abbreviations: CI, confidence interval; DDD, defined daily dose; OR, Odds ratio.

¹ Adjusted for age and calendar time (by risk-set matching and the conditional analysis).

² Adjusted for age and calendar time (by risk-set matching and the conditional analysis) and other covariates listed in the appendix S3.