Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Age-standardized characteristics (% or mean [SD]) of person-years contributed by women in the Nurses' Health Studies (1980-2015)

	Nurses' Health Study (n= 93,664)			Nurses' Health Study II (n=111,834)		
	No Aspirin (298,000 PY)	Past Aspirin (440,187 PY)	Current Aspirin (1,041,385 PY)	No Aspirin (1,221,705 PY)	Past Aspirin (275,753 PY)	Current Aspirin (387,542 PY)
Current NSAIDs, %	22.7	46.1	35.6	36.5	50.6	50.3
Current acetaminophen, %	28.6	37.9	29.8	22.3	26.5	37.1
Age, years[a]	51.0 (9.8)	61.7 (10.0)	58.7 (11.3)	41.0 (7.6)	48.8 (6.8)	47.9 (8.2)
Non-Hispanic White Race/Ethnicity, %	92.7	93.6	93.9	92.6	94.2	93.7
Postmenopausal, %	68.8	68.4	68.4	18.5	19.0	19.9
Tubal ligation, %	13.5	23.4	19.0	22.8	22.8	24.7
Hysterectomy, %	20.0	20.4	20.3	7.0	7.9	9.2
Family history of breast or ovarian cancer, %	12.9	15.4	14.0	11.3	12.3	11.2
Parous, %	94.4	95.1	95.0	80.6	77.3	75.8
Number of children[b]	3.2 (1.6)	3.1 (1.4)	3.2 (1.5)	2.3 (1.0)	2.2 (0.9)	2.2 (0.9)
Ever used OCs, %	40.3	57.6	50.9	85.9	89.2	89.0
Duration of OC use (years)[c]	4.2 (3.6)	4.0 (3.8)	4.0 (3.9)	5.1 (4.6)	6.0 (5.2)	5.5 (4.9)
Estrogen HT use, %[d]	20.6	24.1	23.1	7.9	8.9	9.0
Estrogen HT use (years)[e]	6.9 (8.9)	6.8 (5.8)	6.5 (6.1)	4.1 (5.5)	4.3 (3.0)	4.2 (2.8)
Estrogen-progestin HT use, %[d]	14.7	32.4	25.8	29.4	29.8	31.5
Estrogen-progestin HT use (years)[e]	5.6 (5.9)	5.4 (3.7)	5.6 (4.0)	3.5 (3.8)	3.6 (2.3)	3.6 (2.2)
Other HT use, %[d]	19.1	21.3	21.3	9.7	10.9	9.3
Other HT use (years)[e]	3.3 (4.7)	3.0 (2.6)	3.1 (2.9)	2.0 (2.3)	2.1(1.3)	2.1 (1.3)
Current Smoker, %	19.8	14.5	17.0	8.9	9.7	11.9
Body mass index (kg/m^2)	25.0 (4.7)	26.1 (5.3)	25.9 (5.1)	25.7 (5.8)	26.4 (6.2)	26.7 (6.5)
Waist circumference (cm)	82.4(16.3)	83.2(12.6)	83.5(12.9)	81.3(14.7)	81.3(13.4)	83.5(14.1)
Physical activity (MET-hrs/week)	16.9 (22.5)	16.4 (16.2)	16.8 (16.6)	22.0 (25.8)	22.5 (23.9)	22.4 (26.4)
Sedentary Behavior (hrs/week)						

- 0-9, %	13.0	11.0	12.1	10.7	6.7	10.1
- 10-19, %	22.8	23.0	23.3	31.0	29.8	29.7
- 20-39, %	33.6	35.1	34.1	34.6	35.9	34.7
- 40+, %	30.5	30.9	30.4	23.6	27.7	25.4
Inflammatory diet score (quintiles)						
- Q1, %	23.3	29.9	29.1	24.9	27.8	25.6
- Q2, %	15.4	18.2	17.4	16.4	16.5	15.8
- Q3, %	14.3	15.9	15.3	17.9	16.5	17.0
- Q4, %	14.0	14.4	13.8	18.0	16.6	17.4
- Q5, %	33.0	21.6	24.4	22.8	22.6	24.1
Recent physical exam, %	82.7	84.9	83.7	83.1	81.8	85.0
Beta blockers, %	10.5	11.0	15.2	3.3	4.4	7.1
Thiazide diuretics, %	10.8	11.2	13.0	3.4	4.5	6.5
Calcium channel blockers, %	6.2	6.4	8.8	2.1	2.5	4.8
History of hypertension, %	28.2	34.8	36.8	12.4	16.7	21.8
History of high cholesterol, %	28.2	41.1	38.1	23.7	29.5	32.9
MI or angina, %	4.8	5.0	8.1	1.0	1.7	2.9
Stroke, %	1.1	1.2	1.5	0.3	0.7	1.3
History of diabetes, %	4.4	5.6	6.5	1.8	2.6	4.8
Rheumatoid arthritis, %	6.5	7.8	6.7	1.9	2.8	2.6
Other arthritis, %	28.2	35.9	33.4	13.3	16.4	17.7
Non-GI autoimmune disease, %	7.3	10.3	8.4	3.3	4.4	4.5
Ulcerative colitis, %	1.6	1.6	1.3	1.5	1.7	1.6
History of gastric or duodenal ulcer, %	10.8	9.0	6.6	4.0	5.3	5.2
Irregular Menstruation, %	12.9	13.4	12.8	22.8	23.4	23.2
History of Endometriosis[f]	-	-	-	6.5	9.1	7.9

[a]Value is not age-adjusted
[b]Number of children among parous women
[c]Duration of OC use among past and current OC users
[d]HT use among postmenopausal women
[e]Duration of HT use among past and current HT users
[f]Endometriosis evaluated in the Nurses' Health Study II only

eTable 2. Analgesic use and risk of ovarian cancer in the Nurses' Health Studies, by menopausal status at the time of analgesic assessment

	Aspirin (1980-2015)				NSAIDs (1989-2015)				Acetaminophen (1989-2015)			
	Premenopausal		Postmenopausal[a]		Premenopausal		Postmenopausal[a]		Premenopausal		Postmenopausal[a]	
	Cases	Multivariate-adjusted HR (95% CI)[b]	Cases	Multivariate-adjusted HR (95% CI)[b]	Cases	Multivariate-adjusted HR (95% CI)[b]	Cases	Multivariate-adjusted HR (95% CI)[b]	Cases	Multivariate-adjusted HR (95% CI)[b]	Cases	Multivariate-adjusted HR (95% CI)[b]
Duration (years)												
<1	358	1.00 (ref)	359	1.00 (ref)	155	1.00 (ref)	298	1.00 (ref)	197	1.00 (ref)	458	1.00 (ref)
1-4	153	1.01 (0.83, 1.23)	94	1.14 (0.90, 1.44)	143	1.08 (0.85, 1.36)	193	1.70 (1.41, 2.04)	135	0.93 (0.74, 1.16)	65	1.07 (0.80, 1.44)
5-9	101	1.15 (0.90, 1.45)	119	1.39 (1.13, 1.72)	85	1.15 (0.86, 1.54)	129	1.65 (1.33, 2.04)	67	1.12 (0.84, 1.50)	25	0.97 (0.62, 1.51)
10-15[c]	30	0.90 (0.61, 1.32)	89	1.40 (1.11, 1.78)	37	1.20 (0.80, 1.80)	88	1.80 (1.39, 2.33)	21	1.12 (0.70, 1.80)	--	--
≥15	93	1.35 (1.05, 1.72)	189	1.42 (1.18, 1.71)	--	--	--	--	--	--	--	--
p-trend		0.04		<0.01		0.32		<0.01		0.40		0.89
Days per week (cumulative average)[d]												
<2	439	1.00 (ref)	350	1.00 (ref)	261	1.00 (ref)	447	1.00 (ref)	305	1.00 (ref)	499	1.00 (ref)
3-4	91	1.13 (0.90, 1.42)	221	1.19 (1.00, 1.41)	70	1.12 (0.85, 1.46)	97	1.09 (0.87, 1.37)	39	1.11 (0.79, 1.55)	78	1.13 (0.89, 1.44)
≥5	29	1.14 (0.78, 1.67)	99	0.92 (0.73, 1.15)	24	1.41 (0.92, 2.16)	57	1.21 (0.91, 1.60)	7	1.21 (0.57, 2.58)	20	0.82 (0.52, 1.28)
p-trend		0.27		0.97		0.11		0.16		0.45		0.93
Tablets per week (cumulative average)[d]												
<1	330	1.00 (ref)	234	1.00 (ref)	44	1.00 (ref)	140	1.00 (ref)	72	1.00 (ref)	164	1.00 (ref)
1-3	159	1.14 (0.93, 1.39)	276	1.32 (1.10, 1.57)	18	0.61 (0.35, 1.07)	55	1.32 (0.96, 1.83)	28	1.34 (0.83, 2.14)	65	1.33 (0.97, 1.81)
4-5	47	0.99 (0.72, 1.34)	84	1.27 (0.98, 1.63)	14	0.73 (0.40, 1.34)	37	1.54 (1.06, 2.24)	9	0.78 (0.33, 1.82)	29	1.21 (0.77, 1.89)

6-9	36	1.13 (0.80, 1.61)	74	1.24 (0.95, 1.62)	18	1.77 (1.00, 3.12)	20	1.16 (0.72, 1.88)	4	1.19 (0.43, 3.33)	19	1.29 (0.79, 2.10)
≥10	64	1.22 (0.93, 1.60)	56	0.91 (0.68, 1.23)	32	1.32 (0.82, 2.13)	59	1.44 (1.05, 1.97)	7	0.49 (0.15, 1.59)	39	1.45 (1.00, 2.11)
p-trend		0.18		0.76		0.03		0.03		0.34		0.05

[a]Analysis restricted to postmenopausal cases

[b]Models allowed for variation in baseline hazards by cohort, age in months (continuous) and calendar years (continuous), and adjusted for menopausal status, parity (ever/never and number of children), duration of oral contraceptive use (never, <1, 1 to 5, >5 years), duration of postmenopausal hormone use by type, history of tubal ligation (yes, no), history of hysterectomy (yes, no), family history of breast cancer or ovarian cancer (yes, no), BMI (<20, 20 to <25, 25 to <30, ≥30)

[c]Top category of duration analysis for NSAIDs and acetaminophen is ≥10 years

[d]Cumulative averages were calculated using premenopausal or postmenopausal person-years only; aspirin cumulative average days per week follow-up 1984-2015 and NSAID cumulative average tablets per week follow-up 2000-2015

eTable 3. Analgesic use and risk of ovarian cancer in the Nurses' Health Studies, further adjusted for inflammatory factors

		Low-dose Aspirin (2000-2015)			Standard-dose Aspirin (2000-2015)			NSAIDs (1989-2015)	
		Main Analysis[a]	Further Adjusted for Inflammatory Factors[b]		Main Analysis[a]	Further Adjusted for Inflammatory Factors[b]		Main Analysis[a]	Further Adjusted for Inflammatory Factors[b]
	Cases	HR (95% CI)	HR (95% CI)	Cases	HR (95% CI)	HR (95% CI)	Cases	HR (95% CI)	HR (95% CI)
Current use									
None	287	1.00 (ref)	1.00 (ref)	276	1.00 (ref)	1.00 (ref)	106	1.00 (ref)	1.00 (ref)
Past	22	0.65 (0.35-1.19)	0.64 (0.35-1.18)	57	1.34 (0.90-1.99)	1.32 (0.88-1.96)	167	1.20 (0.87-1.66)	1.20 (0.86-1.67)
Current	122	0.95 (0.70-1.27)	0.94 (0.69-1.26)	91	1.28 (0.92-1.77)	1.23 (0.89-1.71)	266	1.32 (0.96-1.80)	1.31 (0.95-1.81)
Duration (years)									
<1	324	1.00 (ref)	1.00 (ref)	328	1.00 (ref)	1.00 (ref)	126	1.00 (ref)	1.00 (ref)
1-4	71	0.78 (0.53-1.14)	0.77 (0.52-1.12)	88	1.19 (0.84-1.69)	1.16 (0.82-1.66)	138	1.23 (0.89-1.70)	1.23 (0.88-1.70)
5-9[c]	22	0.91 (0.51-1.66)	0.90 (0.50-1.64)	24	2.12 (1.21-3.69)	2.00 (1.14-3.51)	150	1.25 (0.90-1.73)	1.23 (0.88-1.71)
≥10	--	--	--	--	--	--	130	1.22 (0.85-1.75)	1.20 (0.82-1.75)
p-trend		0.53	0.50		0.008	0.02		0.43	0.52
Days per week (cumulative average)									
<2	362	1.00 (ref)	1.00 (ref)	355	1.00 (ref)	1.00 (ref)	407	1.00 (ref)	1.00 (ref)
3-4	57	0.86 (0.58-1.28)	0.86 (0.58-1.29)	45	1.54 (1.04-2.27)	1.50 (1.01-2.22)	104	0.83 (0.60-1.15)	0.81 (0.58-1.13)
≥5	47	0.98 (0.66-1.46)	0.96 (0.64-1.43)	36	1.34 (0.84-2.16)	1.23 (0.76-1.99)	42	1.30 (0.83-2.04)	1.26 (0.79-2.02)
p-trend		0.74	0.68		0.05	0.12		0.83	0.96
Tablets per week (cumulative average)[d]									
<1	320	1.00 (ref)	1.00 (ref)	316	1.00 (ref)	1.00 (ref)	171	1.00 (ref)	1.00 (ref)

1-3	41	1.04 (0.67-1.62)	1.06 (0.68-1.65)	38	1.06 (0.67-1.69)	1.05 (0.66-1.67)	79	0.99 (0.67-1.45)	0.98 (0.66-1.45)
4-5	30	0.96 (0.57-1.63)	0.96 (0.56-1.63)	21	1.27 (0.69-2.32)	1.24 (0.67-2.28)	45	1.22 (0.77-1.91)	1.21 (0.76-1.90)
6-9	26	1.11 (0.64-1.92)	1.12 (0.65-1.94)	21	2.46 (1.40-4.35)	2.32 (1.31-4.13)	51	1.52 (0.95-2.42)	1.52 (0.94-2.44)
≥10	30	0.89 (0.53-1.48)	0.87 (0.52-1.46)	27	1.26 (0.74-2.14)	1.15 (0.67-1.97)	76	1.21 (0.81-1.80)	1.20 (0.79-1.81)
p-trend		0.78	0.74		0.05	0.12		0.14	0.18
Tablet-days									
None	287	1.00 (ref)	1.00 (ref)	276	1.00 (ref)	1.00 (ref)	199	1.00 (ref)	1.00 (ref)
1-499	21	1.33 (0.78-2.28)	1.31 (0.76-2.26)	33	1.04 (0.63-1.70)	1.05 (0.64-1.73)	59	1.01 (0.68-1.52)	1.01 (0.67-1.52)
500-999	6	0.36 (0.05-2.62)	0.38 (0.05-2.73)	6	1.08 (0.39-2.99)	1.05 (0.38-2.91)	18	0.75 (0.36-1.56)	0.75 (0.36-1.56)
1000-2499	61	0.93 (0.64-1.34)	0.91 (0.63-1.31)	53	1.38 (0.93-2.05)	1.32 (0.88-1.97)	65	1.17 (0.81-1.68)	1.18 (0.81-1.72)
≥2500	27	0.85 (0.48-1.49)	0.84 (0.48-1.48)	22	1.82 (1.02-3.23)	1.73 (0.97-3.11)	58	1.27 (0.80-2.02)	1.30 (0.81-2.09)
p-trend		0.46	0.42		0.01	0.03		0.22	0.19

[a]Models allowed for variation in baseline hazards by cohort, age in months (continuous) and calendar years (continuous), and adjusted for menopausal status, parity (ever/never and number of children), duration of oral contraceptive use (never, <1, 1 to 5, >5 years), duration of postmenopausal hormone use by type, history of tubal ligation (yes, no), history of hysterectomy (yes, no), family history of breast cancer or ovarian cancer (yes, no), BMI (<20, 20 to <25, 25 to <30, ≥30)

[b]Model a further adjusted for history of hypertension (yes, no), history of diabetes (yes, no), history of arthritis (yes, no), history of non-GI autoimmune disease (yes, no), history of ulcerative colitis (yes, no), history of gastric or duodenal ulcer (yes, no), history of myocardial infarction or angina (yes, no), history of stroke (yes, no), history of high cholesterol (yes, no), history of irregular menstruation (yes, no), waist circumference (continuous), physical activity in MET hours per week (<3, 3-8.9, 9-17.9, 18-26.9, 27+), sedentary behavior in hours per week (0-9, 10-19, 20-39, 40+), inflammatory diet score (quintiles), smoking (current, past, never)

[c]Top category for duration of low-dose aspirin and regular dose aspirin was ≥5 years

[d] NSAID tablets per week follow-up was 2000-2015

eTable 4. Aspirin or NSAID use and risk of ovarian cancer in the Nurses' Health Studies, by tumor histotype								
	Aspirin (1980-2015)				NSAIDs (1989-2015)			
	Type II		Type I		Type II		Type I	
	Cases	Multivariable-adjusted HR (95% CI)[a]	Cases	Multivariable-adjusted HR (95% CI)[a]	Cases	Multivariable-adjusted HR (95% CI)[a]	Cases	Multivariable-adjusted HR (95% CI)[a]
Current regular use								
None	152	1.00 (ref)	93	1.00 (ref)	176	1.00 (ref)	69	1.00 (ref)
Past	176	0.86 (0.66-1.10)	60	1.06 (0.72-1.55)	138	1.12 (0.88-1.43)	48	1.10 (0.73-1.65)
Current	378	0.94 (0.76-1.18)	112	0.98 (0.71-1.36)	260	1.31 (1.06-1.61)	87	1.09 (0.77-1.54)
p-heterogeneity				0.59				0.60
Duration (years)								
<1	189	1.00 (ref)	109	1.00 (ref)	204	1.00 (ref)	77	1.00 (ref)
1-4	97	0.93 (0.72-1.20)	46	1.05 (0.73-1.50)	153	1.19 (0.96-1.48)	75	1.39 (0.99-1.94)
5-9	113	1.05 (0.81-1.36)	40	1.23 (0.82-1.84)	133	1.40 (1.10-1.77)	36	0.92 (0.60-1.41)
10-15[b]	75	1.05 (0.78-1.42)	18	1.05 (0.61-1.81)	95	1.61 (1.21-2.14)	23	1.00 (0.59-1.70)
≥15	166	1.11 (0.86-1.42)	38	1.16 (0.74-1.80)	--	--	--	--
p-trend		0.30		0.51		0.001		0.51
p-heterogeneity				0.95				0.02
Days per week (cumulative average)[c]								
<2	413	1.00 (ref)	160	1.00 (ref)	425	1.00 (ref)	146	1.00 (ref)
3-4	184	1.02 (0.85-1.23)	48	1.09 (0.77-1.53)	98	1.17 (0.94-1.47)	29	0.85 (0.57-1.28)
≥5	45	0.84 (0.61-1.14)	113	0.95 (0.53-1.70)	43	1.25 (0.91-1.72)	8	0.68 (0.33-1.40)
p-trend		0.48		0.89		0.07		0.21
p-heterogeneity				0.65				0.05
Tablets per week (cumulative average)[c]								
<1	269	1.00 (ref)	100	1.00 (ref)	109	1.00 (ref)	37	1.00 (ref)
1-3	238	1.17 (0.98-1.41)	60	1.12 (0.79-1.57)	55	1.40 (1.00-1.96)	16	0.92 (0.50-1.67)
4-5	76	1.23 (0.94-1.59)	27	1.55 (1.00-2.40)	31	1.48 (0.98-2.23)	9	0.88 (0.42-1.84)
6-9	63	1.10 (0.83-1.46)	11	0.78 (0.41-1.48)	26	1.52 (0.97-2.38)	8	1.18 (0.54-2.62)
≥10	43	0.96 (0.69-1.33)	20	1.30 (0.79-2.13)	55	1.65 (1.18-2.31)	16	1.08 (0.59-1.98)
p-trend		0.91		0.40		0.003		0.69
p-heterogeneity				0.51				0.29

[a]Models allowed for variation in baseline hazards by cohort, age in months (continuous) and calendar years (continuous), and adjusted for menopausal status, parity (ever/never and number of children), duration of oral contraceptive use (never, <1, 1 to 5, >5 years), duration of postmenopausal hormone use by type, history of tubal ligation (yes, no), history of hysterectomy (yes, no), family history of breast cancer or ovarian cancer (yes, no), BMI (<20, 20 to <25, 25 to <30, ≥30)

[b]Top category of duration analysis for NSAIDs is ≥10 years
[c]Aspirin days per week follow-up 1984-2015; NSAID tablets per week follow-up 2000-2015

eTable 5. Acetaminophen and risk of ovarian cancer in the Nurses' Health Studies, by tumor histotype

	Type II		Type I	
	Cases	Multivariate-adjusted HR (95% CI)[a]	Cases	Multivariate-adjusted HR (95% CI)[a]
Current regular use				
None	189	1.00 (ref)	91	1.00 (ref)
Past	189	1.20 (0.96-1.49)	58	0.89 (0.62-1.28)
Current	180	1.17 (0.94-1.44)	49	0.78 (0.55-1.12)
p-heterogeneity				0.14
Duration (years)				
<1	226	1.00 (ref)	104	1.00 (ref)
1-4	174	1.18 (0.96-1.44)	53	0.81 (0.57-1.13)
5-9	132	1.32 (1.06-1.66)	42	1.03 (0.71-1.50)
≥10	53	1.20 (0.87-1.66)	13	0.81 (0.44-1.48)
p-trend		0.09		0.76
p-heterogeneity				0.28
Days per week (cumulative average)				
<2	483	1.00 (ref)	162	1.00 (ref)
3-4	57	0.98 (0.74-1.29)	18	0.97 (0.60-1.59)
≥5	16	1.02 (0.62-1.68)	2	0.43 (0.11-1.73)
p-trend		0.96		0.35
p-heterogeneity				0.41
Tablets per week (cumulative average)[b]				
<1	139	1.00 (ref)	59	1.00 (ref)
1-3	58	1.32 (0.96-1.80)	11	0.60 (0.31-1.15)
4-5	23	1.20 (0.76-1.88)	8	1.09 (0.52-2.29)
6-9	15	1.19 (0.69-2.05)	6	1.9 (0.63-3.54)
≥10	30	1.33 (0.89-2.00)	7	0.78 (0.35-1.74)
p-trend		0.15		0.87
p-heterogeneity				0.41

[a]Models allowed for variation in baseline hazards by cohort, age in months (continuous) and calendar years (continuous), and adjusted for menopausal status, parity (ever/never and number of children), duration of oral contraceptive use (never, <1, 1 to 5, >5 years), duration of postmenopausal hormone use by type, history of tubal ligation (yes, no), history of hysterectomy (yes, no), family history of breast cancer or ovarian cancer (yes, no), BMI (<20, 20 to <25, 25 to <30, ≥30)
[b] Cumulative average tablets per week follow-up 2000-2015