Supplemental Online Content

Ajufo E, Ayers CR, Vigen R, et al. Value of coronary artery calcium scanning in association with the net benefit of aspirin in primary prevention of atherosclerotic cardiovascular disease. *JAMA Cardiol*. Published online October 28, 2020. doi:10.1001/jamacardio.2020.4939

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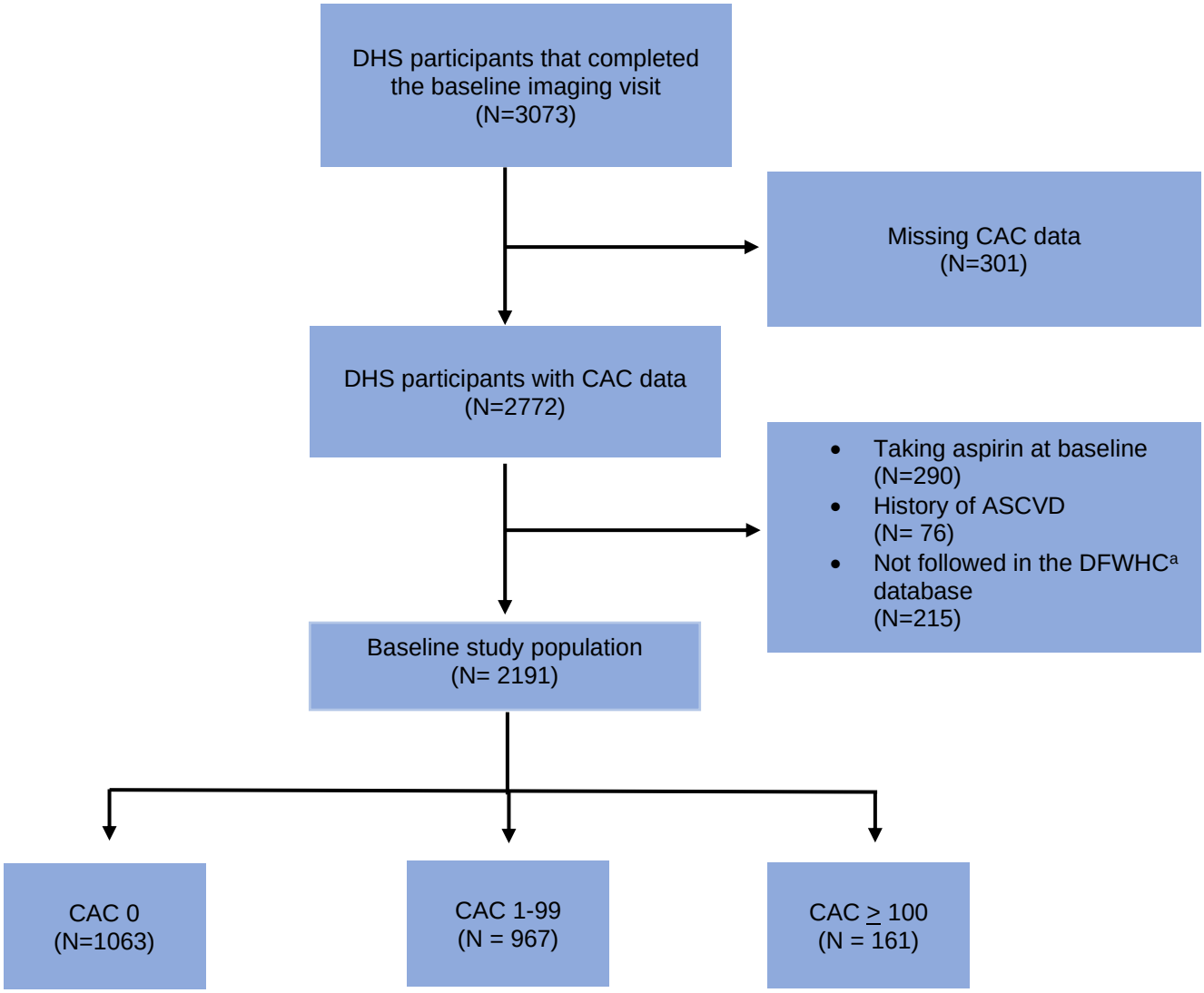
eFigure 1. Participant selection



[a] ASCVD, Atherosclerotic cardiovascular disease; CAC, coronary artery calcium; DHS, Dallas Heart Study; DFWHC, Dallas Fort Worth Hospital coalition database

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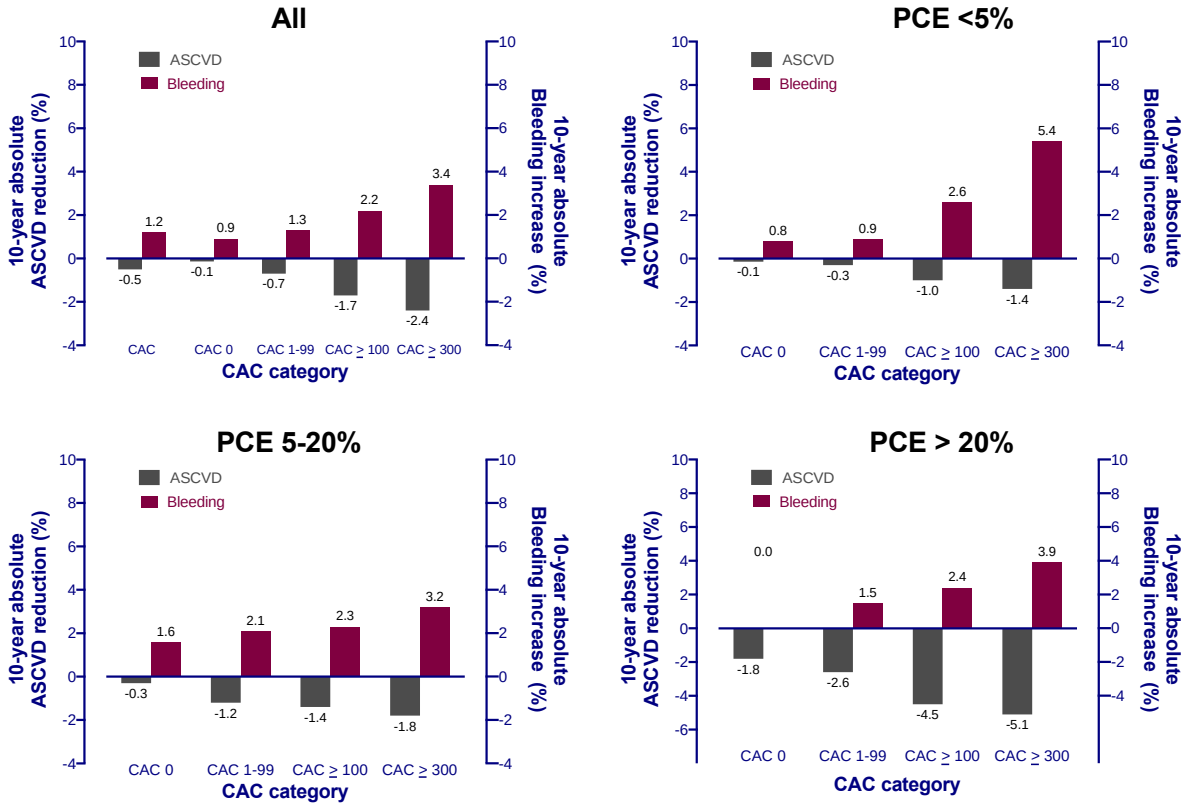
eFigure 2. Estimated increase in bleeding event rate vs reduction in ASCVD event rate with aspirin use for primary prevention in DHS participants stratified by ASCVD risk and CAC (*including CAC ≥300 category*)



Estimates were generated by applying an 11% relative risk reduction to 10-year ASCVD event rates and a 43% relative risk increase to 10-year bleeding event rates.
Abbreviations: PCE, pooled cohort equation

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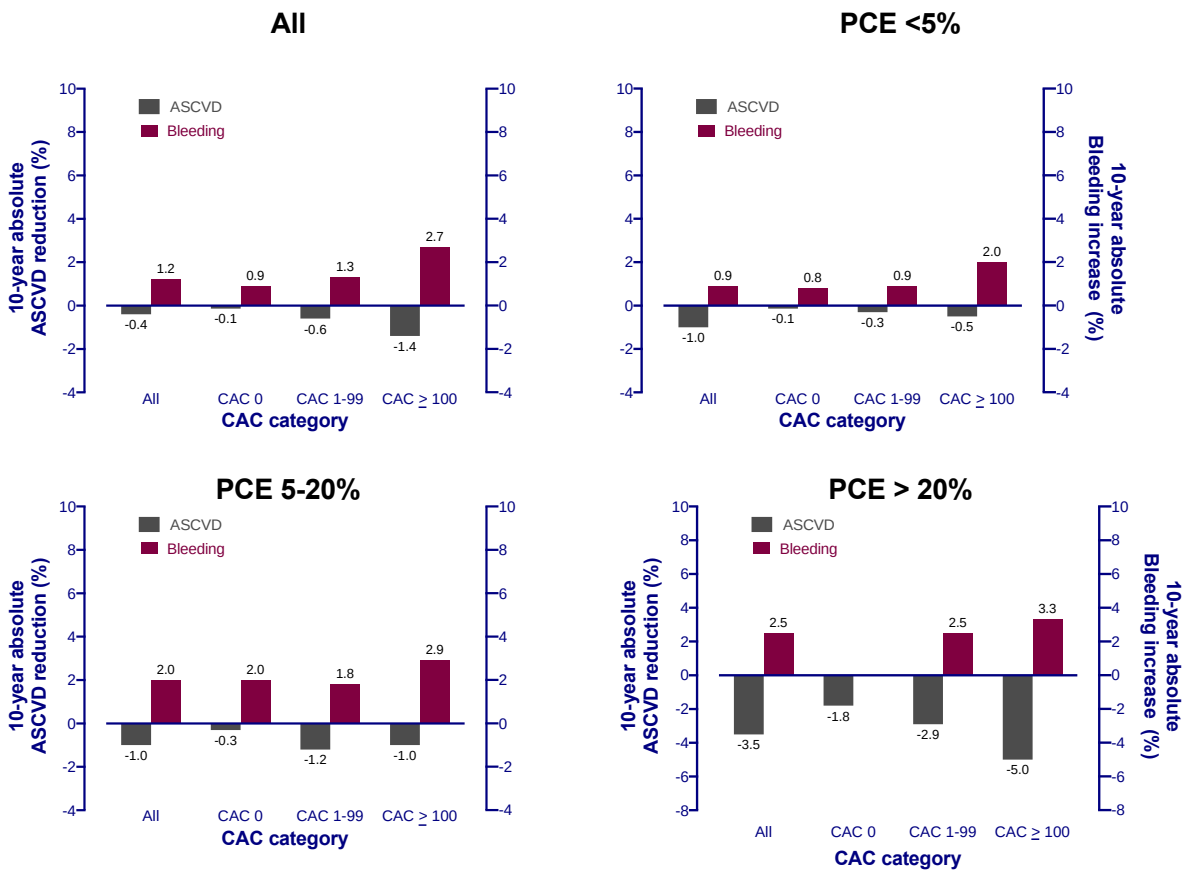
eFigure 3. Estimated increase in bleeding event rate vs reduction in ASCVD event rate with aspirin use for primary prevention in DHS participants without interval aspirin uptake[a]



Estimates were generated by applying an 11% relative risk reduction to 10-year ASCVD event rates and a 43% relative risk increase to 10-year bleeding event rates, N=1912.
[a] Participants were confirmed not to be on aspirin at the baseline DHS-2 visit seven years after the baseline DHS-1 visit.
Abbreviations: PCE, pooled cohort equation

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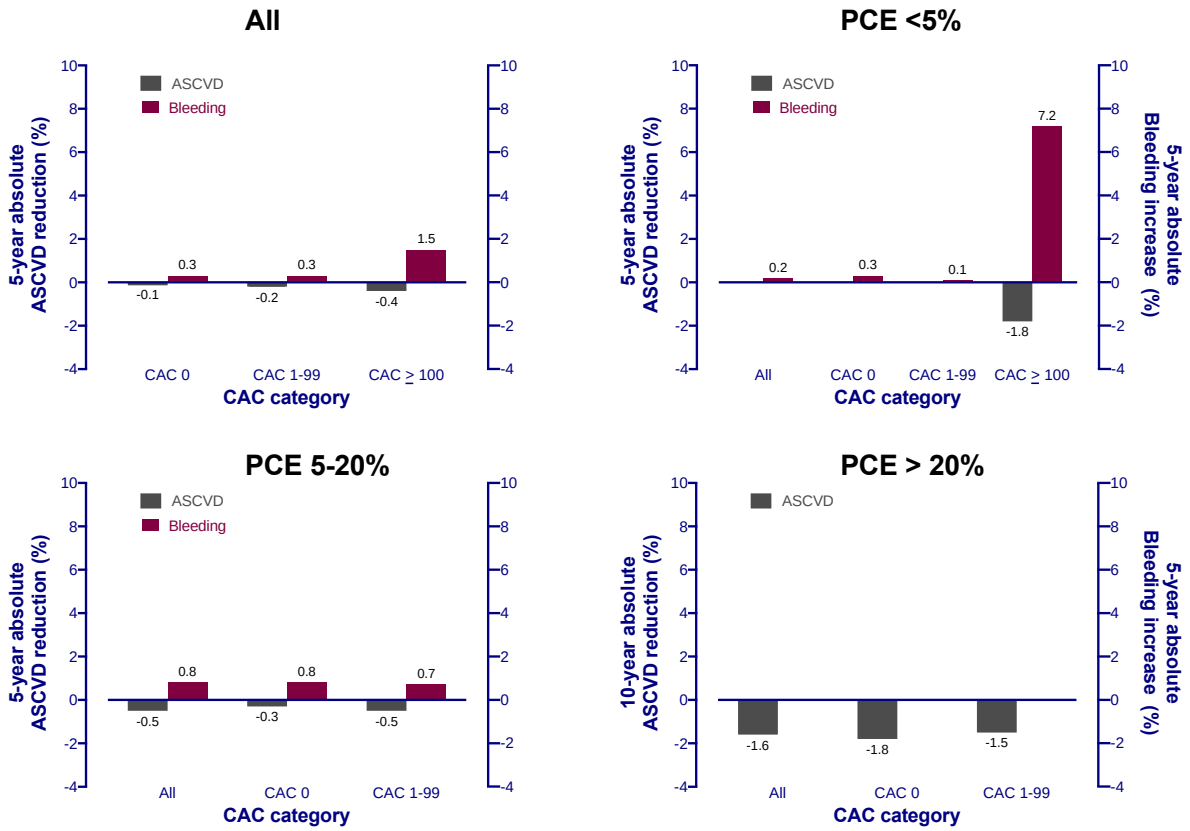
eFigure 4. Estimated increase in 5-year bleeding event rate vs reduction in adjudicated 5-year ASCVD event rate with aspirin use for primary prevention stratified by CAC



Estimates were generated by applying an 11% relative risk reduction to 5-year ASCVD event rates and a 43% relative risk increase to 5-year bleeding event rates

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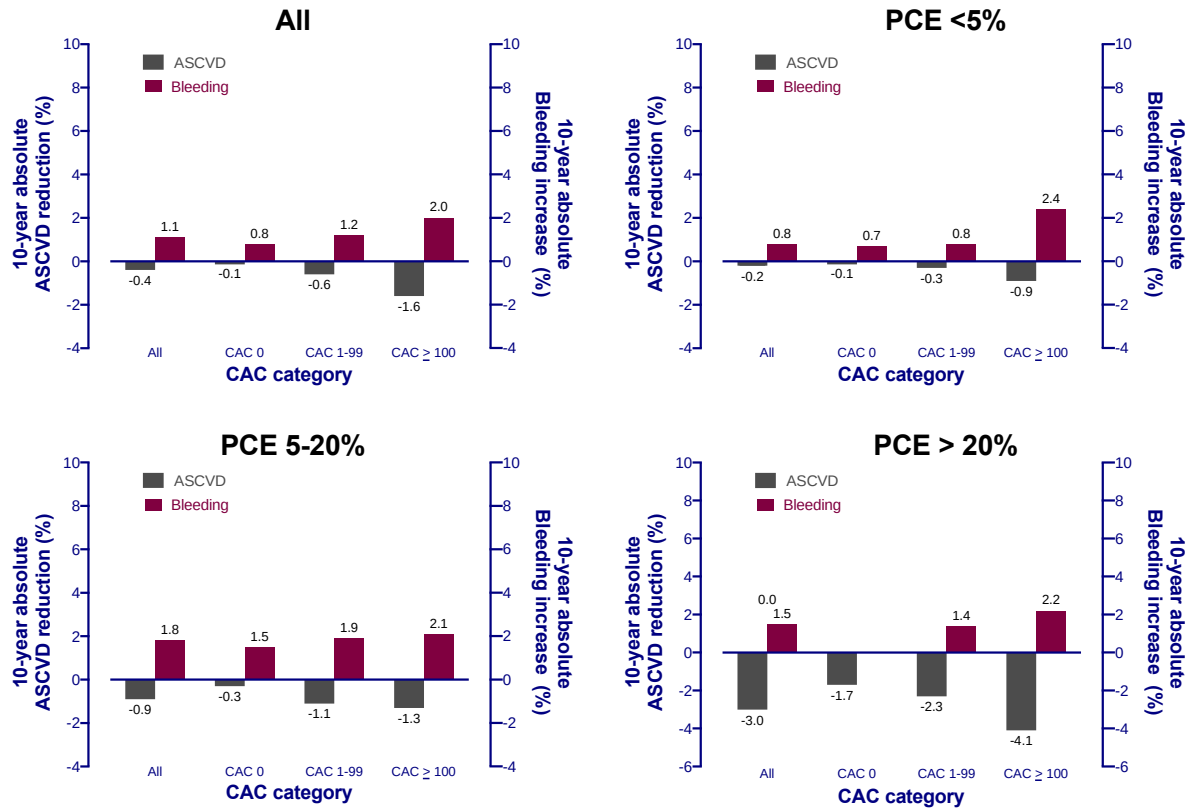
eFigure 5. Estimated increase in bleeding event rate vs reduction in ASCVD event rate with aspirin use for primary prevention in DHS participants stratified by ASCVD risk and CAC (*aspirin effect estimates taken from contemporary aspirin trials)**



*Estimates were generated by applying post-hoc effect estimates from a meta-analysis of aspirin trials conducted after 2000 - 10% relative risk reduction to 10-year ASCVD event rates and a 39% relative risk increase to 10-year bleeding event rates.

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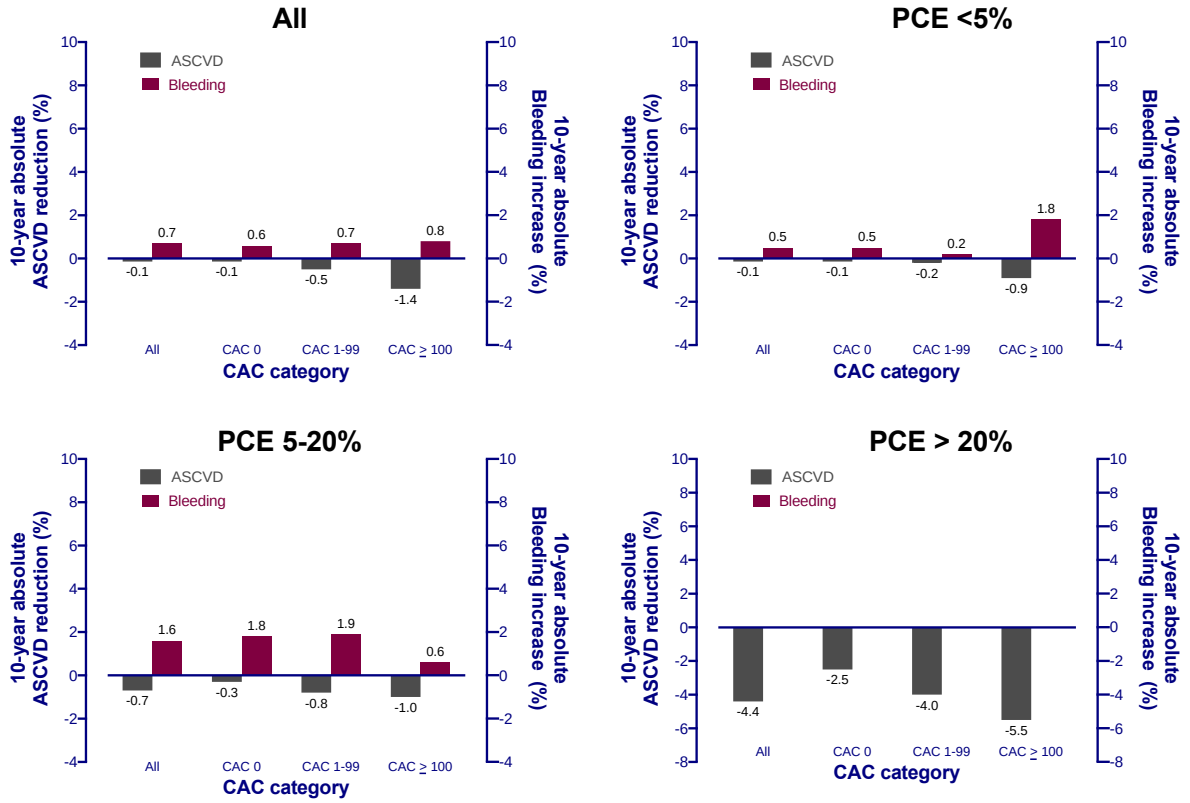
eFigure 6. Estimated increase in bleeding event rate vs reduction in ASCVD event rate with aspirin use for primary prevention in DHS participants at lower bleeding risk stratified by ASCVD risk and CAC (*aspirin effect estimates taken from contemporary aspirin trials)**



*Estimates were generated by applying post-hoc effect estimates from a meta-analysis of aspirin trials conducted after 2000 - 10% relative risk reduction to 10-year ASCVD event rates and a 39% relative risk increase to 10-year bleeding event rates.

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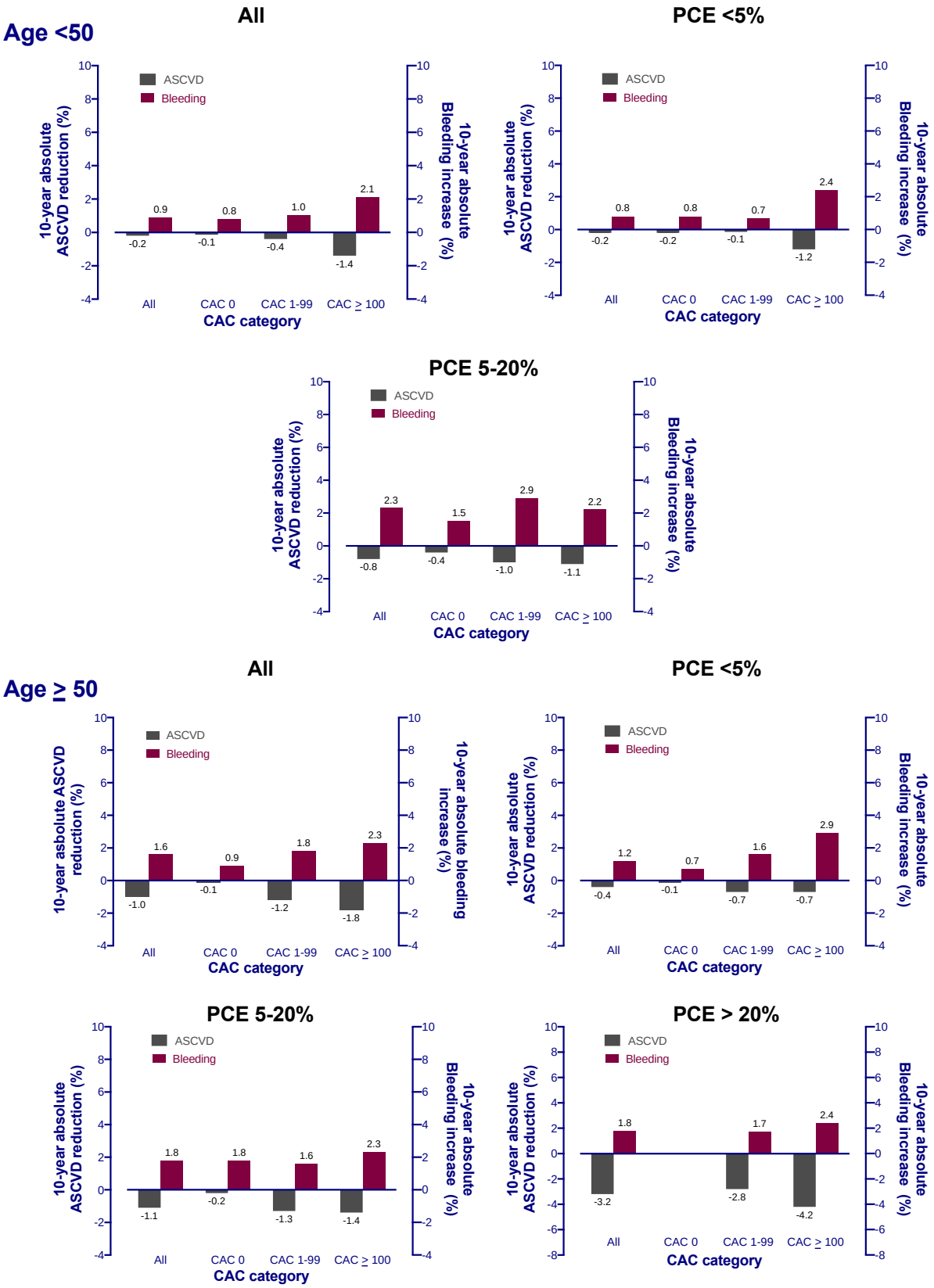
eFigure 7. Estimated increase in bleeding event rate vs reduction in ASCVD event rate with aspirin use for primary prevention in DHS participants stratified by age, ASCVD risk and CAC



Estimates were generated by applying an 11% relative risk reduction to 10-year ASCVD event rates and a 43% relative risk increase to 10-year bleeding event rates. The number of individuals in each subgroup were as follows: Age <50 - All (N= 1547),

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PCE <5% (N=1304), PCE 5-20% (N=189), PCE > 20% (N=5); Age ≥ 50 - All (N=647), PCE <5% (N=243), PCE 5-20% (N=319), PCE ≥ 20% (N=56). There were too few events to construct a figure for the Age <50, PCE ≥ 20% subgroup.
Abbreviations: PCE, pooled cohort equation

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eTable 1. ICD codes used to identify bleeding events from the DFWHC and NDI databases

	ICD-9	ICD-10
Gastrointestinal		
Peptic ulcer with bleeding and/or perforation	Gastric: 531.0, 531.01, 531.10, 531.11, 531.20, 531.21, 531.50, 531.51, 531.60, 531.61, 531.40, 531.41 Duodenal: 532.0, 532.01, 532.10, 532.11, 532.20, 532.21, 532.50, 532.51, 532.60, 532.61, 532.40, 532.41 Gastrojejunal: 534.0, 534.01, 534.10, 534.11, 534.20, 534.21, 534.40, 534.41, 534.50, 534.51, 534.60, 534.61 Unspecificied site: 533.00, 533.01, 533.10, 533.11, 533.20, 533.21, 533.40, 533.41, 533.50, 533.51, 533.60, 533.661	Gastric: K25.0, K25.1, K25.2, K25.4, K25.5, K25.6 Duodenal: K26.0, K26.1, K26.2, K26.4, K26.5, K26.6 Gastrojejunal: K28.0, K28.1, K28.2, K28.4, K28.5, K28.6 Peptic: K27.0, K27.1, K27.2, K27.4, K27.5, K27.6
Diverticulitis with bleeding or divertiuclosis with bleeding	562.02, 562.03, 562.12, 562.13	K57.01, K57.13, K57.11, K57.21, K57.31, K57.33, K57.41, K57.51, K57.53, K57.81, K57.91, K57.93
Angiodysplasia with bleeding	537.83, 569.85	K31.82, K55.22
Mallory-Weiss tear	530.7	K22.6
Gastritis with bleeding, gastroduodenitis with bleeding or duodenitis with bleeding	535.01, 535.11, 535.31, 535.41, 535.51, 535.61	K29.0, K29.21, K29.31, K29.41, K29.51, K29.61, K29.81, K29.71, K29.91
Hemorrhage of anus and rectum	569.3	K62.5
Hematemesis	578	K92.0
Malena	578.1	K92.1
Gastrointestinal hemorrhage, unspecified	578.9	K92.2
Esophageal varcies with bleeding	456.0, 456.20	I85.01, I85.11
Esophageal hemorrhage	530.82	
Intracranial Bleeding		
Subarachnoid hemorrhage	I60	430
Intracerebral hemorrhage	I61	431
Other nontraumatic intracranial hemorrhage	I62	432.0, 432.1, 432.9
Sequelae of subarachnoid hemorrhage	I69.0	
Sequelae of intracerebral hemorrhage	I69.1	
Sequelae of other intracranial hemorrhage	I69.2	
Other Bleeding		
Ocular (vitreous and retinal)	H35.6, H43.1	362.81, 379.23
Respiratory passage (including epistaxis and hemoptysis)	R04	784.7, 784.8, 786.3
Hemopericardium/hemoperitoneum	I31.2, K66.1	423.0, 568.81
Hemarthrosis	M25.0	719.10, 719.11, 719.12, 719.13, 719.14, 719.15, 719.16, 719.17, 719.18, 719.19

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eTable 2. Bleeding event categories

Bleeding Type	Non-fatal	Fatal	Total
All	92	24	116
Gastrointestinal	68	13	81
Intracerebral	12	6	18
Other	12	5	17

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eTable 3. ASCVD event rate and hazard ratios stratified by CAC

CAC	N	ASCVD, n	ASCVD event rate, 1000 person-years (95% CI)	Unadjusted ASCVD HR (95% CI)	p Value	Adjusted ASCVD HR (95% CI)[a]	p Value
All	2191	123	5.1 (5.1-5.1)	-	-	-	-
0	1063	17	1.3 (1.3-1.3)	1	-	1	-
1-99	967	72	6.27 (6.2-6.3)	4.8 (2.8-8.2)	<0.01	2.5 (1.4-4.3)	<0.01
≥ 100	161	34	19.3 (19.1-19.5)	5.3 (3.6-7.9)	<0.01	2.0 (1.3-3.0)	<0.01

[a]Model adjusted for age, sex, Race/Ethnicity, diabetes mellitus, current smoking, total cholesterol, HDL cholesterol, anti-hypertensive use, systolic blood pressure, statin use

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eTable 4. Bleeding event rate and hazard ratios stratified by CAC in DHS participants without interval aspirin uptake[a]

CAC	N	Bleeding events, n	Bleeding event rate, 1000 person-years (95% CI)	Unadjusted Bleeding HR (95% CI)	p Value	Adjusted Bleeding HR (95% CI)[b]	p Value
All	1912	93	1.9 (1.9-1.9)	-	-	=	
0	*963*	*31*	*1.9 (1.9-2.0)*	*1*	-	*1*	-
1-99	832	50	3.7 (3.7-3.8)	1.9 (1.2-3.0)	<0.01	1.0 (0.6-1.7)	0.95
≥ 100	117	12	7.8 (7.7-7.9)	2.7 (1.5-5.0)	<0.01	1.3 (0.7-2.6)	0.39

[a] The subgroup of participants not on aspirin at the baseline DHS-2 visit seven years after the baseline DHS-1 visit.
[b] Model adjusted for age, sex, race/Ethnicity, SBP, anti-hypertensive use, smoking status, diabetes mellitus, PUD, PPI/Antacid, corticosteroid.

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	ALL				PCE <5%				PCE 5-20%				PCE ≥ 20%			
CAC	**All**	**0**	**1-99**	**≥100**	**All**	**0**	**1-99**	**≥100**	**All**	**0**	**1-99**	**≥100**	**All**	**0**	**1-99**	**≥100**
All																
Participants, N	2191	1063	967	161	1547	908	606	33	508	108	303	97	61	6	30	25
ASCVD events, n	94	11	58	25	27	7	17	3	47	3	32	12	18	1	7	10
10Y ASCVD event rate (%)	4.3	1.0	6.0	15.7	1.8	0.8	2.8	9.1	9.3	2.8	10.6	12.5	29.7	16.8	23.3	41.1
Bleeding events, n	65	23	34	8	35	19	14	2	25	4	16	5	2	0	1	1
10Y bleeding event rate (%)	2.7	2.0	3.1	5.2	2.0	1.9	2.0	6.1	4.7	3.8	4.8	5.3	3.8	0	3.6	5.6
No interval aspirin uptake																
Participants, N	1912	963	832	117	1397	833	542	22	415	89	250	76	41	6	19	16
ASCVD events, n	70	7	48	15	20	4	15	1	36	2	27	7	13	1	5	7
10Y ASCVD event rate (%)	3.7	0.7	5.8	13.0	1.5	0.5	2.8	4.6	8.7	2.3	10.9	9.3	32.0	16.7	26.3	45.0
Bleeding events, n	59	22	30	7	33	18	14	1	21	4	12	5	2	0	1	1
10Y bleeding event rate (%)	2.8	2.1	3.1	6.3	2.1	1.9	2.2	4.6	4.7	4.6	4.1	6.8	5.7	0	5.9	7.7
Age <50																
Participants, N	1547	882	624	41	1304	789	497	18	189	60	109	20	5	1	3	1
ASCVD events, n	34	9	20	5	18	6	10	2	14	2	10	2	2	1	0	1
10Y ASCVD event rate (%)	2.2	1.0	3.2	12.3	1.4	0.8	2.0	11.1	7.5	3.3	9.2	10.0	40	100	0	100
Bleeding events, n	38	19	17	2	28	17	10	1	10	2	7	1	0	0	0	0
10Y bleeding event rate (%)	2.2	1.9	2.4	4.9	1.9	1.9	1.6	5.6	5.4	3.4	6.7	5.0	0	0	0	0

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Age ≥ 50																
Participants, N	644	181	343	120	243	119	109	15	319	48	194	77	56	5	27	24
ASCVD events, n	60	2	38	20	9	1	7	1	33	1	22	10	16	0	7	9
10Y ASCVD event rate (%)	9.4	1.1	11.1	16.8	3.7	0.8	6.5	6.7	10.4	2.1	11.4	13.1	28.8	0	25.9	38.4
Bleeding events, n	27	4	17	6	7	2	4	1	15	2	9	4	2	0	1	1
10Y bleeding event rate (%)	3.8	2.2	4.2	5.3	2.9	1.7	3.7	6.7	4.2	4.3	3.7	5.4	4.1	0	4.0	5.6
Lower bleeding risk																
Participants, N	1430	752	579	99	1050	647	381	22	294	67	164	63	25	4	10	11
ASCVD events, n	48	8	26	14	14	5	7	2	21	2	13	6	11	1	4	6
10Y ASCVD event rate (%)	0.5	1.1	4.5	14.3	1.35	0.7	1.9	9.1	7.2	3.0	7.9	9.5	44.0	25.0	40.0	54.6
Bleeding events, n	26	12	12	2	12	9	2	1	12	3	8	1	0	0	0	0
10Y bleeding event rate (%)	1.8	1.6	1.9	2.1	1.2	1.4	0.5	4.6	4.1	4.5	4.9	1.6	0	0	0	0
Higher bleeding risk																
Participants, N	761	311	388	62	497	261	225	11	214	41	139	34	36	2	20	14
ASCVD events, n	46	3	32	11	13	2	10	1	26	1	19	6	7	0	3	4
10Y ASCVD event rate (%)	6.1	1.0	8.3	17.9	2.6	0.8	4.5	9.1	12.2	2.4	13.8	17.7	19.7	0	15.0	29.9
Bleeding events, n	39	11	22	6	23	10	12	1	13	1	8	4	2	0	1	1
10Y bleeding event rate (%)	4.5	2.9	4.8	10.2	3.9	3.1	4.5	9.1	5.4	2.6	4.6	12.1	6.6	0	5.6	10.0

eTable 5. Observed ASCVD and bleeding events at 10 years in various subgroups

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