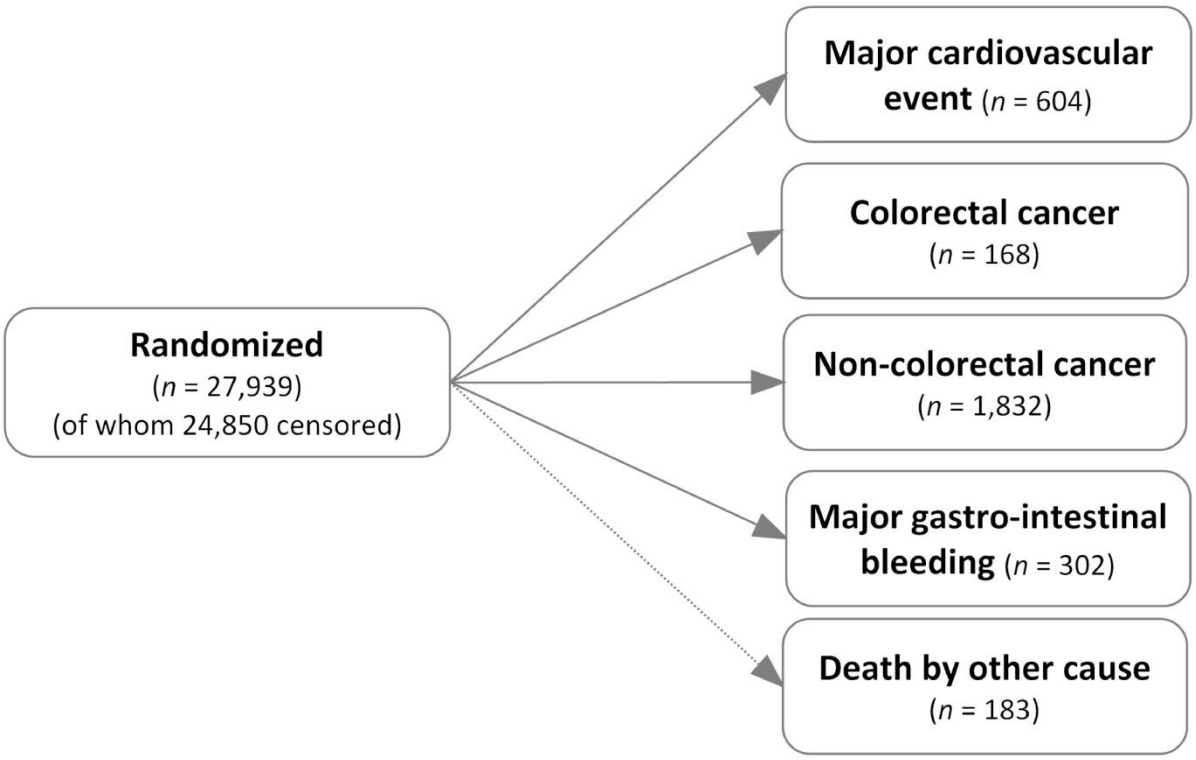
Appendix 2

Supplemental figures



Appendix 2.1 | Competing risks framework with number of events during trial period (*i.e.* from baseline through 31 March 2004, average follow-up of 10.1 years) in women included in the Women's Health Study who provided an adequate baseline plasma sample. Models for the prediction of absolute effects of aspirin on major cardiovascular events, colorectal cancer, non-colorectal cancer and major gastro-intestinal bleeding were developed. No separate model was developed for prediction of the effects on death by other causes, since no effects of aspirin on this outcome was expected, given that all relevant outcomes (major cardiovascular events, colorectal cancer, non-colorectal cancer and major gastro-intestinal bleeding) are already taken into account. Death by other causes was taken into account as competing risks outcome when modelling the other outcomes, because not taking competing risks into account may lead to bias in predictions of absolute risks.

Appendix 2.2 | Models for prediction of 10-year absolute risk reduction with aspirin treatment

Predicted 10-year absolute risk reduction = Total risk without aspirin treatment – Total risk with aspirin treatment, where

Total risk without aspirin treatment:	*Total of model risk estimates for all outcomes, when aspirin treatment is set to 'FALSE'.*
Total risk on aspirin treatment:	*Total of model risk estimates for all outcomes, when aspirin treatment is set to 'TRUE'.*

Model for prediction of 10-year major cardiovascular event risk
(1 - exp(- (0.01068 * exp(A – 20.51836)))) * 100%, where

A = 0.07750 * age (years) + 0.91719 [if current smoker] – 0.02174* body mass index (kg/m^2) + 3.27143 * natural logarithm(systolic blood pressure, mmHg) + 0.25540 [if using blood pressure lowering medication] + 0.28204 [if family history of premature myocardial infarction] + 0.83017 * natural logarithm(total cholesterol, mg/dL) – 0.90235 * natural logarithm(high-density lipoprotein cholesterol, mg/dL) + 0.11419 * natural logarithm(high-sensitivity C-reactive protein, mg/L) + 0.17444 * hemoglobin A1c (%) [if diabetic] –0.09592 [if using aspirin]

Model for prediction of 10-year colorectal cancer risk
(1 - exp(- (0.00287 * exp(B – 4.854)))) * 100%, where

B = 0.06907 * age (years) + 0.15647 [if ever smoker] + 0.03173 * body mass index (kg/m^2) + 0.00180 * height (inches) – 0.01487 [if diabetic] + 0.03258 * no. of alcoholic drinks per day + 0.28102 [if peri- / postmenopausal] – 0.26464 [if ever used hormone replacement therapy] + 0.12076 [if family history of colorectal cancer] – 0.05372 [if using aspirin]

Model for prediction of 10-year non-colorectal cancer risk
(1 - exp(- (0.05554 * exp(C – 3.40691)))) * 100%, where

C = 0.04287 * age (years) + 0.14222 [if ever smoker] + 0.00125 * body mass index (kg/m^2) + 0.01469 * height (inches) – 0.14474 [if diabetic] + 0.07571 * no. of alcoholic drinks per day – 0.14239 [if peri- / postmenopausal] + 0.04985 [if ever used hormone replacement therapy] + 0.00181 [if family history of cancer] + 0.046578 [if using aspirin]

Model for prediction of 10-year major gastro-intestinal bleeding risk
(1 - exp(- (0.00742 * exp(D – 4.53537)))) * 100%, where

D = 0.06209 * age (years) + 0.22339 [if current smoker] + 0.03316 * body mass index (kg/m^2) + 0.26552 [if diabetic] + 0.00652 * no. of alcoholic drinks per day + 0.21780 [if history of dyspepsia] + 0.45399 [if using aspirin]

Outcomes were modelled in a competing risks framework, mutually accounting for all outcomes as well as death by other causes (Appendix 2.1), because not taking competing risks into account may lead to bias in predictions of absolute risks and non-additivity of risks for the individual outcomes[23 24]. No separate model was developed for prediction of the effects of aspirin on death by other causes, since no effects of aspirin on this outcome was expected, given that all relevant outcomes (major cardiovascular events, colorectal cancer, non-colorectal cancer and major gastro-intestinal bleeding) are already taken into account.

Appendix 2.3 | Models for prediction of 15-year absolute risk reduction with aspirin treatment

Predicted 15-year absolute risk reduction = Total risk without aspirin treatment – Total risk with aspirin treatment, where

Total risk without aspirin treatment:	*Total of model risk estimates for all outcomes, when aspirin treatment is set to 'FALSE'.*
Total risk on aspirin treatment:	*Total of model risk estimates for all outcomes, when aspirin treatment is set to 'TRUE'.*

Model for prediction of 15-year major cardiovascular event risk
(1 - exp(- (0.01602 * exp(A – 20.51836)))) * 100%, where

A = 0.07750 * age (years) + 0.91719 [if current smoker] – 0.02174* body mass index (kg/m^2) + 3.27143 * natural logarithm(systolic blood pressure, mmHg) + 0.25540 [if using blood pressure lowering medication] + 0.28204 [if family history of premature myocardial infarction] + 0.83017 * natural logarithm(total cholesterol, mg/dL) – 0.90235 * natural logarithm(high-density lipoprotein cholesterol, mg/dL) + 0.11419 * natural logarithm(high-sensitivity C-reactive protein, mg/L) + 0.17444 * hemoglobin A1c (%) [if diabetic] –0.09592 [if using aspirin]

Model for prediction of 15-year colorectal cancer risk
(1 - exp(- (0.00428 * exp(B – 6.89174)))) * 100%, where

B = 0.05465 * age (years) + 0.18407 [if ever smoker] + 0.03713 * body mass index (kg/m^2) + 0.03973 * height (inches) – 0.27643 [if diabetic] + 0.15733 * no. of alcoholic drinks per day + 0.62717 [if peri- / postmenopausal] – 0.29949 [if ever used hormone replacement therapy] + 0.14094 [if family history of colorectal cancer] – 0.14483 [if using aspirin]

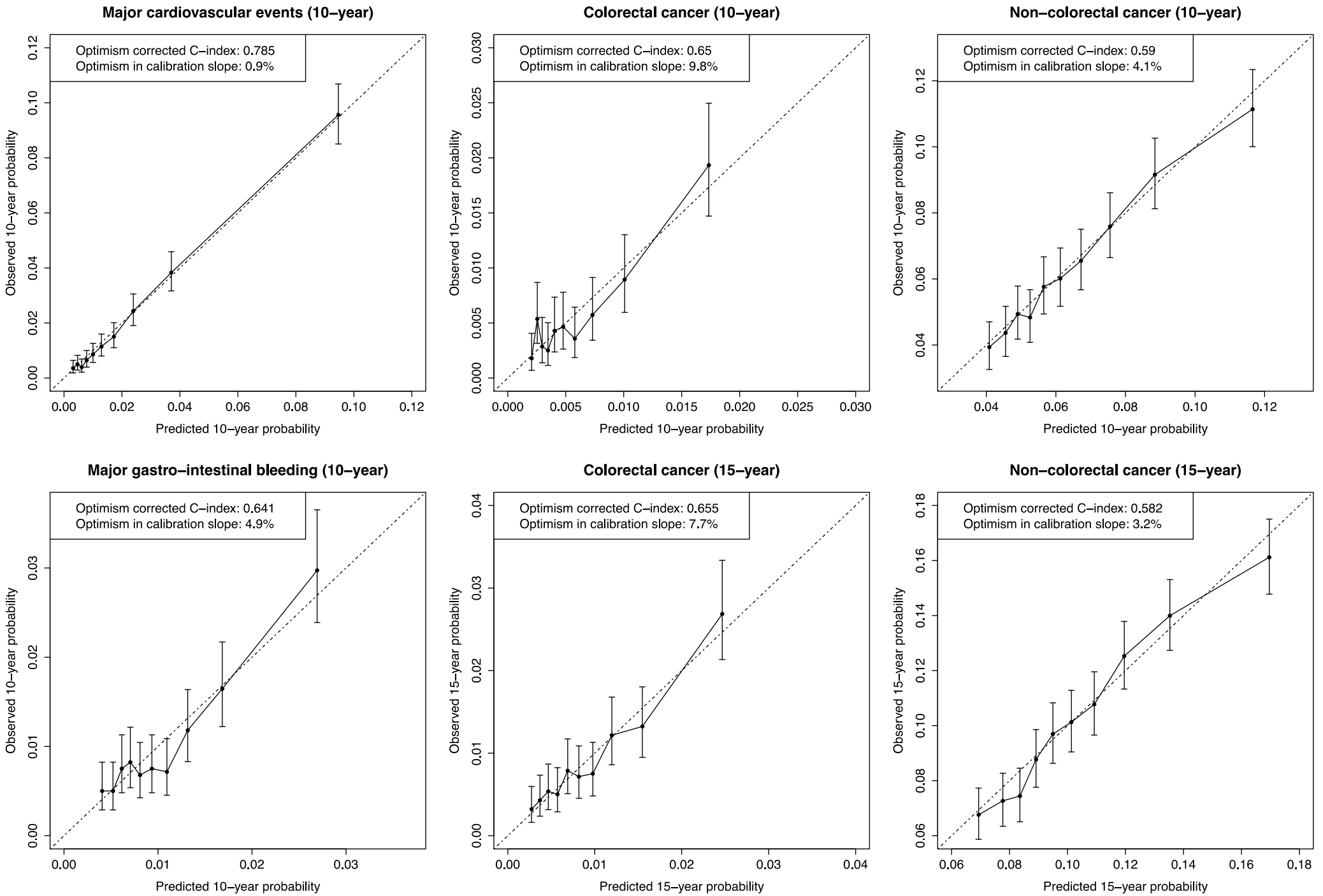
Model for prediction of 15-year non-colorectal cancer risk
(1 - exp(- (0.09493 * exp(C – 3.61989)))) * 100%, where

C = 0.03598 * age (years) + 0.17283 [if ever smoker] + 0.00735 * body mass index (kg/m^2) + 0.02162 * height (inches) – 0.03080 [if diabetic] + 0.09586 * no. of alcoholic drinks per day – 0.13779 [if peri- / postmenopausal] + 0.06473 [if ever used hormone replacement therapy] + 0.06062 [if family history of cancer] + 0.01568 [if using aspirin]

Model for prediction of 15-year major gastro-intestinal bleeding risk
(1 - exp(- (0.01113 * exp(D – 4.53537)))) * 100%, where

D = 0.06209 * age (years) + 0.22339 [if current smoker] + 0.03316 * body mass index (kg/m^2) + 0.26552 [if diabetic] + 0.00652 * no. of alcoholic drinks per day + 0.21780 [if history of dyspepsia] + 0.45399 [if using aspirin]

Outcomes were modelled in a competing risks framework, mutually accounting for all outcomes as well as death by other causes (Appendix 2.1), because not taking competing risks into account may lead to bias in predictions of absolute risks and non-additivity of risks for the individual outcomes[23 24]. No separate model was developed for prediction of the effects of aspirin on death by other causes, since no effects of aspirin on this outcome was expected, given that all relevant outcomes (major cardiovascular events, colorectal cancer, non-colorectal cancer and major gastro-intestinal bleeding) are already taken into account.



Appendix 2.4 | Calibration plots. Axis scales differ between plots. Plots were created with R-code adjusted from: *N.P. Bleda. Interval-censored semi-competing risks data : a novel approach for modelling bladder cancer. Thesis, Universitat Politècnica de Catalunya, Barcelona, June 2010.*

Appendix 2.5 (A) | Observed absolute risks, absolute risk reductions and numbers needed to treat/harm for aspirin

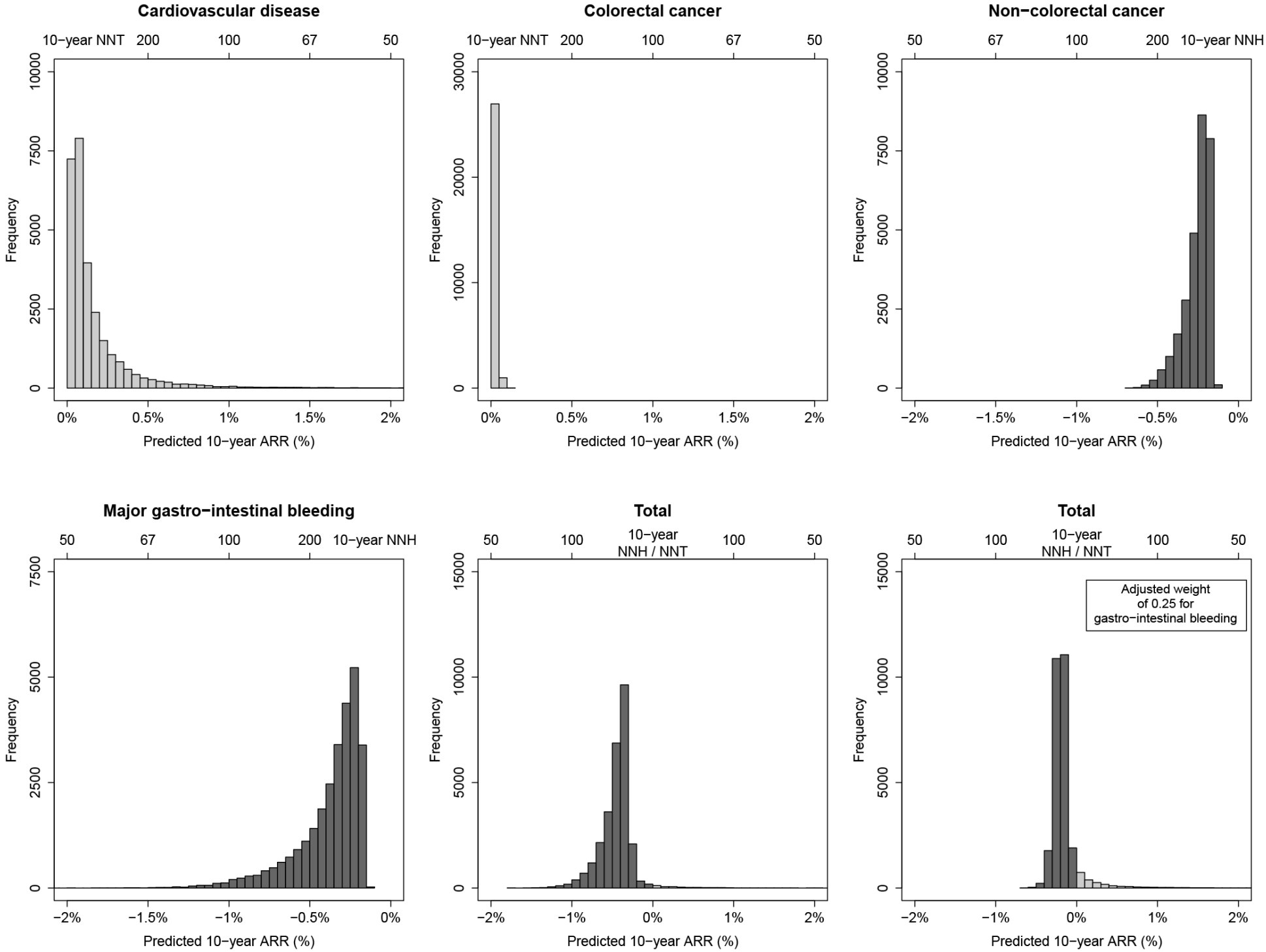
		Major cardiovascular disease	Colorectal cancer	Non-colorectal cancer	Major gastro-intestinal bleeding
		Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)
Total study population					
10-year	AR without aspirin (%)	2.27 (2.03 to 2.53)	0.61 (0.49 to 0.75)	6.40 (6.00 to 6.82)	0.83 (0.69 to 0.99)
	AR with aspirin (%)	2.09 (1.86 to 2.34)	0.60 (0.48 to 0.74)	6.67 (6.26 to 7.10)	1.33 (1.15 to 1.53)
	ARR (%)	0.18 (0.02 to 0.95)	0.01 (0.00 to 32.05)	-0.27 (-0.86 to 0.32)	-0.50 (-0.26 to -0.75)
	[a]NNT or [b]NNH	550 (106 to >1000) [a]	>1000 (3 to >1000) [a]	370[b] (117[b] to 317[a])	199 (134 to 390) [b]
15-year	AR without aspirin (%)	3.38 (3.14 to 3.64)	1.01 (0.85 to 1.18)	10.44 (9.93 to 10.96)	1.24 (1.09 to 1.40)
	AR with aspirin (%)	3.11 (2.88 to 3.36)	0.86 (0.72 to 1.03)	10.52 (10.01 to 11.04)	1.99 (1.80 to 2.19)
	ARR (%)	0.27 (0.06 to 0.86)	0.14 (0.02 to 0.59)	-0.08 (-0.80 to 0.64)	-0.75 (-0.50 to -1.00)
	[a]NNT or [b]NNH	371 (116 to >1000) [a]	709 (170 to >1000) [a]	>1000[b] (124[b] to 156[a])	133 (100 to 198) [b]
Women <65 years					
10-year	AR without aspirin (%)	1.66 (1.45 to 1.90)	0.51 (0.40 to 0.65)	5.75 (5.34 to 6.17)	0.69 (0.55 to 0.85)
	AR with aspirin (%)	1.70 (1.49 to 1.95)	0.47 (0.36 to 0.60)	6.23 (5.82 to 6.67)	1.11 (0.94 to 1.31)
	ARR (%)	-0.04 (-0.37 to 0.28)	0.05 (0.00 to 0.96)	-0.49 (-1.08 to 0.11)	-0.43 (-0.19 to -0.66)
	[a]NNT or [b]NNH	>1000[b] (273[b] to 354[a])	>1000 (105 to >1000) [a]	205[b] (92[b] to 937[a])	235 (151 to 531) [b]
15-year	AR without aspirin (%)	2.48 (2.26 to 2.72)	0.88 (0.73 to 1.06)	9.62 (9.11 to 10.15)	1.03 (0.89 to 1.18)
	AR with aspirin (%)	2.55 (2.32 to 2.78)	0.71 (0.57 to 0.87)	9.94 (9.42 to 10.48)	1.66 (1.48 to 1.86)
	ARR (%)	-0.06 (-0.39 to 0.26)	0.17 (0.04 to 0.55)	-0.32 (-1.06 to 0.42)	-0.64 (-0.40 to -0.87)
	[a]NNT or [b]NNH	>1000[b] (259[b] to 382[a])	581 (181 to >1000) [a]	312[b] (94[b] to 237[a])	157 (114 to 251) [b]
Women ≥65 years					
10-year	AR without aspirin (%)	7.39 (6.12 to 8.82)	1.43 (0.92 to 2.15)	11.93 (10.32 to 13.66)	2.02 (1.39 to 2.86)
	AR with aspirin (%)	5.25 (4.18 to 6.49)	1.71 (1.13 to 2.47)	10.29 (8.81 to 11.91)	3.15 (2.34 to 4.14)
	ARR (%)	2.14 (0.85 to 4.52)	-0.27 (-1.17 to 0.63)	1.64 (0.31 to 5.34)	-1.12 (-2.28 to 0.04)
	[a]NNT or [b]NNH	47 (22 to 118) [a]	369[b] (85[b] to 158[a])	61 (19 to 321) [a]	89[b] (44[b] to >1000[a])
15-year	AR without aspirin (%)	10.88 (9.58 to 12.28)	2.06 (1.42 to 2.89)	17.44 (15.52 to 19.45)	3.02 (2.35 to 3.82)
	AR with aspirin (%)	7.77 (6.67 to 8.97)	2.17 (1.51 to 3.01)	15.39 (13.59 to 17.30)	4.68 (3.84 to 5.64)
	ARR (%)	3.11 (1.67 to 5.27)	-0.11 (-1.15 to 0.93)	2.05 (0.43 to 6.28)	-1.66 (-0.50 to -2.82)
	[a]NNT or [b]NNH	32 (19 to 60) [a]	924[b] (87[b] to 107[a])	49 (16 to 235) [a]	60 (35 to 199) [b]
Never smokers					
10-year	AR without aspirin (%)	1.85 (1.55 to 2.18)	0.57 (0.42 to 0.77)	5.43 (4.92 to 5.97)	0.69 (0.52 to 0.91)
	AR with aspirin (%)	1.53 (1.26 to 1.84)	0.54 (0.39 to 0.73)	6.63 (6.06 to 7.22)	1.16 (0.93 to 1.43)
	ARR (%)	0.32 (0.07 to 1.05)	0.03 (0.00 to 3.86)	-1.20 (-0.41 to -1.98)	-0.46 (-0.15 to -0.78)
	[a]NNT or [b]NNH	314 (95 to >1000) [a]	>1000 (26 to >1000) [a]	83 (50 to 242) [b]	215 (128 to 685) [b]
15-year	AR without aspirin (%)	2.76 (2.46 to 3.09)	0.92 (0.72 to 1.16)	9.05 (8.40 to 9.73)	1.04 (0.86 to 1.25)
	AR with aspirin (%)	2.29 (2.01 to 2.59)	0.72 (0.55 to 0.94)	9.90 (9.22 to 10.61)	1.73 (1.49 to 2.00)
	ARR (%)	0.47 (0.18 to 1.09)	0.20 (0.04 to 0.75)	-0.85 (-1.81 to 0.11)	-0.69 (-0.37 to -1.01)
	[a]NNT or [b]NNH	211 (92 to 565) [a]	509 (134 to >1000) [a]	117[b] (55[b] to 911[a])	144 (99 to 267) [b]
Past smokers					
10-year	AR without aspirin (%)	2.27 (1.88 to 2.71)	0.76 (0.55 to 1.03)	7.01 (6.33 to 7.75)	1.00 (0.75 to 1.30)
	AR with aspirin (%)	1.96 (1.60 to 2.37)	0.74 (0.53 to 1.01)	6.08 (5.44 to 6.76)	1.50 (1.19 to 1.86)
	ARR (%)	0.31 (0.04 to 1.48)	0.02 (0.00 to 24.90)	0.94 (0.30 to 2.37)	-0.50 (-0.07 to -0.93)
	[a]NNT or [b]NNH	321 (68 to >1000) [a]	>1000 (4 to >1000) [a]	107 (42 to 339) [a]	200 (107 to >1000) [b]
15-year	AR without aspirin (%)	3.38 (2.99 to 3.81)	1.21 (0.94 to 1.54)	11.50 (10.64 to 12.40)	1.49 (1.23 to 1.78)
	AR with aspirin (%)	2.92 (2.55 to 3.32)	1.06 (0.81 to 1.37)	10.28 (9.46 to 11.13)	2.24 (1.92 to 2.59)
	ARR (%)	0.46 (0.12 to 1.38)	0.15 (0.01 to 1.40)	1.22 (0.40 to 2.98)	-0.75 (-0.31 to -1.18)
	[a]NNT or [b]NNH	216 (72 to 853) [a]	662 (71 to >1000) [a]	82 (34 to 250) [a]	134 (85 to 322) [b]
Current smokers					
10-year	AR without aspirin (%)	4.12 (3.22 to 5.18)	0.31 (0.12 to 0.69)	8.72 (7.41 to 10.16)	0.89 (0.51 to 1.47)
	AR with aspirin (%)	4.98 (3.99 to 6.14)	0.44 (0.20 to 0.87)	8.75 (7.43 to 10.20)	1.57 (1.04 to 2.27)
	ARR (%)	-0.86 (-2.31 to 0.59)	-0.13 (-0.55 to 0.29)	-0.03 (-1.99 to 1.92)	-0.68 (-1.44 to 0.09)
	[a]NNT or [b]NNH	-116 (-43 to 169) [a]	-758 (-181 to 348) [a]	<-1000 (50 to 52) [b]	148 (-69 to >1000) [b]
15-year	AR without aspirin (%)	6.12 (5.19 to 7.15)	0.75 (0.41 to 1.28)	13.28 (11.66 to 14.99)	1.33 (0.93 to 1.87)
	AR with aspirin (%)	7.38 (6.36 to 8.50)	0.88 (0.51 to 1.44)	14.06 (12.40 to 15.83)	2.34 (1.79 to 3.01)
	ARR (%)	-1.26 (-2.71 to 0.19)	-0.13 (-0.75 to 0.50)	-0.79 (-3.18 to 1.60)	-1.01 (-0.24 to -1.78)
	[a]NNT or [b]NNH	-79 (-37 to 524) [a]	-783 (-133 to 201) [a]	127 (31 to 62) [b]	99 (56 to 420) [b]

CI: Confidence interval ; AR: Absolute risk ; ARR: Absolute risk reduction ; [a]NNT: Number needed to treat ; [b]NNH: Number needed to harm. Risks were estimated based on the cumulative incidence function, accounting for competing risks.

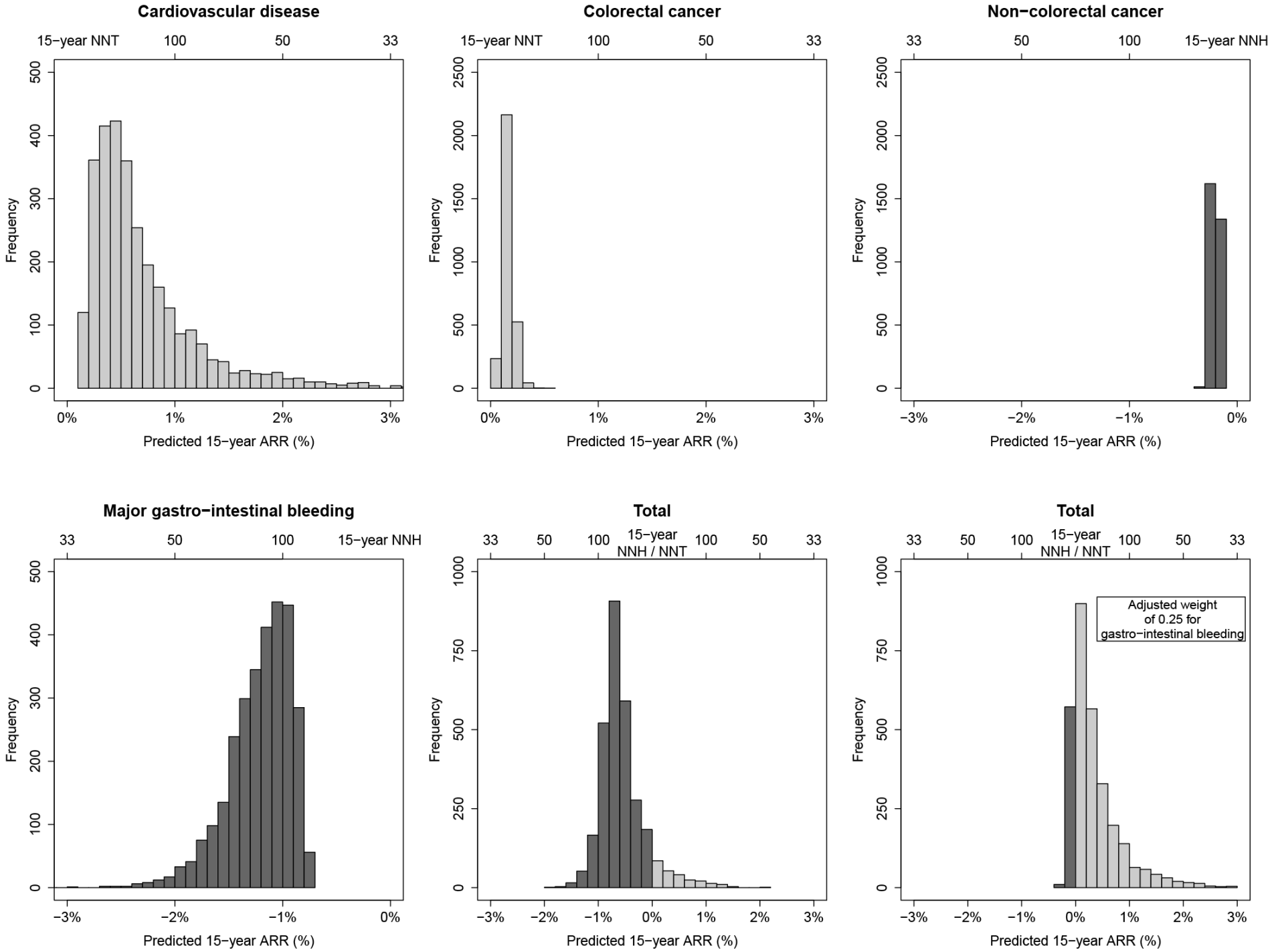
Appendix 2.5 (B) | Observed absolute risks, absolute risk reductions and numbers needed to treat/harm for aspirin

		Total	Total adjusted weight of 0.5 for gastro-intestinal bleeding	Total adjusted weight of 0.25 for gastro-intestinal bleeding	Total adjusted weight of 0.1 for gastro-intestinal bleeding
		Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)	Estimate (95% CI)
Total study population					
10-year	AR without aspirin (%)	10.11 (9.59 to 10.64)	9.69 (9.18 to 10.22)	9.49 (8.97 to 10.01)	9.36 (8.85 to 9.89)
	AR with aspirin (%)	10.69 (10.16 to 11.23)	10.02 (9.50 to 10.57)	9.69 (9.16 to 10.23)	9.49 (8.96 to 10.03)
	ARR (%)	-0.58 (-1.33 to 0.17)	-0.33 (-1.08 to 0.42)	-0.20 (-0.95 to 0.54)	-0.13 (-0.88 to 0.62)
	[a]iNNT or [b]iNNH	172[b] (605[b] to 75[a])	302[b] (93[b] to 240[a])	488[b] (105[b] to 184[a])	772[b] (114[b] to 162[a])
15-year	AR without aspirin (%)	16.07 (15.46 to 16.68)	15.45 (14.84 to 16.07)	15.14 (14.53 to 15.76)	14.95 (14.35 to 15.57)
	AR with aspirin (%)	16.49 (15.87 to 17.11)	15.49 (14.88 to 16.12)	15.00 (14.38 to 15.62)	14.70 (14.09 to 15.32)
	ARR (%)	-0.42 (-1.29 to 0.45)	-0.05 (-0.92 to 0.82)	0.14 (0.00 to 7.59)	0.25 (0.00 to 3.43)
	[a]iNNT or [b]iNNH	238[b] (223[b] to 78[a])	>1000[b] (109[b] to 121[a])	703 (13 to >1000) [a]	393 (29 to >1000) [a]
Women <65 years					
10-year	AR without aspirin (%)	8.61 (8.11 to 9.13)	8.26 (7.76 to 8.78)	8.09 (7.59 to 8.61)	7.99 (7.49 to 8.51)
	AR with aspirin (%)	9.52 (8.99 to 10.06)	8.96 (8.44 to 9.51)	8.68 (8.16 to 9.23)	8.52 (7.99 to 9.06)
	ARR (%)	-0.91 (-0.17 to -1.65)	-0.70 (-1.44 to 0.04)	-0.59 (-1.33 to 0.15)	-0.53 (-1.27 to 0.21)
	[a]iNNT or [b]iNNH	110 (61 to 583) [b]	143[b] (70[b] to >1000[a])	169[b] (75[b] to 676[a])	190[b] (79[b] to 472[a])
15-year	AR without aspirin (%)	14.02 (13.41 to 14.63)	13.50 (12.90 to 14.12)	13.25 (12.64 to 13.86)	13.09 (12.49 to 13.71)
	AR with aspirin (%)	14.86 (14.25 to 15.49)	14.03 (13.41 to 14.66)	13.62 (13.00 to 14.25)	13.37 (12.75 to 14.00)
	ARR (%)	-0.85 (-1.72 to 0.03)	-0.53 (-1.40 to 0.34)	-0.37 (-1.24 to 0.50)	-0.27 (-1.15 to 0.60)
	[a]iNNT or [b]iNNH	118[b] (58[b] to >1000[a])	189[b] (71[b] to 291[a])	271[b] (81[b] to 199[a])	365[b] (87[b] to 167[a])
Women ≥65 years					
10-year	AR without aspirin (%)	22.78 (20.47 to 25.17)	21.77 (19.46 to 24.16)	21.26 (18.96 to 23.66)	20.96 (18.66 to 23.36)
	AR with aspirin (%)	20.39 (18.21 to 22.67)	18.82 (16.64 to 21.10)	18.03 (15.86 to 20.32)	17.56 (15.39 to 19.85)
	ARR (%)	2.39 (0.46 to 7.46)	2.95 (0.81 to 7.58)	3.23 (1.01 to 7.71)	3.40 (1.13 to 7.81)
	[a]iNNT or [b]iNNH	42 (13 to 215) [a]	34 (13 to 123) [a]	31 (13 to 99) [a]	29 (13 to 89) [a]
15-year	AR without aspirin (%)	33.40 (30.81 to 36.01)	31.89 (29.30 to 34.50)	31.13 (28.55 to 33.75)	30.68 (28.10 to 33.30)
	AR with aspirin (%)	30.01 (27.55 to 32.50)	27.67 (25.22 to 30.16)	26.50 (24.05 to 29.00)	25.79 (23.35 to 28.30)
	ARR (%)	3.39 (0.98 to 8.42)	4.22 (1.59 to 8.90)	4.64 (1.92 to 9.19)	4.89 (2.13 to 9.38)
	[a]iNNT or [b]iNNH	29 (12 to 102) [a]	24 (11 to 63) [a]	22 (11 to 52) [a]	20 (11 to 47) [a]
Never smokers					
10-year	AR without aspirin (%)	8.54 (7.89 to 9.23)	8.20 (7.54 to 8.88)	8.02 (7.37 to 8.71)	7.92 (7.27 to 8.61)
	AR with aspirin (%)	9.85 (9.15 to 10.59)	9.27 (8.57 to 10.01)	8.99 (8.29 to 9.72)	8.81 (8.11 to 9.54)
	ARR (%)	-1.31 (-0.33 to -2.29)	-1.08 (-0.10 to -2.06)	-0.96 (-1.94 to 0.02)	-0.89 (-1.87 to 0.09)
	[a]iNNT or [b]iNNH	76 (44 to 304) [b]	93 (49 to >1000) [b]	104[b] (52[b] to >1000[a])	112[b] (53[b] to >1000[a])
15-year	AR without aspirin (%)	13.77 (12.99 to 14.57)	13.25 (12.47 to 14.05)	12.99 (12.21 to 13.79)	12.83 (12.05 to 13.64)
	AR with aspirin (%)	14.64 (13.84 to 15.47)	13.78 (12.97 to 14.60)	13.34 (12.54 to 14.17)	13.08 (12.28 to 13.91)
	ARR (%)	-0.87 (-2.01 to 0.26)	-0.53 (-1.67 to 0.61)	-0.36 (-1.49 to 0.78)	-0.25 (-1.39 to 0.89)
	[a]iNNT or [b]iNNH	114[b] (50[b] to 380[a])	189[b] (60[b] to 164[a])	282[b] (67[b] to 128[a])	398[b] (72[b] to 113[a])
Past smokers					
10-year	AR without aspirin (%)	11.04 (10.16 to 11.96)	10.54 (9.66 to 11.46)	10.29 (9.41 to 11.21)	10.14 (9.26 to 11.06)
	AR with aspirin (%)	10.26 (9.42 to 11.15)	9.52 (8.67 to 10.41)	9.14 (8.30 to 10.03)	8.92 (8.08 to 9.81)
	ARR (%)	0.77 (0.11 to 3.06)	1.02 (0.25 to 2.99)	1.15 (0.33 to 3.02)	1.22 (0.39 to 3.04)
	[a]iNNT or [b]iNNH	130 (33 to 885) [a]	98 (33 to 398) [a]	87 (33 to 300) [a]	82 (33 to 259) [a]
15-year	AR without aspirin (%)	17.58 (16.54 to 18.65)	16.84 (15.79 to 17.91)	16.46 (15.42 to 17.54)	16.24 (15.20 to 17.31)
	AR with aspirin (%)	16.49 (15.49 to 17.53)	15.38 (14.37 to 16.41)	14.82 (13.81 to 15.85)	14.48 (13.48 to 15.52)
	ARR (%)	1.09 (0.23 to 3.49)	1.46 (0.47 to 3.57)	1.65 (0.61 to 3.67)	1.76 (0.70 to 3.74)
	[a]iNNT or [b]iNNH	92 (29 to 442) [a]	68 (28 to 213) [a]	61 (27 to 164) [a]	57 (27 to 144) [a]
Current smokers					
10-year	AR without aspirin (%)	14.04 (12.32 to 15.87)	13.60 (11.88 to 15.43)	13.37 (11.66 to 15.20)	13.24 (11.53 to 15.07)
	AR with aspirin (%)	15.74 (13.91 to 17.68)	14.96 (13.13 to 16.90)	14.57 (12.74 to 16.51)	14.33 (12.51 to 16.27)
	ARR (%)	-1.70 (-4.29 to 0.89)	-1.36 (-3.95 to 1.23)	-1.19 (-3.78 to 1.40)	-1.09 (-3.68 to 1.50)
	[a]iNNT or [b]iNNH	59[b] (23[b] to 112[a])	73[b] (25[b] to 82[a])	84 (26 to 72)	92[b] (27[b] to 67[a])
15-year	AR without aspirin (%)	21.48 (19.49 to 23.55)	20.82 (18.82 to 22.88)	20.48 (18.49 to 22.55)	20.28 (18.29 to 22.35)
	AR with aspirin (%)	24.67 (22.53 to 26.85)	23.50 (21.37 to 25.69)	22.91 (20.78 to 25.10)	22.56 (20.43 to 24.75)
	ARR (%)	-3.18 (-0.21 to -6.15)	-2.68 (-5.65 to 0.29)	-2.43 (-5.39 to 0.54)	-2.28 (-5.24 to 0.69)
	[a]iNNT or [b]iNNH	31 (16 to 466) [b]	37[b] (18[b] to 346[a])	41 (19 to 185) [a]	44[b] (19[b] to 145[a])

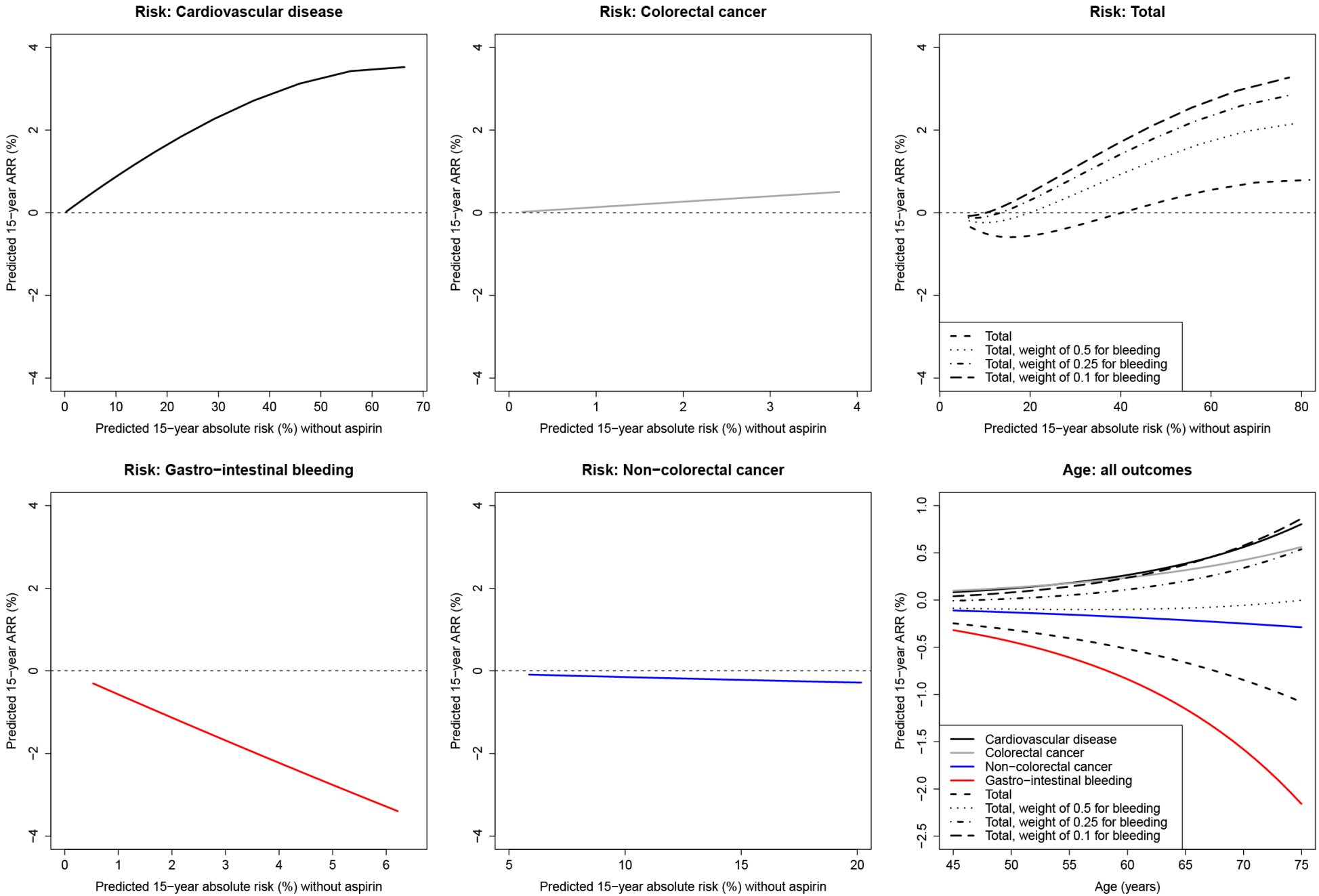
CI: Confidence interval ; AR: Absolute risk ; ARR: Absolute risk reduction ; [a]NNT: Number needed to treat ; [b]NNH: Number needed to harm. Risks were estimated based on the cumulative incidence function, accounting for competing risks.



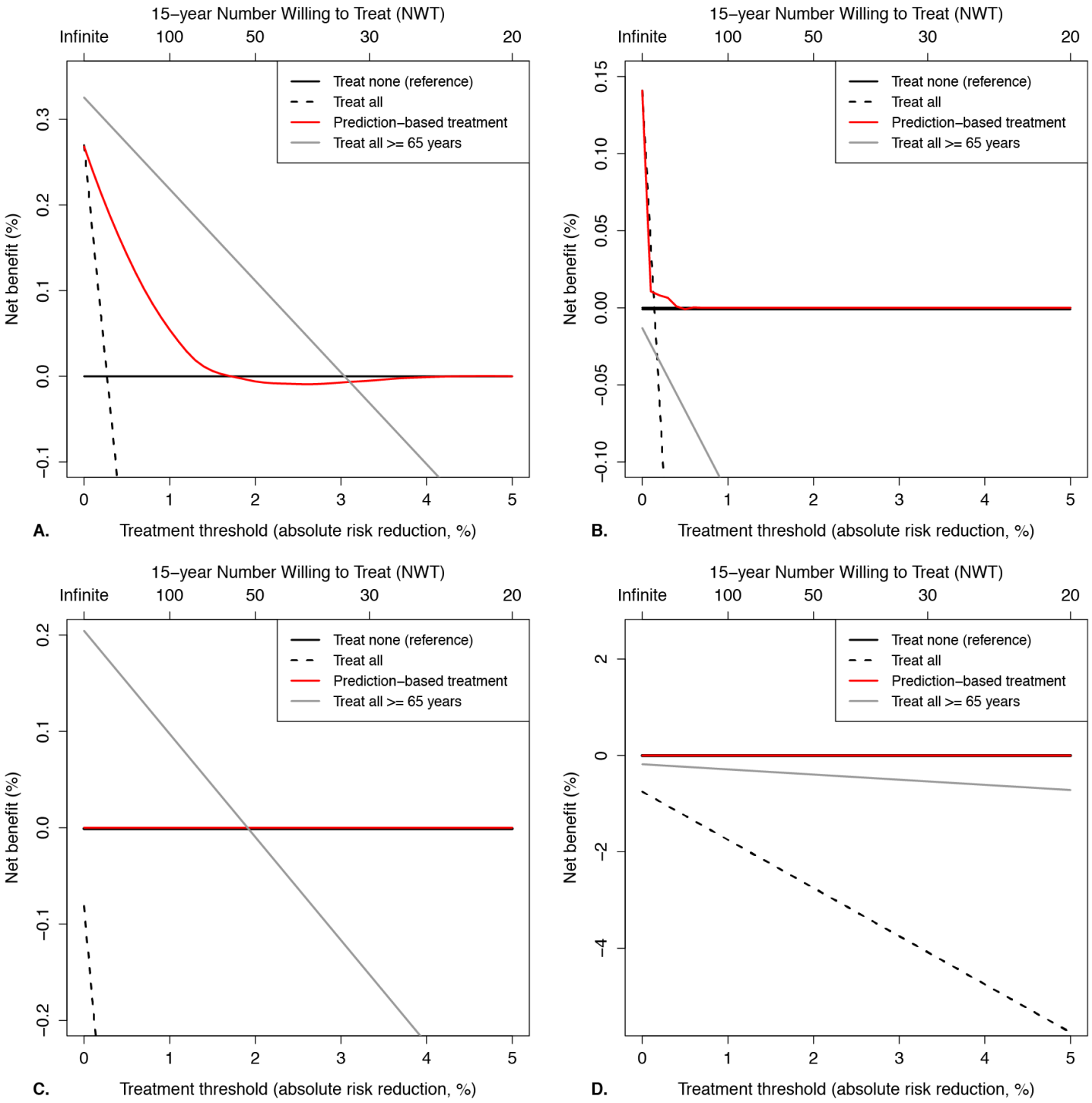
Appendix 2.6 | Distribution of predicted 10-year absolute risk reduction for major cardiovascular events, colorectal cancer and major gastro-intestinal bleeding with aspirin



Appendix 2.7 | Distribution of predicted 15-year absolute risk reduction for major cardiovascular events, colorectal cancer, non-colorectal cancer and major gastro-intestinal bleeding with aspirin treatment in participants of the Women's Health Study of 65 years and older. ARR: absolute risk reduction ; NNT/NNH: Number needed to treat/harm.



Appendix 2.8 | Effect of baseline risk and age on predicted 15-year absolute risk reduction. ARR: absolute risk reduction. ARR in plot for age apply to an average participant of the Women's Health Study (i.e. a 55-year old postmenopausal woman who never smoked, does not have diabetes, history of dyspepsia or a family no family history of premature myocardial infarction or cancer, has a height of 65 inches, a BMI of 26 kg/m2 and a systolic blood pressure of 124 mmHg and does not receive treatment for hypertension, with a serum level of high sensitivity C-reactive protein of 2·0 mg/L, total cholesterol of 212 mg/dL and a HDL-cholesterol of 54 mg/dL, drinks 2 alcoholic beverages per week and has never received hormone replacement therapy) with alternating age.



Appendix 2.9 | Decision curves for different aspirin treatment strategies for the individual outcomes: **A.** Major cardiovascular events ; **B.** Colorectal cancer ; **C**. Non-colorectal cancer ; **D.** Major gastro-intestinal bleeding. Reading the net benefit plot starts with choosing a treatment threshold, that is the absolute risk reduction (ARR) at which one would opt for treatment, or number-willing-to-treat (NWT). A NWT of 30 implies that one is willing to treat 30 women to prevent at least 1 event. Positive net benefit means that the treatment strategy led to a more favourable trade-off between benefits (observed decrease in event rate) and harms (the proportion of patients receiving treatment weighted by the reciprocal of the treatment threshold). Since for non-colorectal cancer and major gastro-intestinal bleeding all patients had a negative predicted absolute risk prediction (meaning that their risk of those outcomes increases with aspirin), none will selected for treatment over the full range of threshold values when applying prediction-based treatment and the net benefit for this treatment strategy is equal to zero.