

Patient preferences of low-dose aspirin for cardiovascular disease and colorectal cancer prevention in Italy: A latent class analysis

Tommi Tervonen, PhD^{1,2}, Pareen Vora, PhD³, Jaein Seo, PharmD⁴, Nicolas Krucien, PhD¹, Kevin Marsh, PhD¹, Raffaele De Caterina, MD, PhD^{5,6}, Ulrike Wissinger, MD, PhD³, Montse Soriano Gabarró, MD, MSc³

¹Patient-Centered Research, Evidera, London, UK

²Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands

³Epidemiology, Bayer AG, Berlin, Germany

⁴Patient-Centered Research, Evidera, Bethesda, MD, USA

⁵Cardiology Division, University of Pisa and Pisa University Hospital, Pisa, Italy

⁶Fondazione VillaSerena per la Ricerca, Città Sant'Angelo, Pescara, Italy

Corresponding author: Tommi Tervonen, Evidera, The Ark, 201 Talgarth Rd, London W6 8BJ, UK, Email:

Tommi.Tervonen@evidera.com. Tel: +44 2085 765 026. Fax: +44 20 8576 5195.

Online Resource 1. Attribute and level development

Potential attributes for prevention of CVD identified in the literature

Potential attribute	Agent							
	Aspirin	Anti-coagulant	Anti-HTN	Anti-platelet	Anti-thrombotic	Statins	VKA DOAC	N/A
Benefit attributes								
Prevention of stroke	1,2,3	4,6,7,8			12,13			
Prevention of myocardial infarction	2	6,7,8		11	13			18
Prevention of cardiovascular disease		9	10					16
Prevention of colorectal cancer	2							
Prevention of cardiogenic shock								17
Prevention of chronic heart failure								17
Prevention of re-venous thromboembolism							15	
Prevention of re-myocardial infarction								17
Prevention of re-ischemia					13			
Survival gain						14		
Prevention of death				11				
Prevention of death from myocardial infarction of stroke		6						
Risk attributes								
Risk of bleeding	1,3	4,5,6,7,8		11	12,13		15	17
Side effects		9	10					16
All-cause death		8			13			17
Bleeding death		6,7						
Dyspnoea				11				
Blood clot in the leg		8						

A search of PubMed and EMBASE for qualitative and quantitative preference studies in adult patients with cardiovascular disease, colorectal cancer and other gastrointestinal cancers gave 564 hits. The abstracts for these potentially relevant references were screened and 524 of them were excluded. Full text was obtained for the remaining 40 reference. Full text screening resulted in a further 21 references being excluded. The remaining 19 references were used to identify attributes for the DCE survey.

DOAC, direct oral anticoagulant; HTN, hypertension; VKA, vitamin K antagonist; N/A, not applicable

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Additional reference with no potentially relevant attributes

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Level construction

Outcome risk data was extracted from the safety and efficacy analyses in published literature to inform the levels. Ranges of levels for the benefit attributes were chosen to take into account both the estimated untreated (baseline) risks and altered risks as a result of treatment with low-dose aspirin.

Myocardial infarction (heart attack) and ischemic stroke

Two distinct sets of levels were used for CVD events due to differing baseline risks: one for the primary CVD prevention population and one for the secondary CVD prevention population. For the purposes of constructing the levels, the baseline CVD risk for primary CVD prevention was assumed to be 20%, in line with the inclusion criteria. This baseline risk was then further split between myocardial infarction and stroke according to the proportion of all CVD events that were myocardial infarctions and strokes (62% and 38%, respectively) (1). We used data for all strokes instead of ischemic stroke because the data source included many unknown strokes. The baseline risk of myocardial infarction in the primary CVD prevention population (12%) was obtained by multiplying the overall 10-year CVD risk (20%) by the proportion of all CVD events that were myocardial infarctions (62%). The risk of myocardial infarction with low-dose aspirin treatment in the primary prevention population (10%) was derived by multiplying the risk of myocardial infarction with placebo (12%) in the primary CVD prevention population by the rate ratio between aspirin and placebo (0.82) (1). These calculations informed the myocardial infarction 10-year risk levels 10/15/20% in the primary CVD prevention population and 40/50/60% in the secondary CVD prevention population. The baseline risk of stroke in the primary CVD prevention population (8%) was obtained by multiplying the 10-year CVD risk (20%) by the proportion of all CVD events that were stroke (38%). The risk of stroke with low-dose aspirin treatment in the primary prevention population (7%) was derived in the same manner as the risk of myocardial infarction with aspirin. For secondary prevention, yearly risk estimates (pooled from multi-year studies) were multiplied by 10 to obtain the 10-year risk (1). These calculations informed the ischemic stroke 10-year risk levels of 5/10/15% in the primary CVD prevention population and 15/25/30% in the secondary CVD prevention population.

Colorectal Cancer (CRC)

In a recent cohort study with patients aged 40 years or older, the incidence of CRC was 16.74 per 10,000 person-years (2). From this, we estimated the untreated baseline risk of CRC over 10 years in older populations to be at least 2%. The same study found that use of low-dose aspirin reduced the risk of CRC, with a risk ratio of 0.66. These data informed the 10-year CRC risk levels of 1/2/3%.

Adverse effects

Risks of peptic ulcer, gastrointestinal (stomach) bleeding, and intracranial haemorrhage (bleeding in the brain) have been reported in studies with varying follow-up times. Increases in the risk of gastrointestinal bleeding and peptic ulcer due to aspirin use have been reported in a systematic review (3), where aspirin was found to increase the incidence of peptic ulcer by up to 0.78 per 1000 person years and gastrointestinal bleeding by up to 4.92 per 1000 person years. The risk of intracranial haemorrhage were reported in another systematic review examining age- and sex-specific rates of intracranial haemorrhage (4), where aspirin was associated with an incidence of 1.69-8.04 cases per 10,000 person years compared with 1.26-8.25 cases per 10,000 person years in the comparison cohort. The rate of aspirin intolerance varies in different populations and has been reported to be between 2% and 23% in patients with asthma (5). The rate is very low in the general population and risk of aspirin-related severe allergic reaction (anaphylaxis) has been reported to be at most 0.9% in people without asthma (5). Given the variation in study follow-up times, the expected attribution of risk over exposure for some adverse effects (intracranial haemorrhage, peptic ulcer, gastrointestinal bleeding) but not for others (severe allergic reaction), and small differences in baseline and on-treatment risks for some adverse effects (intracranial haemorrhage), the levels for all adverse effects were expressed as categorical “no risk” and “increased risk”.

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Online Resource 2. Attribute descriptions in Section 1 of the DCE

Heart attack

A heart attack is usually caused by a blood clot, which stops the blood from flowing to a part of your heart muscle, causing damage to that part of the heart.

The most common symptom of a heart attack is severe chest pain, which often feels like a heavy pressure on your chest. The pain may be similar to more general chest pain experienced when performing rigorous activity, but it is usually more severe and lasts longer. You may also sweat, feel sick, feel faint, and be short of breath.

A heart attack may lead to temporary or lasting disability, such as reduced mobility, decreased stamina, and fatigue. If you experience a heart attack, you will be hospitalised for medical care. After having a heart attack, you are more likely to have a new heart attack or other forms of heart conditions.

In this survey, we will describe various treatments for which patients may have different chances of experiencing a heart attack. The chances of experiencing a heart attack in the next ten years that we will ask you to consider are:

Primary prevention	Secondary prevention
• 10% (10 out of 100) • 15% (15 out of 100) • 20% (20 out of 100)	• 40% (40 out of 100) • 50% (50 out of 100) • 60% (60 out of 100)

[Note: only one set of chances was presented, depending on which prevention category the participants were in]

Colorectal cancer

Colorectal cancer often begins as a growth called a ‘polyp’, which may become cancer over time. About one third of people having colorectal cancer die in the following 5 years.

The most common symptoms of colorectal cancer are stomach pain or gas pains; change in bowel habits; blood in stools; feeling weak or tired; and black or dark-coloured stools.

Early colorectal cancer screening can help find a polyp or cancer early enough to treat it easier and cannot be replaced with any choice of cancer prevention.

If you have colorectal cancer, you will receive chemotherapy or surgery. Once having had colorectal cancer, you are more likely to develop new cancers in other areas of the colon and rectum.

In this survey, we will describe various treatments for which patients may have different chances of experiencing a colorectal cancer. The chances of experiencing colorectal cancer in the next ten years that we will ask you to consider are:

- 1% (1 out of 100)
- 2% (2 out of 100)
- 3% (3 out of 100)

To put this into perspectives, in Italy, the overall chance of dying from any causes in the ten-year period is

- [Primary prevention] around 1%
- [Secondary prevention] around 2%

And the overall chance of experiencing cancer in the ten-year period before the age of 75 is around 27% (27 out of 100).

Stroke

A stroke can happen if something keeps the blood from flowing as it should in the brain, causing damage to that part of the brain.

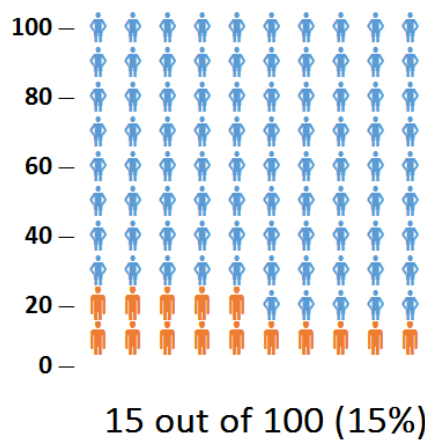
A stroke usually happens suddenly; a person suffering a stroke exhibits several of signs: numbness or weakness on one side of the body, a very bad headache, dizziness, loss of balance, trouble talking or understanding what people are saying, and trouble seeing.

A stroke may lead to temporary or lasting disability, such as paralysis, reduced mobility, and problems with thinking, memory, and speech.

If you experience a stroke, you will be hospitalised for medical care. After having a stroke, you are more likely to have a new stroke.

In this survey, we will describe various treatments for which patients may have different chances of experiencing a stroke. The chance of experiencing a stroke in the next 10 years that we will ask you to consider are:

Primary prevention	Secondary prevention
• 5% (5 out of 100) • 10% (10 out of 100) • 15% (15 out of 100)	• 15% (15 out of 100) • 20% (20 out of 100) • 30% (30 out of 100)

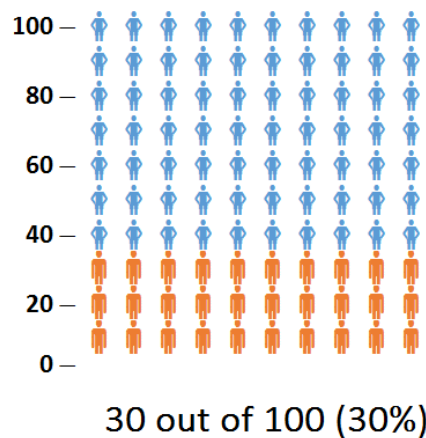


You will be presented with the following graphics to help you think about these chances.

- The grid contains 100 people, each of which represents a person who has taken a treatment to prevent heart disease.
- Each **orange person**  shows a person who would have experienced a stroke **ten** years of treatment. In this example, 15 people out of 100.
- Each **blue person**  shows a person who will not have a stroke after ten years of treatment. In this example 85 people out of 100.

Before we move onto the next outcome, please review the example below. How many of these people **will have experienced** a stroke after taking the treatment for ten years?

- ☐ 30 out of 100
- ☐ 50 out of 100
- ☐ 70 out of 100
- ☐ 95 out of 100



Side effects

In this survey, the treatment described can cause the following undesirable effects with a small chance of 1 in 100 people (1%). We will ask you to consider treatments for which these effects might occur ( Increased risk) or might not occur (No risk). These are stomach bleeding, stomach ulcers, bleeding in the brain and severe allergic reactions.

Bleeding in the brain

Bleeding in the brain known as intracranial haemorrhage occurs from a broken blood vessel within the brain.

Symptoms may suddenly appear or gradually worsen. The symptoms include sudden tingling, weakness in an arm or leg, numbness, difficulty speaking, loss of balance, and a sudden severe headache with vomiting.

Any type of bleeding inside the brain is a medical emergency, and someone should call 112 for emergency medical help. It can lead to death, but those who survive may suffer long-term problems with their nervous systems, such as weakness in one side of the body, or trouble with balance, if not recovered well.

Stomach ulcer

A stomach ulcer is a sore in the lining of your stomach or small intestine which results from acids damaging the walls of the stomach or small intestine.

Symptoms start between meals or during the night and lasts for minutes to hours. You may feel discomfort or pain which can be dull, sharp, or burning.

If you have a stomach ulcer, your doctor will prescribe antacids, proton pump inhibitors (PPIs) to relieve pain, heal the ulcer, and prevent complications. Complications of ulcers include bleeding, perforation, and blockage to the passage of food.

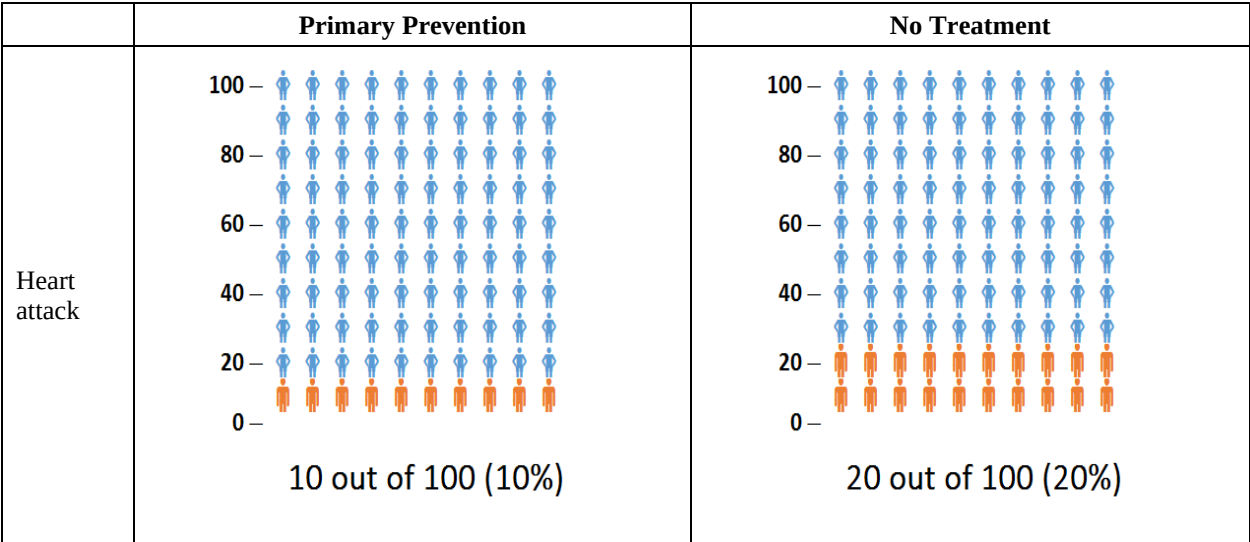
Stomach bleeding

This may involve bleeding in the throat, stomach, intestines, and anus.

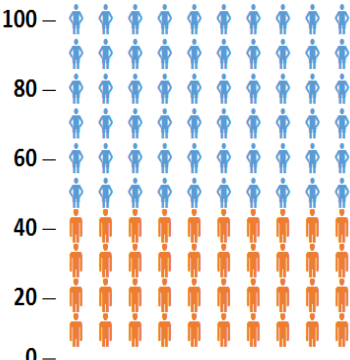
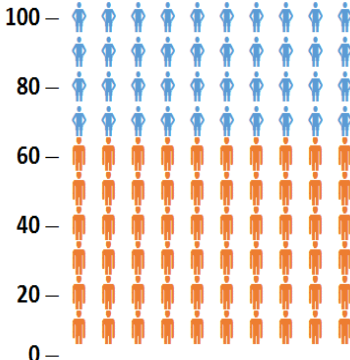
Symptoms of bleeding may include light-headedness, shortness of breath, chest pain, confusion, cold clammy skin, respiratory congestion, and darkened stool.

If you have stomach bleeding, you will receive a blood transfusion requiring hospitalisation or procedure in an outpatient clinic. In most cases, people recover from bleeding after a transfusion. However, in some severe cases, people have longer term health effects due to damage to other body organs that did not receive enough blood flow during the bleeding episode.

Suppose there was a treatment that could reduce the risk of having a heart attack to 10% [Primary prevention] / 40% [Secondary prevention], which however, some the treatment could cause an increased risk of having stomach bleeding.



	Primary Prevention	No Treatment
Stomach bleeding	 Increased risk	No risk

	Secondary Prevention	No Treatment (Secondary Prevention)
Heart attack	 40 out of 100 (40%)	 60 out of 100 (60%)
Stomach bleeding	 Increased risk	No risk

Would you take the treatment?

- ☐ Definitely not
- ☐ Probably not
- ☐ Not sure
- ☐ Probably yes
- ☐ Definitely yes

Severe allergic reaction

A severe allergic reaction, known as anaphylaxis, is potentially life-threatening and needs to be treated right away.

Within seconds or minutes of exposure to something you are allergic to, you may experience trouble breathing, rapid heartbeat, itching, swelling, tightness of the throat, and a weak pulse.

If you have a severe allergic reaction, you need an epinephrine shot as soon as possible, and someone should call 112 for emergency medical help. Future reactions might be more severe than the first reaction.

Online Resource 3. Analysis of optimal number of latent classes

	Latent classes	Parameters	LL	BIC	AIC	AIC3	AICc	CAIC
Primary CVD prevention group	1	9	-5605.1	11288.3	11228.1	11237.1	11228.2	11297.3
	2	19	-4645.5	9456	9329	9348	9329.2	9475
	3	29	-4393.2	9038.2	8844.5	8873.5	8844.8	9067.2
	4	39	-4302.8	8944.2	8683.6	8722.6	8684.1	8983.2
	5	49	-4287.7	9000.8	8673.5	8722.5	8674.3	9049.8
	6	59	-4241.2	8994.5	8600.3	8659.3	8601.5	9053.5
Secondary CVD prevention group	1	9	-5803.2	11685	11624.5	11633.5	11624.5	11694
	2	19	-4058	8281.9	8154.1	8173.1	8154.2	8300.9
	3	29	-3795.3	7843.6	7648.5	7677.5	7648.8	7872.6
	4	39	-3778.1	7896.6	7634.2	7673.2	7634.7	7935.6
	5	49	-3733.6	7894.9	7565.2	7614.2	7566	7943.9
	6	59	-3716.6	7948.1	7551.2	7610.2	7552.3	8007.1

LL, log-likelihood; BIC, Bayesian information criterion; AIC, Akaike information criterion; AICc, corrected AIC; CAIC, consistent AIC.

Online Resource 4. Validity assessments

		Primary CVD prevention (N=491)			Secondary CVD prevention (N=514)		
	Full sample (N=1005)	Total (N=491)	Taking low- dose aspirin (N=230)	Not taking low-dose aspirin (N=261)	Total (N=514)	Taking low- dose aspirin (N=258)	Not taking low-dose aspirin (N=256)
Dominance question, n (%)							
Correct	946 (94)	449 (91)	211 (92)	238 (91)	497 (97)	252 (98)	245 (96)
Incorrect	59 (6)	42 (9)	19 (8)	23 (9)	17 (3)	6 (2)	11 (4)
Repeated question, n (%)							
Same Answers	665 (66)	322 (66)	150 (65)	172 (66)	343 (67)	166 (64)	177 (69)
Different Answers	340 (34)	169 (34)	80 (35)	89 (34)	171 (33)	92 (36)	79 (31)
Always choosing the alternative better on one attribute, n (%)							
Stroke	4 (0)	4 (1)	4 (2)	0 (0)	0 (0)	0 (0)	0 (0)
Heart attack	18 (2)	11 (2)	8 (3)	3 (1)	7 (1)	6 (2)	1 (0)
Colorectal cancer	3 (0)	3 (1)	2 (1)	1 (0)	0 (0)	0 (0)	0 (0)
Stomach bleeding	14 (1)	7 (1)	5 (2)	2 (1)	7 (1)	3 (1)	4 (2)
Stomach ulcer	11 (1)	7 (1)	3 (1)	4 (2)	4 (1)	1 (0)	3 (1)
Bleeding in the brain	86 (9)	40 (8)	18 (8)	22 (8)	46 (9)	23 (9)	23 (9)
Severe allergic reaction	9 (1)	5 (1)	1 (0)	4 (2)	4 (1)	1 (0)	3 (1)
None	860 (86)	414 (84)	189 (82)	225 (86)	446 (87)	224 (87)	222 (87)
Always choosing A / B / no treatment, n (%)							
Always choosing A or always choosing B	11 (1)	7 (1)	2 (1)	5 (2)	4 (1)	1 (0)	3 (1)
Always choosing no treatment	144 (14)	33 (7)	14 (6)	19 (7)	111 (22)	58 (22)	53 (21)
Not always choosing the same option	850 (85)	451 (92)	214 (93)	237 (91)	399 (78)	199 (77)	200 (78)
Choice proportions (including serial non-respondents ^a), %							
Treatment A	29	34	35	33	24	24	24
Treatment B	35	41	41	40	29	29	29

No treatment	37	26	24	27	48	48	48
Choice proportions (excluding serial non-respondents^a), %							
Treatment A	34	36	37	36	30	31	30
Treatment B	40	43	44	42	36	37	36
No treatment	27	21	19	22	33	33	34
Time taken to complete the DCE survey (minutes.seconds), n (%)							
<3.00	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
3.00-4.59	2 (0)	1 (0)	1 (0)	0 (0)	1 (0)	1 (0)	0 (0)
5.00-6.59	31 (3)	23 (5)	20 (9)	3 (1)	8 (2)	5 (2)	3 (1)
7.00-9.59	41 (4)	12 (2)	6 (3)	6 (2)	29 (6)	15 (6)	14 (5)
10.00-14.59	101 (10)	40 (8)	19 (8)	21 (8)	61 (12)	30 (12)	31 (12)
15.00-19.59	88 (9)	39 (8)	12 (5)	27 (10)	49 (10)	28 (11)	21 (8)
≥20.00	742 (74)	376 (77)	172 (75)	204 (78)	366 (71)	179 (69)	187 (73)
Health literacy question 1:							
<i>How often do you have someone help you read hospital materials?, n (%)</i>							
Always	106 (11)	47 (10)	22 (10)	25 (10)	59 (11)	30 (12)	29 (11)
Often	234 (23)	83 (17)	40 (17)	43 (16)	151 (29)	69 (27)	82 (32)
Sometimes	362 (36)	181 (37)	86 (37)	95 (36)	181 (35)	93 (36)	88 (34)
Occasionally	198 (20)	113 (23)	47 (20)	66 (25)	85 (17)	47 (18)	38 (15)
Never	105 (10)	67 (14)	35 (15)	32 (12)	38 (7)	19 (7)	19 (7)
Health literacy question 2:							
<i>How confident are you filling out medical forms by yourself?, n (%)</i>							
Extremely	75 (7)	42 (9)	17 (7)	25 (10)	33 (6)	20 (8)	13 (5)
Quite a bit	180 (18)	98 (20)	45 (20)	53 (20)	82 (16)	41 (16)	41 (16)
Somewhat	411 (41)	241 (49)	117 (51)	124 (48)	170 (33)	80 (31)	90 (35)
A little bit	268 (27)	88 (18)	40 (17)	48 (18)	180 (35)	91 (35)	89 (35)
Not at all	71 (7)	22 (4)	11 (5)	11 (4)	49 (10)	26 (10)	23 (9)

Health literacy question 3:***How often do you have problems learning about your medical condition because of difficulty understanding medical information?, n (%)***

Always	46 (5)	19 (4)	9 (4)	10 (4)	27 (5)	13 (5)	14 (5)
Often	213 (21)	81 (16)	31 (13)	50 (19)	132 (26)	70 (27)	62 (24)
Sometimes	469 (47)	233 (47)	120 (52)	113 (43)	236 (46)	112 (43)	124 (48)
Occasionally	201 (20)	119 (24)	49 (21)	70 (27)	82 (16)	37 (14)	45 (18)
Never	76 (8)	39 (8)	21 (9)	18 (7)	37 (7)	26 (10)	11 (4)

Health literacy, n (%)^b

Adequate	356 (35)	209 (43)	94 (41)	115 (44)	147 (29)	73 (28)	74 (29)
Inadequate	649 (65)	282 (57)	136 (59)	146 (56)	367 (71)	185 (72)	182 (71)

Numeracy question 1:***Which of the following numbers represents the biggest probability/likelihood of getting a disease?, n (%)***

Correct	446 (44)	280 (57)	129 (56)	151 (58)	166 (32)	76 (29)	90 (35)
Incorrect	559 (56)	211 (43)	101 (44)	110 (42)	348 (68)	182 (71)	166 (65)

Numeracy question 2:***Which of the following represents the biggest probability/likelihood of getting a disease?, n (%)***

Correct	799 (80)	375 (76)	180 (78)	195 (75)	424 (82)	204 (79)	220 (86)
Incorrect	206 (20)	116 (24)	50 (22)	66 (25)	90 (18)	54 (21)	36 (14)

Numeracy question 3:***If the chance of getting a disease is 10%, how many people would be expected to get the disease out of 100?, n (%)***

Correct	963 (96)	471 (96)	222 (97)	249 (95)	492 (96)	248 (96)	244 (95)
Incorrect	42 (4)	20 (4)	8 (3)	12 (5)	22 (4)	10 (4)	12 (5)

Numeracy question 4:***If the chance of getting a disease is 10%, how many people would be expected to get the disease out of 1000?, n (%)***

Correct	836 (83)	416 (85)	189 (82)	227 (87)	420 (82)	209 (81)	211 (82)
Incorrect	169 (17)	75 (15)	41 (18)	34 (13)	94 (18)	49 (19)	45 (18)

Numeracy question 5:***If the chance of getting a disease is 20 out of 100, this would be the same as having a [answer]% chance of getting the disease, n (%)***

Correct	874 (87)	428 (87)	202 (88)	226 (87)	446 (87)	228 (88)	218 (85)
Incorrect	131 (13)	63 (13)	28 (12)	35 (13)	68 (13)	30 (12)	38 (15)

Numeracy, n (%)^c							
Adequate	910 (91)	447 (91)	210 (91)	237 (91)	463 (90)	229 (89)	234 (91)
Inadequate	95 (9)	44 (9)	20 (9)	24 (9)	51 (10)	29 (11)	22 (9)

Abbreviations: CRC = colorectal cancer; DCE = discrete choice experiment

^a Respondents who always chose the no-treatment option (N=144)

^b Answers to the 3 health literacy questions were each scored on a scale from 0 points (Always [Questions 1 and 3] or Not at all [Question 2] to 4 points (Never [Questions 1 and 3] or Extremely [Question 2]). Adequate health literacy was defined as an average score of >2 , whereas inadequate health literacy was defined as an average score of ≤ 2 .

^c Answers to the 5 numeracy questions were each scored as correct = 1 point and incorrect = 0 points. Adequate numeracy was defined as a total score of ≥ 3 , whereas inadequate numeracy was defined as a total score of <3 .

Online Resource 5. Four-class latent class logit model for the primary CVD prevention group

Attribute	Level	Class 1 (n=182, 37%)		Class 2 (n=126, 26%)		Class 3 (n=93, 19%)		Class 4 (n=90, 18%)	
		RI		RI		RI		RI	
		MLE (SE; 95% CI)	(95% CI)	MLE (SE; 95% CI)	(95% CI)	MLE (SE; 95% CI)	(95% CI)	MLE (SE; 95% CI)	(95% CI)
Alternative-specific constants	Treatment	-0.22 (0.08; -0.38, -0.07)**		0.14 (0.09; -0.04, 0.32)		-0.05 (0.18; -0.41, 0.31)		-0.47 (0.12; -0.70, -0.24)***	
	No treatment	-1.99 (0.17; -2.33, -1.64)***		-1.50 (0.40; -2.28, -0.72)***		0.46 (0.37; -0.27, 1.19)		-2.32 (0.39; -3.09, -1.56)***	
Ischaemic stroke	1% decrease in risk	0.08 (0.01; 0.05, 0.10)***	10% (7.0, 12.0)	0.21 (0.02; 0.16, 0.26)***	29% (26.0, 31.8)	-0.00 (0.02; -0.05, 0.04)	0% (-3.6, 4.2)	0.02 (0.01; -0.01, 0.05)	16% (-2.9, 34.0)
Myocardial infarction	1% decrease in risk	0.10 (0.01; 0.07, 0.12)***	12% (9.1, 14.6)	0.26 (0.03; 0.20, 0.31)***	35% (32.0, 38.5)	0.04 (0.02; -0.01, 0.08)	6% (-0.7, 11.7)	-0.00 (0.01; -0.03, 0.02)	2% (-7.9, 12.2)
Colorectal cancer	1% decrease in risk	0.16 (0.05; 0.05, 0.26)**	4% (1.5, 6.4)	0.34 (0.07; 0.20, 0.49)***	9% (6.1, 12.7)	0.14 (0.11; -0.07, 0.36)	4% (-1.0, 9.4)	0.18 (0.06; 0.05, 0.30)**	25% (10.9, 39.9)
Gastrointestinal bleeding	Increased risk		16% (13.7, 17.6)		6% (3.1, 8.2)		23% (18.5, 28.2)		13% (0.8, 25.9)
	No risk	1.26 (0.11; 1.05, 1.46)***		0.41 (0.10; 0.21, 0.61)***		1.58 (0.27; 1.05, 2.10)***		0.19 (0.09; 0.01, 0.36)*	
Peptic ulcer	Increased risk		15% (12.8, 16.5)		7% (3.9, 9.4)		16% (10.4, 20.7)		10% (0.0, 20.5)
	No risk	1.18 (0.09; 1.00, 1.36)***		0.49 (0.11; 0.26, 0.71)***		1.05 (0.25; 0.55, 1.55)***		0.14 (0.09; -0.04, 0.32)	
Intracranial bleeding	Increased risk		28% (25.7, 30.4)		8% (4.9, 10.1)		32% (26.4, 38.3)		20% (3.6, 37.2)
	No risk	2.26 (0.13; 2.00, 2.51)***		0.55 (0.09; 0.36, 0.73)***		2.19 (0.30; 1.60, 2.78)***		0.29 (0.17; -0.04, 0.62)	

Attribute	Level	Class 1 (n=182, 37%)		Class 2 (n=126, 26%)		Class 3 (n=93, 19%)		Class 4 (n=90, 18%)	
		RI		RI		RI		RI	
		MLE (SE; 95% CI)	(95% CI)	MLE (SE; 95% CI)	(95% CI)	MLE (SE; 95% CI)	(95% CI)	MLE (SE; 95% CI)	(95% CI)
Severe allergic reaction	Increased risk		16% (14.7, 18.1)		7% (0.31, 0.66)		19% (14.1, 23.6)		13% (1.7, 24.0)
	No risk	1.32 (0.10; 1.12, 1.51)***		0.49 (0.09; 0.31, 0.66)***		1.27 (0.23; 0.81, 1.73)***		0.18 (0.11; -0.03, 0.39)	
Class membership constant		Reference		-0.48 (0.05)***		-0.77 (0.04)***		-0.83 (0.06)***	

Bayesian information criterion = 8945

CI, confidence interval; MLE, maximum likelihood estimate; RI, relative importance; SE, standard error.

* P < 0.05, ** P < 0.01, *** P < 0.001 (z-test)

Online Resource 6. Comparison of relative importance profiles across classes**Primary CVD prevention group**

Test	Chi-square of Wald test	P-value
Class 1 vs. Class 2	1127.8	< 0.001
Class 1 vs. Class 3	154.4	< 0.001
Class 1 vs. Class 4	452.5	< 0.001
Class 2 vs. Class 1	779.0	< 0.001
Class 2 vs. Class 3	1382.5	< 0.001
Class 2 vs. Class 4	729.9	< 0.001
Class 3 vs. Class 1	38.4	< 0.001
Class 3 vs. Class 2	454.3	< 0.001
Class 3 vs. Class 4	165.2	< 0.001
Class 4 vs. Class 1	14.5	0.043
Class 4 vs. Class 2	53.8	< 0.001
Class 4 vs. Class 3	17.8	0.013

Secondary CVD prevention group

Test	Chi-square of Wald test	P-value
Class 1 vs. Class 2	337.1	< 0.001
Class 1 vs. Class 3	72.4	< 0.001
Class 2 vs. Class 1	727.8	< 0.001
Class 2 vs. Class 3	230.3	< 0.001
Class 3 vs. Class 1	247.5	< 0.001
Class 3 vs. Class 2	276.0	< 0.001

Online Resource 7. Comparison of participant characteristics across latent classes for the primary CVD prevention group

Characteristic	P-value (chi-square test)	Class composition, n (%)			
		Class 1 (N=182)	Class 2 (N=126)	Class 3 (N=93)	Class 4 (N=90)
Age: ≤55 years (vs. 56-64)	0.082	30 (16)	19 (15)	12 (13)	24 (27)
Age: ≥65 years (vs. 56-64)		87 (48)	57 (45)	41 (44)	28 (31)
Total cholesterol level: 292-320 mg/dL (vs. 131-291 mg/dL)	0.059	118 (65)	91 (72)	74 (80)	59 (66)
Comorbidities: diabetes type 2 (vs. no)	0.029	69 (38)	60 (48)	44 (47)	27 (30)
Current medications for heart condition: cholesterol lowering drugs (vs. no)	0.786	157 (86)	108 (86)	81 (87)	74 (82)
Current medications for heart condition: antihypertensive drugs (vs. no)	0.549	169 (93)	113 (90)	82 (88)	80 (89)
Current medications for heart condition: low-dose aspirin (vs. no)	0.044	73 (40)	70 (56)	41 (44)	46 (51)
Current medications for other condition: ibuprofen (vs. no)	0.638	87 (48)	57 (45)	37 (40)	39 (43)
Current medications for other condition: stomach acid reducing drugs (vs. no)	0.132	51 (28)	34 (27)	37 (40)	24 (27)
Current medications for other condition: none (vs. Some)	0.785	71 (39)	52 (41)	38 (41)	41 (46)
Duration of taking medications for heart condition: ≥5 years (vs. <5 years)	0.661	150 (82)	109 (87)	75 (81)	76 (84)
Education: higher education (vs. primary/high school)	0.019	38 (21)	41 (33)	31 (33)	33 (37)
Exercise/week: none (vs. 1-2 h)	0.402	60 (33)	40 (32)	35 (38)	24 (27)
Exercise/week: ≥3 h (vs. 1-2 h)		65 (36)	40 (32)	22 (24)	31 (34)
Overall health: fair/poor (vs. excellent/very good/good)	0.859	83 (46)	62 (49)	47 (51)	44 (49)
Health literacy: inadequate (vs. adequate)	0.147	96 (53)	69 (55)	58 (62)	59 (66)
Sex: male (vs. female)	0.101	93 (51)	61 (48)	37 (40)	52 (58)
Marital status: married (vs. widowed/divorced/separated/single)	0.801	129 (71)	89 (71)	69 (74)	68 (76)
Past medications for heart condition: cholesterol lowering drugs (vs. no)	0.695	99 (54)	65 (52)	53 (57)	44 (49)
Past medications for heart condition: antihypertensive drugs (vs. no)	0.001	110 (60)	52 (41)	58 (62)	42 (47)

Characteristic	P-value (chi-square test)	Class composition, n (%)			
		Class 1 (N=182)	Class 2 (N=126)	Class 3 (N=93)	Class 4 (N=90)
Past medications for heart condition: low-dose aspirin (vs. no)	0.617	49 (27)	33 (26)	30 (32)	29 (32)
Past medications for heart condition: none (vs. some)	0.495	37 (20)	35 (28)	21 (23)	22 (24)
Smoking status: never (vs. former/current smoker)	0.774	89 (49)	63 (50)	46 (49)	39 (43)
Systolic blood pressure: 170-199 mmHg (vs. 91-169 mmHg)	0.888	141 (77)	96 (76)	75 (81)	70 (78)

Online Resource 8. Three-class latent class logit model for the secondary CVD prevention group

Attribute	Level	Class 1 (n=189, 37%)		Class 2 (n=181, 35%)		Class 3 (n=144, 28%)	
		RI (95% CI)		RI (95% CI)		RI (95% CI)	
		MLE (SE; 95% CI)	CI	MLE (SE; 95% CI)	CI	MLE (SE; 95% CI)	CI
Alternative-specific constants	Treatment A	-0.17 (0.21; -0.58, 0.24)		-0.15 (0.05; -0.26, -0.05)**		-0.39 (0.09; -0.58, -0.21)***	
	No treatment	0.17 (0.52; -0.84, 1.19)		-2.36 (0.17; -2.68, -2.03)***		-1.01 (0.17; -1.36, -0.67)***	
Ischaemic stroke	1% decrease in risk	-0.02 (0.02; -0.06, 0.01)	3% (-0.4, 6.2)	0.04 (0.01; 0.03, 0.05)***	15% (11.9, 18.2)	0.05 (0.01; 0.04, 0.07)***	10% (7.1, 12.3)
Myocardial infarction	1% decrease in risk	0.03 (0.01; 0.01, 0.06)*	5% (0.8, 8.9)	0.06 (0.00; 0.05, 0.07)***	28% (24.7, 31.1)	0.05 (0.01; 0.04, 0.07)***	13% (10.3, 16.5)
Colorectal cancer	1% decrease in risk	0.06 (0.12; -0.17, 0.29)	1% (-1.4, 3.2)	0.18 (0.04; 0.10, 0.25)***	8% (5.1, 11.6)	0.08 (0.06; -0.03, 0.20)	2% (-0.4, 4.6)
Gastrointestinal bleeding	Increased risk						
	No risk	4.03 (0.54; 2.98, 5.09)***	31% (26.1, 35.8)	0.415 (0.06; 0.29, 0.52)***	9% (7.1, 11.8)	1.34 (0.12; 1.10, 1.58)***	17% (14.5, 18.7)
Peptic ulcer	Increased risk						
	No risk	1.68 (0.41; 0.88, 2.48)***	13% (9.0, 16.8)	0.51 (0.06; 0.39, 0.62)***	12% (9.4, 14.2)	1.23 (0.11; 1.01, 1.46)***	15% (13.2, 17.5)
Intracranial bleeding	Increased risk						
	No risk	4.02 (0.54; 2.97, 5.07)***	31% (26.0, 35.7)	0.73 (0.06; 0.61, 0.85)***	17% (14.5, 19.6)	2.25 (0.14; 1.98, 2.52)***	28% (25.6, 30.4)

Attribute	Level	Class 1 (n=189, 37%)		Class 2 (n=181, 35%)		Class 3 (n=144, 28%)	
		MLE (SE; 95% CI)	RI (95% CI)	MLE (SE; 95% CI)	RI (95% CI)	MLE (SE; 95% CI)	RI (95% CI)
Severe allergic reaction	Increased risk						
	No risk	2.18 (0.40; 1.40, 2.96)***	17% (13.2, 20.2)	0.45 (0.06; 0.33, 0.56)***	10% (8.0, 12.9)	1.19 (0.10; 0.99, 1.40)***	15% (12.7, 17.0)
Class membership constant		Reference		-0.04 (0.03)		-0.29 (0.03)***	

Bayesian information criterion = 7843

CI, confidence interval; MLE, maximum likelihood estimate; RI, relative importance; SE, standard error.

* P < 0.05, ** P < 0.01, *** P < 0.001 (z-test)

Online Resource 9. Comparison of participant characteristics across latent classes for the secondary CVD prevention group

Characteristic	P-value (chi-square test)	Class composition, n (%)		
		Class 1 (N=189)	Class 2 (N=181)	Class 3 (N=144)
Age: ≤55 years (vs. 56-64)	<0.001	59 (31)	22 (12)	23 (16)
Age: ≥65 years (vs. 56-64)		29 (15)	115 (64)	82 (57)
Comorbidities: atherosclerosis (vs. no)	<0.001	56 (30)	7 (4)	21 (15)
Comorbidities: history of myocardial infarction (vs. no)	<0.001	41 (22)	78 (43)	66 (46)
Comorbidities: hospitalization (vs. no)	<0.001	157 (83)	23 (13)	37 (26)
Comorbidities: kidney failure (vs. no)	<0.001	58 (31)	1 (1)	2 (1)
Comorbidities: transient ischemic attack (vs. no)	<0.001	75 (40)	29 (16)	33 (23)
Comorbidities: ischaemic stroke (vs. no)	0.009	11 (6)	28 (15)	19 (13)
Comorbidities: unstable angina (vs. no)	<0.001	46 (24)	9 (5)	16 (11)
Comorbidities: stable angina (vs. no)	0.005	74 (39)	43 (24)	42 (29)
Comorbidities: congestive heart failure (vs. no)	<0.001	80 (42)	3 (2)	15 (10)
Comorbidities: diabetes type 2 (vs. no)	0.028	49 (26)	33 (18)	21 (15)
Comorbidities: deep vein thrombosis (vs. no)	<0.001	64 (34)	0 (0)	10 (7)
Comorbidities: heart arrhythmias (vs. no)	<0.001	124 (66)	6 (3)	21 (15)
Comorbidities: heart valve problems (vs. no)	<0.001	75 (40)	3 (2)	11 (8)
Comorbidities: hypertension (vs. no)	<0.001	178 (94)	108 (60)	108 (75)
Comorbidities: hypercholesterolemia (vs. no)	<0.001	168 (89)	92 (51)	84 (58)
Current medications for heart condition: cholesterol lowering drugs (vs. no)	<0.001	174 (92)	104 (57)	89 (62)
Current medications for heart condition: antihypertensive drugs (vs. no)	<0.001	180 (95)	113 (62)	104 (72)
Current medications for heart condition: low-dose aspirin (vs. no)	0.459	99 (52)	93 (51)	66 (46)

Characteristic	P-value (chi-square test)	Class composition, n (%)		
		Class 1 (N=189)	Class 2 (N=181)	Class 3 (N=144)
Current medications for heart condition: blood thinning drugs (vs. no)	0.977	70 (37)	68 (38)	55 (38)
Current medications for other condition: ibuprofen (vs. no)	<0.001	7 (4)	70 (39)	50 (35)
Current medications for other condition: stomach acid reducing drugs (vs. no)	0.147	55 (29)	69 (38)	53 (37)
Current medications for other condition: none (vs. some)	<0.001	130 (69)	63 (35)	62 (43)
Duration of taking medications for heart condition: ≥ 5 years (vs. < 5 years)	<0.001	23 (12)	140 (77)	109 (76)
Education: primary school (vs. high school)		70 (37)	50 (28)	48 (33)
Education: higher education (vs. high school)	0.028	23 (12)	45 (25)	28 (19)
Exercise/week: none (vs. 1-2 h)		86 (46)	67 (37)	60 (42)
Exercise/week: ≥ 3 h (vs. 1-2 h)	<0.001	4 (2)	58 (32)	29 (20)
Overall health: fair/poor (vs. excellent/very good/good)	0.039	129 (68)	103 (57)	98 (68)
Health literacy: inadequate (vs. adequate)	<0.001	164 (87)	109 (60)	94 (65)
Sex: male (vs. female)	0.523	104 (55)	89 (49)	74 (51)
Marital status: married (vs. widowed/divorced/separated/single)	0.340	149 (79)	134 (74)	104 (72)
Past medications for heart condition: cholesterol lowering drugs (vs. no)	<0.001	173 (92)	96 (53)	86 (60)
Past medications for heart condition: antihypertensive drugs (vs. no)	<0.001	156 (83)	93 (51)	87 (60)
Past medications for heart condition: low-dose aspirin (vs. no)	0.083	59 (31)	73 (40)	43 (30)
Past medications for heart condition: blood thinning drugs (vs. no)	<0.001	11 (6)	34 (19)	42 (29)
Past medications for heart condition: none (vs. some)	<0.001	4 (2)	31 (17)	21 (15)
Smoking status: former smoker (vs. current smoker)		90 (48)	28 (15)	38 (26)
Smoking status: never (vs. current smoker)	<0.001	17 (9)	121 (67)	76 (53)