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Review

Assessing risk of myocardial infarction and stroke: new data from the Prospective Cardiovascular Münster (PROCAM) study‡

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Abstract

Objectives Based on the data of the Prospective Cardiovascular Münster (PROCAM) study, a prospective study of men and women at work in the north-west of Germany, we aimed (i) to develop a refined scoring scheme for calculating the risk of acute coronary events among adult and elderly men and women; and (ii) to generate a new scoring scheme for calculating the risk of ischaemic stroke or transient ischaemic attack (TIA).

Methods The coronary risk score was derived from a Weibull function using data from 18 460 men and 8515 women who were recruited before 1996 and had a mean follow-up period of 12 ± 6 years. The stroke score was derived using a Cox proportional hazards model using data of 5905 men and 2225 women aged 35–65 years with at least 10 years of unbroken follow-up.

Results The coronary risk score was based on 511 major coronary events, 462 (168 fatal, 294 non-fatal) in men and 49 (18 fatal, 31 non-fatal) in women and included the risk factors LDL cholesterol, HDL cholesterol, systolic blood pressure, smoking status, triglycerides and diabetes mellitus status. It was accurate in both sexes over an age range from 20 to 75 years with an area under the receiver-operating characteristics (ROC) curve of 0·82. The stroke score was based on 85 cerebral ischaemic events (21 TIAs, 64 ischaemic strokes) and included the risk factors age, sex, diabetes mellitus status, smoking status and systolic blood pressure. It had an area under the ROC curve of 0·78 and identified a high-risk group comprising only 4% of the study population that contained 31% of all cerebral ischaemic events.

Conclusion Both new PROCAM risk scores provide simple and effective ways to assess the risk of acute coronary events and ischaemic stroke in the general population and will improve the ability of physicians to target measures in an effort to prevent these potentially devastating conditions.

Keywords coronary heart disease, epidemiology, myocardial infarction, stroke.

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Introduction

Individual risk factors such as the total cholesterol or the systolic blood pressure level have poor power to predict cardiovascular events such as myocardial infarction or ischaemic stroke. For this reason, much effort has gone into developing algorithms and scores for calculating risk based on a multiplicity of risk factors [1,2]. These have considerably increased predictive power and have helped to improve prevention of cardiovascular disease and its complications

Some years ago, we developed a risk score for coronary events based on a Cox proportional hazards model, which incorporated outcome data derived from 10 years of unbroken follow-up among participants in the Prospective Cardiovascular Münster (PROCAM) study [3]. While this score has been widely adapted, particularly in Europe, the fact that it was derived from the PROCAM cohort of middle-aged men has limited its applicability to women in general and to men outside this age range, particularly to men above the age of 65 years, who bear a considerable risk of suffering a coronary event.

The first objective of the present study was therefore to develop an updated coronary risk score based on a Weibull function. This removes the statistical constraint that previously limited us to an analysis among the 35–65 years age group in PROCAM, allowing us to incorporate data from participants of all ages. This is an advantage that has previously been exploited by others, notably the SCORE project of the European Society of Cardiology [2] and in some of the risk scores derived from the Framingham study [4,5]. In addition, the technique of first developing a common algorithm for calculating relative risk in both men and women and then, in a second step developing a Weibull function for each sex separately (following the example of the SCORE project [2]) now allows us for the first time to develop a risk score for women based on the PROCAM data.

Coronary and cerebral ischaemic events share a number of commonalities in terms of their risk profiles [6]. However, in contrast to the situation with coronary heart disease, where risk scores have proliferated [1–3], few comprehensive scores have been developed for the calculation of risk of cerebral ischaemic events. Indeed, the stroke score that is still most widely used was published by the Framingham group in 1991 [7] based on data that is at least 30 years old (and in most cases, a lot older) today. Since publication of the Framingham stroke score, two other scores have been developed in prospective studies using different sets of stroke risk factors [8,9], but neither has seen widespread use. As noted in recent guidelines on primary prevention of ischaemic stroke [10], 'it is clear that an ideal stroke risk-assessment tool that is generally applicable, simple and widely accepted does not exist.' Our second aim in the present study was therefore to develop a simple prediction score based on the incidences of cerebral ischaemic events in the PROCAM population in order to provide physicians with a simple tool that will enable them to more accurately target measures to prevent this devastating illness.

Methods

Recruitment of participants

Recruitment to the PROCAM study [11,12] was started in 1978 and completed in 1995 for both cohorts analysed in the present report. During this time, 26 975 employees (18 460 men, 8515 women) of 52 companies and local government authorities were examined. At time of entry into the study, the participants ranged in age between 20 and 78 years. Details of the examination procedure are reported elsewhere [13]. Briefly, the examination at study entry included case history using standardized questionnaires, measurement of blood pressure and anthropometric data, a resting electrocardiogram and collection of a blood sample after a 12-h fast for the determination of more than 20 laboratory parameters. Participation was voluntary and participation ranged between 40% and 80% (on average 60%) of all employees. All findings were reported to the participants' general practitioners and also the participants were informed in case of abnormal findings, but the investigators neither carried out nor arranged for any intervention. Subjects with a history of angina pectoris (defined using the World Health Organisation 'Rose questionnaire' [14]), myocardial infarction (self-reported or based on results of an electrocardiogram) or stroke (self-reported) were excluded. In each case in which evidence of morbidity or mortality was obtained from the completed follow-up questionnaires, hospital records and records of the attending physicians were collected and reviewed. For the coronary risk score, the follow-up periods ranged from 23 days to 27 years, with a mean of 11·7 years and a median of 9·4 years. While the coronary risk score was based on the entire PROCAM population, the stroke score was based on the cohort of 5906 men and 2224 women aged 35–65 years at entry who had at least 10 years of unbroken follow-up. This limitation was necessary because of the low incidence of stroke among the men and women outside this cohort.

Definition and classification of 'major coronary event' and stroke

A 'major coronary event' was defined as the occurrence of sudden cardiac death or a definite fatal or non-fatal myocardial infarction on the basis of ECG and/or cardiac enzyme changes. The detailed criteria for defining a sudden coronary death and a definite fatal or non-fatal myocardial infarction have been previously published [15]. A transient ischaemic attack (TIA) was defined as focal neurological symptoms of ischaemic cause that lasted less than 24 h. A definite stroke was defined as a focal neurological deficit that lasted longer than 24 h and was attributable to a vascular event. Strokes were independently classified by two neurologists into ischaemic and haemorrhagic subtypes on the basis of mode of onset, clinical findings and magnetic resonance imaging and/or computerized tomography, which was performed in 83% of stroke cases. Inter-rate reliability (kappa statistic) was 0·74 for total and ischaemic stroke and 1·0 for haemorrhagic stroke. In cases where the clinical data did not allow a distinction between haemorrhagic and ischaemic stroke, strokes were classified as 'undetermined'.

Study outcome

Five hundred and eleven major coronary events were observed after a mean follow-up of 12 ± 6 years. Of these, 462 (168 fatal, 294 non-fatal) occurred in men, while 49 (18 fatal, 31 non-fatal) occurred in women. Eighty-five cerebral ischaemic events (21 TIAs, 64 ischaemic strokes) were observed. Twenty-four patients who suffered a haemorrhagic or undetermined stroke were excluded from the analysis.

Statistical analysis

Data were analysed using the SPSS Release 12·0 and Stata Release 9 software packages.

Weibull model for coronary heart disease

The Weibull proportional hazards model used to calculate coronary risk had two parts, one to model the shape of the baseline survival function, while the other calculated the relative risks associated with each of the risk factors. Stratification for sex was achieved by calculating separate hazard functions for men and women. However, risk factor coefficients were calculated using the whole dataset, including an interaction term between sex and presence of diabetes mellitus. Interaction terms between sex and the other risk variables were not included because they did not reach statistical significance at the 5% level. Continuous independent variables (LDL cholesterol, HDL cholesterol, log-transformed triglycerides and systolic blood pressure) were modelled as continuous variables. We also tested quadratic terms of these variables, but none of these was significant at the 5% level.

The Weibull model has the advantage that the risk estimation equation can be written as a formula. All model predictions were cross-checked by comparison with Cox regression models to ensure that the assumption made by the Weibull regression equation about the shape of the survival function did not comprise the performance of the algorithm. We constructed our hazard function based on age, and not on the time under observation. Using age as the time variable allows us to make estimations over the entire age range displayed by participants during the duration of follow-up. Ten-year risk calculations were based on the conditional probability of major coronary events occurring within the ensuing 10 years, given that the participant had survived to the index age without suffering a myocardial infarction or stroke. Details of the generation of the Weibull function are given in an annex to this paper.

Table 1 Number of major coronary events observed in men and women in PROCAM aged 35–65 years at recruitment following 10 years of follow-up, by risk category as estimated using the Weibull risk function

	Estimated 10-year risk (Weibull model)					
	< 10%		10–20%		> 20%	
	n	%	*n*	%	*n*	%
Men						
No event	4101	97%	515	85%	213	67%
Major coronary event	128	3%	89	15%	104	33%
Women						
No event	2063	99%	45	94%	13	68%
Major coronary event	15	1%	3	6%	6	32%

Cox proportional hazards model for stroke

The cerebral ischaemic event risk score was constructed using the Cox proportional hazards model as previously described [3]. Since the Cox model only allows calculation of relative risk, absolute risk estimates were obtained from Kaplan–Meier survival curves.

Results

Weibull function for major coronary events

In order to determine how well the estimated risk agreed with the observed incidence of major coronary events, we analysed a subgroup of 5150 men and 2145 women aged 35–65 years with a fixed follow-up period of 10 years. Within this period, 321 men and 24 women suffered a major coronary event. Table 1 shows the distribution of observed coronary events within the three groups with calculated 10-year coronary event risks of < 10%, 10–20%, and > 20%. The good agreement between estimated and observed event incidence rates in men is apparent; in women, in large part due to the small number of events, concordance between observed and expected events, although still considerable, was lower than in men.

In order to determine how well the risk predictions generated by the Weibull model correlate with those generated with the previously published PROCAM risk score [3] which, based on a Cox proportional hazards model, we compared the 10-year risk of a major coronary event as calculated using both methods in the cohort of middle-aged men used to generate the PROCAM risk score. Both methods performed equally well, each having an area under the receiver-operating characteristics (ROC) curve of 82·4%. The coefficient of correlation between the risk predictions generated by the Weibull and Cox models was 0·976, with the following regression equation (risk given in percentage):

$$\text{10-year coronary event risk}_{\text{Weibull}} = 0{\cdot}993 \times \text{10-year coronary event risk}_{\text{Cox}} + 0{\cdot}118.$$

Table 2 PROCAM Weibull score for men and women. The points associated with each risk factor are added together and the total number of points is then inserted into Table 3 (men) or Table 4 (women) to obtain the absolute 10-year risk for developing a major coronary event

LDL* cholesterol (mg dL^{-1})		HDL† cholesterol (mg dL^{-1})		Systolic blood pressure (mmHg)		Smoking status	
≤ 100	0	≤ 35	11	< 110	0	No	0
101–105	1	36–37	10	110–119	1	Yes	12
106–110	2	38–39	9	120–129	2		
111–115	3	40–41	8	130–139	3	Family history	
116–120	4	42–43	7	140–149	4		
121–125	5	44–45	6	150–159	5	No	0
126–130	6	46–47	5	160–169	6	Yes	5
131–135	7	48–49	4	170–179	7		
136–140	8	50–51	3	≥ 180	8		
141–145	9	52–53	2				
146–150	10	54–55	1	Fasting blood glucose ≥ 120 mg dL^{-1} or diagnosis of diabetes mellitus			
151–155	11	> 55	0				
156–160	12						
161–165	13	Triglycerides (mg dL^{-1})					
166–170	14	< 100	0	No	0		
171–175	15	100–149	2	Yes (men)	9		
176–180	16	150–199	3	Yes (women)	11		
181–185	17	≥ 200	4				
186–190	18						
191–195	19						
≥ 196	20						

*Low-density lipoprotein, †high-density lipoprotein.

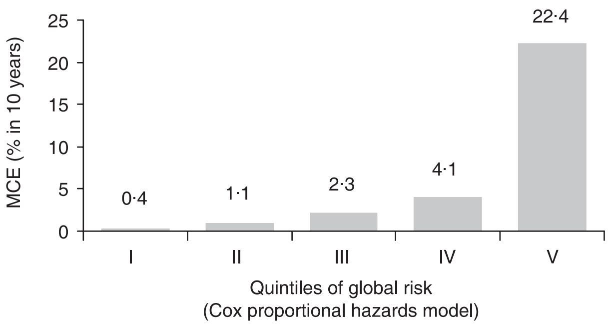

Figure 1 The PROCAM risk algorithm for men (Cox proportional hazards model). Shown are incidences of major coronary events (MCE) (given in percentage within 10 years of follow-up) in each of the five quintiles of global risk as derived from the Cox proportional hazards model for men. The evaluation is based on 406 fatal and non-fatal myocardial infarctions observed in 7152 men aged 35–65 years and includes the independent variables age, systolic blood pressure, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, diabetes mellitus, smoking and family history of cardiovascular disease (CVD).

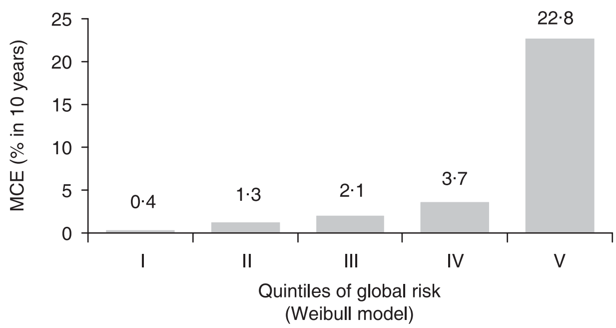

Figure 2 The PROCAM risk algorithm for men (Weibull model). Shown are incidences of major coronary events (given in percentage within 10 years of follow-up) in each of the five quintiles of global risk as derived from the Weibull model for men. The evaluation is based on 462 fatal and non-fatal myocardial infarctions observed in 18 460 men aged 35–65 years and includes the independent variables age, systolic blood pressure, LDL cholesterol, HDL cholesterol, triglycerides, diabetes mellitus, smoking and family history of CVD.

Figures 1 and 2 show the incidence of major coronary events in each of the five quintiles of global risk in PROCAM as derived using the Cox proportional hazards model and the Weibull model for men, respectively.

Construction of PROCAM Weibull risk score

To facilitate the use of the PROCAM Weibull risk score in clinical practice, we prepared the risk score shown in Tables 2–4. In Table 2, the points associated with each risk

Table 3 Ten-year risk of a major coronary event associated with each point score according to the PROCAM Weibull function in men. The point score calculated from Table 2 is located for the appropriate age of the patient and the 10-year risk is read off the top of the chart

	10-year risk of a major coronary event in men				
Age (y)	0–4%	5–9%	10–19%	20–29%	= 30%
20–24	≤ 71				
25	< 66	= 67			
26	< 63	64–71			
27	< 60	61–69	= 70		
28	< 57	58–67	= 68		
29	< 55	56–64	= 65		
30	< 53	54–62	= 63		
31	< 51	52–60	61–62	= 63	
32	< 49	50–58	59–67	= 68	
33	< 47	48–56	57–65	= 66	
34	< 45	46–54	55–63	64–69	= 70
35	< 43	44–52	53–62	63–67	= 68
36	< 41	42–51	52–60	61–66	= 67
37	< 40	41–49	50–58	59–64	= 65
38	< 38	39–48	49–57	58–63	= 64
39	< 37	38–46	47–55	56–61	= 62
40	< 35	36–45	46–54	55–60	= 61
41	< 34	35–43	44–53	54–58	= 59
42	< 33	34–42	43–51	52–57	= 58
43	< 31	32–41	42–50	51–56	= 57
44	< 30	31–39	40–49	50–55	= 56
45	< 29	30–38	39–48	49–53	= 54
46	< 28	29–37	38–46	47–52	= 53
47	< 27	28–36	37–45	46–51	= 52
48	< 26	27–35	36–44	45–50	= 51
49	< 25	26–34	35–43	44–49	= 50
50	< 23	24–33	34–42	43–48	= 49
51	< 23	24–32	33–41	42–47	= 48
52	< 22	23–31	32–40	41–46	= 47
53	< 21	22–30	31–39	40–45	= 46
54	< 20	21–29	30–38	39–44	= 45
55	< 19	20–28	29–37	38–43	= 44
56	< 18	19–27	28–37	38–42	= 43
57	< 17	18–26	27–36	37–41	= 42
58	< 16	17–26	27–35	36–41	= 42
59	< 15	16–25	26–34	35–40	= 41
60	< 15	16–24	25–33	34–39	= 40
61	< 14	15–23	24–33	34–38	= 39
62	< 13	14–22	23–32	33–38	= 39
63	< 12	13–22	23–31	32–37	= 38
64	< 12	13–21	22–30	31–36	= 37
65	< 11	12–20	21–30	31–35	= 36
66	< 10	11–20	21–29	30–35	= 36
67	< 10	11–19	20–28	29–34	= 35
68	< 9	10–18	19–28	29–33	= 34
69	< 8	9–17	18–27	28–33	= 34
70	< 8	9–17	18–26	27–32	= 33
71	< 7	8–16	17–26	27–31	= 32
72	< 6	7–16	17–25	26–31	= 32
73	< 6	7–15	16–24	25–30	= 31
74	< 5	6–14	15–24	25–29	= 30
75	< 4	5–14	15–23	24–29	= 30

Table 4 Ten-year risk of a major coronary event associated with each point score according to the PROCAM Weibull function in women. The point score calculated from Table 2 is located at the appropriate age and the 10-year risk is read off the top of the chart

	10-year risk of a major coronary event in women				
Age (y)	0–4%	5–9%	10–19%	20–29%	= 30%
20–33	≤ 71				
34	< 69	= 70			
35	< 66	= 67			
36	< 64	= 65			
37	< 62	63–70	71		
38	< 59	60–68	= 69		
39	< 57	58–66	= 67		
40	< 55	56–64	= 65		
41	< 53	54–62	= 63		
42	< 51	52–60	61–69	= 70	
43	< 49	50–58	59–67	= 68	
44	< 48	49–56	57–65	= 66	
45	< 46	47–55	56–64	65–69	= 70
46	< 44	45–53	54–62	63–69	= 68
47	< 43	44–51	52–60	61–66	= 67
48	< 41	42–50	51–59	60–64	= 65
49	< 39	40–48	49–57	58–62	= 63
50	< 38	39–47	48–56	57–61	= 62
51	< 36	37–45	46–54	55–60	= 61
52	< 35	36–44	45–53	54–58	= 59
53	< 34	35–42	43–51	52–57	= 58
54	< 32	33–41	42–50	51–55	= 56
55	< 31	32–40	41–49	50–54	= 55
56	< 30	31–39	40–47	48–53	= 54
57	< 28	29–37	38–46	47–51	= 52
58	< 27	28–36	37–45	46–50	= 51
59	< 26	27–35	36–44	45–49	= 50
60	< 25	26–34	35–42	43–48	= 49
61	< 24	25–32	33–41	42–47	= 48
62	< 23	24–31	32–40	41–46	= 47
63	< 21	22–30	31–39	40–45	= 46
64	< 20	21–29	30–38	39–43	= 44
65	< 19	20–28	29–37	38–42	= 43
66	< 18	19–27	28–36	37–41	= 42
67	< 17	18–26	27–35	36–40	= 41
68	< 16	17–25	26–34	35–39	= 40
69	< 15	16–24	25–33	34–38	= 39
70	< 14	15–23	24–32	33–37	= 38
71	< 13	14–22	23–31	32–36	= 37
72	< 12	13–21	22–30	31–35	= 36
73	< 12	13–20	21–29	30–35	= 36
74	< 11	12–19	20–28	29–34	= 35
75	< 10	11–19	20–27	28–33	= 34

factor in both men and women are noted and added together. In a second step, the total number of points is then inserted into Tables 3 and 4 in order to derive the absolute 10-year risk of developing a major coronary event. As with our previous scoring scheme [3], the Weibull risk score contained nearly all of the information contained within the full Weibull risk function using continuous risk variables. The coefficient of correlation between the risk predictions

Table 5 Cox proportional hazards model for stroke: mean values, beta coefficients and hazard ratios of independent risk factors for cerebral ischaemic events in the study population

	Mean value in total population (± SD, where shown)	β-coefficient of Cox model	*P*-value	Hazard ratio (95% confidence interval)
Proportion of women (%)	27·4	–0·626	0·027	0·54 (0·31–0·93)
Age (years)	45·7 ± 6·8	0·109	< 0·001	1·12 (1·08–1·15)
Smoking (%)	29·9	0·852	< 0·001	2·34 (1·52–3·60)
Systolic blood pressure (mmHg)	130·3 ± 18·4	0·022	< 0·001	1·02 (1·01–1·03)
Diabetes mellitus (%)	6·2	0·615	0·040	2·07 (1·03–3·33)

Table 6 PROCAM risk scoring scheme for cerebral ischaemic events. The scheme is applicable to men and women aged 35–65 years

Sex		Cigarette smoking		Systolic blood pressure	
Male	6	No	0	< 140 mmHg	0
Female	0	Yes	9	140–144 mmHg	1
				145–149 mmHg	2
Age* 1 per year		Presence of diabetes mellitus†		150–154 mmHg	3
		No	0	155–159 mmHg	4
		Yes	7	160–164 mmHg	5
				165–169 mmHg	6
				170–174 mmHg	7
				175–179 mmHg	8
				> 180 mmHg	9

*Within the age range of 35–65 years, one point is given for each year of life.

† History of diabetes mellitus or fasting sugar in serum of at least 120 mg dL^{-1}.

Table 7 Ten-year risk of cerebral ischaemic events (ischaemic stroke or transient ischaemic attack) associated with the point score obtained in Table 6

Number of points	Risk of stroke in 10 years (%)	Number of points	Risk of stroke in 10 years (%)
< 42	≤ 0·1	66	2·2
42–46	0·2	67	2·4
47–49	0·3	68	2·7
50–51	0·4	69	3·0
52–53	0·5	70	3·4
54–55	0·6	71	3·8
56	0·7	72	4·2
57	0·8	73	4·7
58	0·9	74	5·2
59	1·0	75	5·8
60	1·1	76	6·5
61	1·3	77	7·3
62	1·4	78	8·1
63	1·6	79	9·0
64	1·7	80	10·0
65	1·9	> 80	> 10·0

generated by the Weibull risk score and the full Weibull models was 0·955 (0·958 in men and 0·907 in women) with the following regression equation (risk given in percentage):

$$\text{10-year coronary event risk}_{\text{Weibull risk score}} = 0{\cdot}901 \times \text{10-year coronary event risk}_{\text{Full Weibull model}} + 0{\cdot}391.$$

The area under the ROC curve was 0·817 for both the full Weibull model and the Weibull score.

Cox model for stroke risk

Of the 57 clinical and laboratory variables measured in the PROCAM study, five (age, sex, cigarette smoking, presence of diabetes mellitus and systolic blood pressure) were found to be independently predictive of stroke risk and were used to construct the risk algorithm. The mean values of these variables, together with the beta coefficients of the Cox model and the hazard ratios are shown in Table 5. In generating our algorithm, we also considered first-order interactions between these independent risk variables. However, none of these interactions exceeded the significance threshold of 0·05. In order to validate the Cox model, we divided our data into five equal and distinct sets. Combinations of four of these five sets were used for generating the model. The final set was used for testing performance of the model on unknown data. This cross-validation procedure was repeated for every possible 4 +1 combination. This internal validation showed that the Cox model performed robustly with results in each subset that did not differ significantly from the model derived in the entire dataset (not shown).

The PROCAM cerebral ischaemic event score (Table 6) derived from the full Cox model is applicable to men and women aged 35–65 years. Table 7 shows the estimated 10-year risk of a cerebral ischaemic event associated with each point score; at very low and very high scores, incidences and case numbers were too small for individual scores to be meaningful; these scores are therefore grouped into two categories of very low and very high scores, respectively.

Figure 3 shows the observed incidence of cerebral ischaemic events in each of four classes of estimated event risk [< 1·0%, 1·0–1·9%, 2·0–3·9%, ≥ 4·0%]. Only 4% of participants had an estimated 10-year cerebral ischaemic event risk of ≥ 4·0%. Nevertheless, this small group contained 31% of all cerebral ischaemic events.

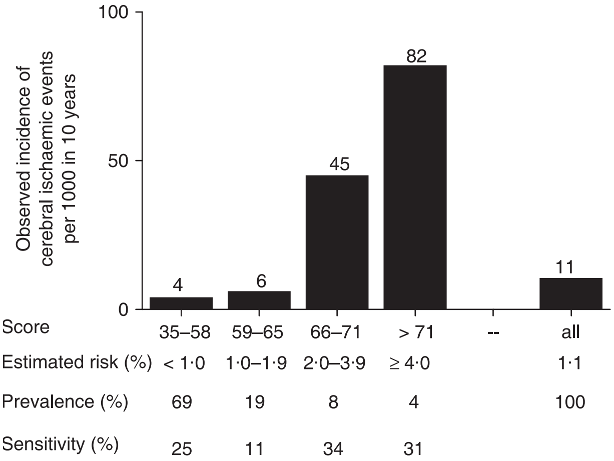

Figure 3 Observed incidence of cerebral ischaemic events per 1000 participants in PROCAM within 10 years for various risk scores. Ten-year cerebral ischaemic event risk categories of < 1·0%, 1·0–1·9%, 2·0–3·9%, and ≥ 4·0% were used. For example, 69% of participants had a score of 35–58, indicating a 10-year estimated cerebral ischaemic event risk of less than 1%. After 10 years of follow-up, only 0·4% of this group suffered a cerebral ischaemic event. Nevertheless, because of its large size, this low-risk group contained 34% of all events. At the opposite extreme, only 4% of participants had a score of greater than 71, indicating a 10-year event risk of 4% or more. After 10 years, 8% of this group had suffered a cerebral ischaemic event. Despite containing not even 4% of the population, this high-risk group contained 31% of all cerebral ischaemic events. The data in this figure were based on 85 fatal and non-fatal strokes and transient ischaemic attacks occurring among 2224 women and 5906 men aged 35–65 years at recruitment into the PROCAM study.

Discussion

The original PROCAM risk algorithm for coronary events was constructed using the Cox proportional hazards model because this model has a number of strengths, including its ability to account for variable duration of follow-up, censoring of subjects, proportionality of event occurrence and time-to-event. While this score has been widely adapted, particularly in Europe, the fact that it was derived from the PROCAM cohort, which consists mainly of middle-aged men, resulted in limitations with respect to its applicability to women in general and to men above the age of 65 years. In order to overcome these limitations, we developed an updated risk score that is based on a Weibull risk function. While our previously presented Cox survival model employed time under observation as the time variable, with age at entry into PROCAM as a risk factor, the Weibull function considered age as a time variable. Therefore, the Weibull algorithm provided a much better means than the Cox model of modelling data from individuals of all ages. The corresponding PROCAM scoring schemes for men and women based on the Weibull distribution contained nearly all the information of the full algorithm (correlation coefficient 0·95) and predicted coronary events with an area under receiver-operating characteristics curve of 0·82 in men and women over an age range between 20 and 75 years.

Cerebral ischaemic events and myocardial infarction share a number of commonalities, since both conditions are due in most cases to the presence of atherosclerosis. However, while myocardial infarction almost always occurs against a background of atherosclerosis of the coronary arteries themselves, cerebral ischaemic events are usually caused not by atherosclerosis of the intracerebral vessels but by plaques in extracranial arteries, in particular the carotids and the aortic root. In addition, ischaemic stroke may be caused by thrombi arising within the heart and by other conditions such as blood dyscrasias. Thus myocardial infarction and cerebral ischaemic events show overlapping but distinct risk factor profiles. For example, atrial fibrillation and sickle cell anaemia are risk factors for cerebral ischaemic events, but not for myocardial infarction, and the relative risk associated with hypertension is greater for cerebral ischaemic events. Notwithstanding these differences, the physician dealing with patients at risk of cerebral ischaemic events is faced with the same task as his or her colleague dealing with patients at risk of myocardial infarction, that is, how to rationally quantify risk within a shifting matrix of mutually interacting risk factors.

In a previous paper, we reported on the incidence of stroke in the PROCAM cohort and on the relative risk for total stroke associated with hypertension, smoking status and presence of diabetes mellitus [6]. In the present report, we extend our results by developing a prediction score based on the incidences of cerebral ischaemic events in the PROCAM population. The cerebral ischaemic event risk score takes into account only five factors (age, sex, presence of cigarette smoking or diabetes mellitus and systolic blood pressure), but nevertheless approaches the performance of contemporary risk scores in predicting major coronary events. Using this score, it was possible to identify a group with a score of more than 71, which, although it comprised only 4% of the population, contained approximately one-third of all cerebral ischaemic events. In this high-risk group, one person in 12 developed a cerebral ischaemic event within 10 years of follow-up (Fig. 3). Conversely, the score allowed identification of a large group comprising 69% of the population (score of 58 or less) in whom the 10-year-risk of stroke was less than a half of one percent. Importantly, the full score was much better at predicting cerebral ischaemic events than either systolic blood pressure or age alone.

Thus, in summary, we present two simple and effective scores for the calculation of cardiovascular risk in the general population, which, we hope, will help to target preventive treatment to those high-risk individuals who need it most.

References

1 Adult Treatment Panel III. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood

Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;**106**:3143–421.
2 Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G *et al*. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. *Eur Heart J* 2003;**24**:987–1003.
3 Assmann G, Cullen P, Schulte H. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) study. *Circulation* 2002;**105**:310–5.
4 Anderson KM, Wilson PWF, Odell PM, Kannel WB. An updated coronary risk profile – a statement for health professionals. *Circulation* 1991;**83**:356–62.
5 d'Agostino RB, Russell MW, Huse DM, Ellison RC, Silbershatz H, Wilson PW *et al*. Primary and subsequent coronary risk appraisal: new results from the Framingham study. *Am Heart J* 2000;**139**:272–81.
6 Berger K, Schulte H, Stögbauer F, Assmann G. Incidence and risk factors for stroke in an occupational cohort: the PROCAM Study. *Prospective Cardiovascular Muenster Study. Stroke* 1998;**29**:1562–6.
7 Wolf PA, d'Agostino RB, Belanger AJ, Kannel WB. Probability of stroke: a risk profile from the Framingham Study. *Stroke* 1991;**22**:312–8.
8 Lumley T, Kronmal RA, Cushman M, Manolio TA, Goldstein S. A stroke prediction score in the elderly: validation and Web-based application. *J Clin Epidemiol* 2002;**55**:129–36.
9 Psaty BM, Anderson M, Kronmal RA, Tracy RP, Orchard T, Fried LP *et al*. The association between lipid levels and the risks of incident myocardial infarction, stroke, and total mortality: The Cardiovascular Health Study. *J Am Geriatr Soc* 2004;**52**:1639–47.
10 Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD *et al*. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: the American Academy of Neurology affirms the value of this guideline. *Stroke* 2006;**37**:1583–633.
11 Assmann G, Cullen P, Schulte H. The Munster Heart Study (PROCAM) – Results of follow-up at 8 years. *Eur Heart J* 1998;**19**:A2–11.
12 Cullen P, Schulte H, Assmann G. The Münster Heart Study (PROCAM). Total mortality in middle-aged men is increased at low total and LDL cholesterol concentrations in smokers but not in nonsmokers. *Circulation* 1997;**96**:2128–36.
13 Assmann G, Schulte H, von Eckardstein A. Hypertriglyceridemia and elevated levels of lipoprotein (a) are risk factors for major coronary events in middle-aged men. *Am J Cardiol* 1996;**77**:1179–84.
14 World Health Organisation. *Cardiovascular Survey Methods*. Geneva, 1997.
15 Assmann G, Cullen P, Evers T, Petzinna D, Schulte H. Importance of arterial pulse pressure as a predictor of coronary heart disease risk in PROCAM. *Eur Heart J* 2005;**26**:2120–6.

