

Drop-out analysis

Methods

In KORA, 486 subjects were lost-to-follow-up without information on incident ASCVD. To rule out possible bias in analysing the ACC/AHA risk score, we performed a sensitivity analysis, analysing the risk profile of these subjects and imputing their missing event status. For this, we used a stratified bootstrapping resampling technique (number of bootstrap samples: $b = 300$) and three imputation scenarios, randomly assigning events with event rate 50%, 20% or 10%. Since we did not have information on survival or censoring time for these subjects, we used the area under the receiver operating characteristic curve (AUC) as a measure of discrimination performance in this sensitivity analysis, as it does not incorporate survival times.¹ We then investigated the impact of the three event rate scenarios on the performance of the ACC/AHA risk score.

Results

Exclusion of subjects with missing information on risk score variables resulted in 5,238 completely observed subjects and 464 (8%) subjects with missing outcome information. Out of seven risk factors included in the ACC/AHA risk equation, we observed significant differences regarding five risk factors (age, total cholesterol, systolic blood pressure, smoking and diabetes) between KORA subjects without follow-up on incident ASCVD events and KORA subjects included in the main analysis. Using the ACC/AHA risk equations, mean estimated 10 year ASCVD risk was greater for KORA subjects without follow-up (11.5%) than for KORA subjects with follow-up (10.0%). Details are depicted in S2 Table.

Results from imputing missing outcome information with event rate 10%, which was closest to the ASCVD risk estimated by the ACC/AHA risk score, showed a calibration performance comparable to the analysis of the completely observed data, however, poorer performance

regarding discriminative power (Complete data: AUC = 0.78 [0.76, 0.81], imputation with 10% event rate: AUC = 0.76 [0.73, 0.78]). Imputation with event rate 20% and 50% improved calibration of the ACC/AHA risk score in KORA, however, with considerably reduced discrimination ability (event rate 20%: AUC = 0.74 [0.72, 0.76]; event rate 50%: AUC = 0.70 [0.68, 0.72]). Results are depicted in S3 Fig.

¹ Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology*. 1982;143(1):29-36.

S2 Table. Risk profile of KORA subjects with and without follow-up on incident ASCVD events.

Characteristic ^a	KORA		p-value ^b
	With follow-up	Without follow-up	
N ^c (%)	5238	464 ^d	
Age ^e (years)	55.9 +- 9.7	57.6 +- 10.2	<0.001
Sex male	49.2 (2623)	44.4 (216)	0.051
Total cholesterol (mg/dL)	234.2 (207.9, 263.7)	240.4 (212.8, 270.4)	0.016
HDL ^f cholesterol (mg/dL)	53.3 (43.8, 65.9)	53.0 (44, 64.3)	0.617
Systolic blood pressure (mmHg)	132.0 (120.5, 146.5)	135.5 (123.5, 148)	<0.01
Intake of antihypertensive drugs	20.4 (1085)	23.2 (112)	0.159
Intake of statins or fibrates	5.1 (270)	6.8 (33)	0.118
Current smoker	21.1 (1122)	25.1 (122)	0.043
Diabetes	4.8 (257)	7.2 (35)	0.028
Average 10 year ASCVD risk (%) according to the ACC/AHA risk score	10.0 ± 10.2	11.5 ± 10.5	<0.001

^aDepicted are absolute numbers (percentage) for categorical and median (first quartile, third quartile) for continuous variables.

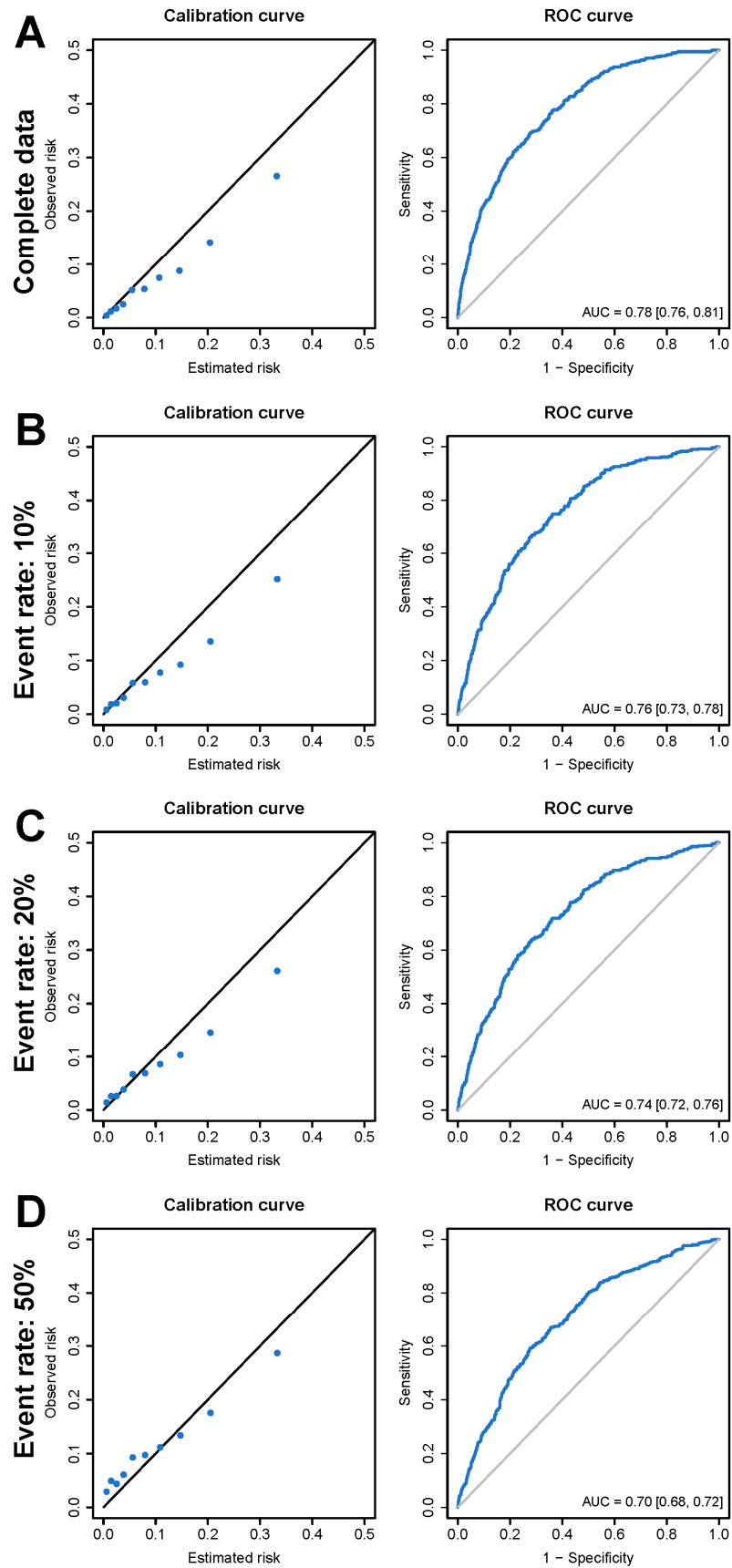
^bp-value from Kruskal-Wallis test for continuous and Chi-square-test for categorical variables.

^cN = Sample size.

^dOf n=486 subjects without follow-up, 22 subjects had to be excluded due to missing information in one or more risk factors.

^eAge (years) is shown as mean ± standard deviation.

^fHDL = High-density lipoprotein.



S3 Fig. Calibration and ROC curve from drop-out analysis. ROC analysis and calibration performance of ACC/AHA risk score after imputation of lost-to-follow-up subjects in KORA: Complete case analysis without imputation (part A), random assignment of event status to lost-to-follow-up subjects with event-rate 10% (part B), 20% (part C) and 50% (part D).