Appendices

1. Detailed information on the different cohorts

1.1 – Baseline information

Appendix 1 - Table 1 shows that individuals from SMART were less healthy and older compared to Morgen and Prospect participants. Moreover, they had significantly higher blood pressure, had diabetes more often, smoked more often and used more medication. On average, the values of the Morgen women regarding their CVD risk factors were slightly lower than the values for the Prospect women, except for smoking. The follow up time across cohorts varied widely because the SMART cohort is an ongoing cohort, whereas Morgen and Prospect are closed cohorts.

Appendix 1 - Table 1: Baseline table for the different cohorts

	SMART men	SMART women	Morgen men	Morgen women	Prospect women
Number individuals	7088	3557	9153	11270	16401
Age (SD)	58.22 (11.61)	55.31 (13.49)	43.32 (11.01)	42.49 (11.25)	57.62 (6.01)
Total cholesterol (SD)	192.65 (51.32)	210.62 (55.82)	205.64 (41.35)	203.94 (40.78)	236.97 (41.38)
High density lipoprotein (SD)	44.88 (12.69)	56.24 (16.59)	45.88 (11.69)	58.32 (14.50)	57.58 (15.62)
Using preventive treatment	44	52%	4%	5%	16%
Systolic blood pressure (SD)	141.26 (20.57)	142.16 (23.49)	125.02 (15.28)	117.89 (16.27)	133.15 (20.02)
Smoking	30%	29%	36%	36%	22%
Diabetes	20%	18%	5%	4%	8%
Follow up time (min-max)	6.99 (0.00-17.49)	7.22 (0.00-17.49)	14.38 (0.04-17.97)	14.93 (0.02-17.97)	14.04 (0.01-17.51)

1.2 - Background information on Framingham Global Risk Score

Appendix 1 - Table 2: Risk predictors

Risk factor	***Description***	***Unit***	***FRS***
Gender	Gender of respondent	0=male, 1=female	X
Age	Age at baseline (rounded)	Years	X
Total cholesterol (TC)	Baseline level, single measurement	mg/dL	X
High-density lipoprotein cholesterol (HDL-C)	One measurement	mg/dL	X
Low-density lipoprotein cholesterol (LDL-C)	One measurement	mg/dL	
Systolic blood pressure (SBP)	Average SBP of two measurements at baseline	mmHg	X
Treatment (trt)	Use of medication for high blood pressure	0 = no, 1 = yes	X
Smoking (smok)	Current smoking status, former smoker is non-smoker	0 = no, 1 = yes	X
Diabetes (diab)	Diabetes mellitus	0 = no, 1 = yes	X

1.3 - Event distribution regarding different cohorts

Only events occurring within 10 years after recruitment were included in the analysis, because the timeline of the CVD risk prediction models used was 10 years. The event distribution varied hugely between the cohorts, for example, SMART individuals suffered more events resulting into a higher observed incidence rate per individual (Appendix 1 - Table 3). Moreover, the percentage fatal CVD events was higher for SMART individuals compared to Morgen and Prospect. There were also differences between men and women. Overall and per cohort, it can be seen that men suffered more non-fatal myocardial infarctions whereas women suffered more from strokes.

Appendix 1 - Table 3: Observed event distribution for the different cohorts

	ICD-10 code	FRS	SMART men	SMART women	Morgen men	Morgen women	Prospect women
			N	N	N	N	N
Morbidity							
Myocardial infarction (MI)	I21,I22	**X**	307 (32.8%)	88 (31.5%)	144 (19.6%)	69 (15.2%)	173 (13.4%)
Other Coronary heart disease (OCHD)	I20,I23, I24,I25	**X**	0 (0%)	0 (0%)	290 (39.5%)	158 (34.73%)	455 (35.4%)
Cardiac arrest	I46,R96	**X**	8 (0.9%)	1 (0.4%)	2 (0.3%)	2 (0.4%)	6 (0.5%)
Ischemic stroke (CVAI)	I63,I65	**X**	240 (25.7%)	97 (34.8%)	64 (8.7%)	60 (13.2%)	195 (15.2%)
Hemorrhagic stroke (CVAH)	I60,I61,I62	**X**	0 (0%)	0 (0%)	13 (1.8%)	29 (6.4%)	55 (4.3%)
Other stroke (OCVA)	I64,I66	**X**	0 (0%)	0 (0%)	29 (4.0%)	19 (4.2%)	32 (2.5%)
Other Cardiovascular diseases (OCVD)	G45,I67,I69, I70-I74,I50	**X**	5 (0.5%)	8 (2.9%)	131 (17.8%)	89 (19.6%)	250 (19.4%)
Mortality							
Myocardial infarction (MI)	I21,I22	**X**	19 (2.0%)	6 (2.2%)	34 (4.6%)	11 (2.4%)	42 3.3%)
Other Coronary heart disease (OCHD)	I20,I23,I24	**X**	0 (0%)	0 (0%)	5 (0.7%)	1 (0.2%)	5 (0.4%)
Cardiac arrest, sudden death	I46,R96	**X**	138 (14.8%)	34 (12.2%)	10 (1.4%)	1 (0.2%)	19 (1.5%)
Ischemic stroke (CVAI)	I63,I65	**X**	18 (1.9%)	5 (1.8%)	2 (0.3%)	1 (0.2%)	5 (0.4%)
Hemorrhagic stroke (CVAH)	I60,I61,I62	**X**	0 (0%)	0 (0%)	2 (0.3%)	4 (0.9%)	9 (0.7%)
Other stroke (OCVA)	I64,I66	**X**	0 (0%)	0 (0%)	1 (0.1%)	2 (0.4%)	21 (1.6%)
Other Cardiovascular diseases (OCVD)	G45,I67,I69, I70-I74,I50	**X**	200 (21.3%)	40 (14.3%)	8 (1.1%)	9 (2.0%)	20 (1.6%)
Total number of			935	279	735	455	1287
Total individuals			7088	3557	9153	11270	16401
Prevalence events (%)			13.19	7.84	8.03	4.04	7.85

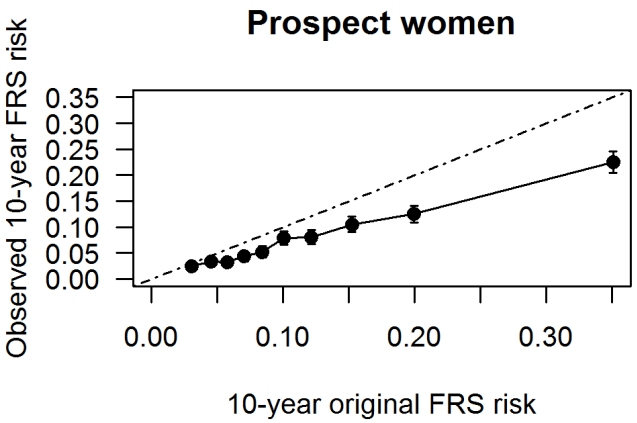
2. Statistical performance

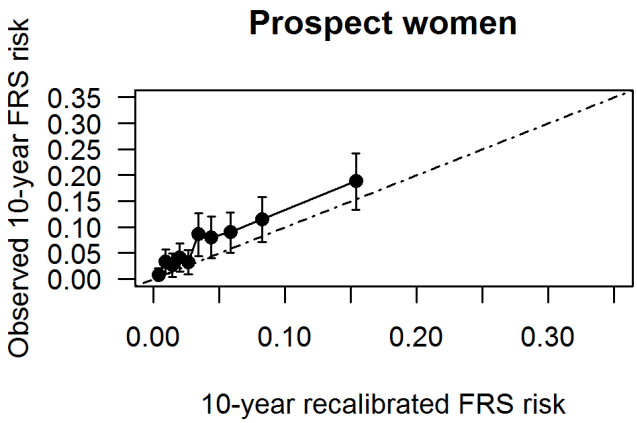
Implementation of a prediction model typically follows updating or recalibration of the model in the target setting, as the target cohort may differ from the original development cohort [1]. Therefore, we recalibrated FRS to the MORGEN and PROSPECT cohorts to ensure that the models provide accurate risk estimates in these cohorts. For the survival data (time-to-event data) considered in this study, recalibrating a prediction model typically involves updating the baseline hazard and centering each predictor around the mean value of all patient characteristics (i.e. linear predictor) in our cohorts, for men and women separately [2]. Furthermore, we incorporated an additional correction factor to ensure that the updated baseline hazards actually reflect the observed probability of survival after 10 years. The regression coefficients of the risk factors of the original FRS model were not changed [3].

Results of the updated values for the linear predictor and baseline hazard can be seen in Appendix 2 - Table 1 (column 2-5). Calibration and discrimination results according to the original and recalibrated model can be found in Appendix 2 - Table 1 (column 6-10). The performance of the subgroups of individuals is good and very similar, see the column "c-statistic". Moreover, the predicted number of events now closely matches the observed number of events. Furthermore, the calibration plots according to FRS for Morgen and Prospect cohort are shown below, see Appendix 2 - Figure 1 and Appendix 2 - Figure 2.

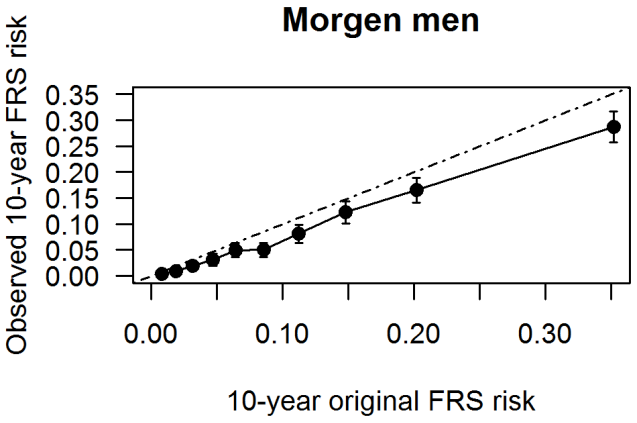
Appendix 2 - Table 1: Statistical performance of FRS for cohort and gender

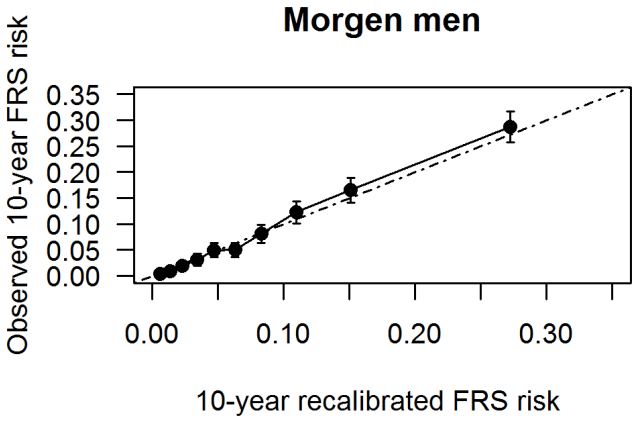
	Linear predictor		**Baseline hazard**		**Observed events**	**Expected events**		**C-statistic**	
	Original model	*Recalibrated model*	*Original model*	*Recalibrated model*		*Original model*	*Recalibrated model*	*Original model*	*Recalibrated model*
Morgen men	24.35	23.44	0.89	0.92	735	978	735	0.78 (0.75; 0.81)	0.78 (0.75; 0.81)
Morgen women	26.97	25.57	0.95	0.96	455	518	455	0.75 (0.70; 0.79)	0.745 (0.70; 0.79)
Prospect women	26.97	26.87	0.95	0.92	1286	1989	1286	0.70 (0.67; 0.73)	0.70 (0.67; 0.73)

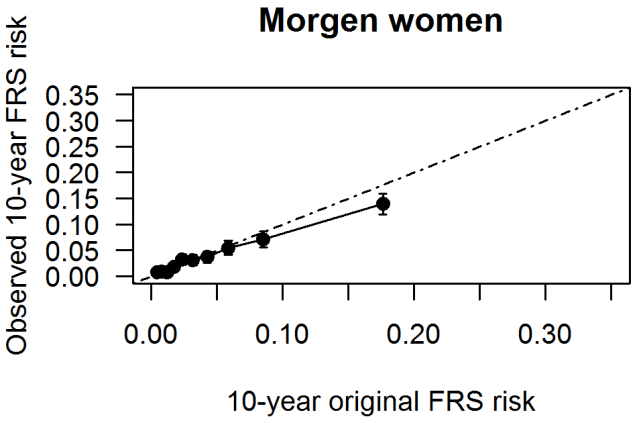


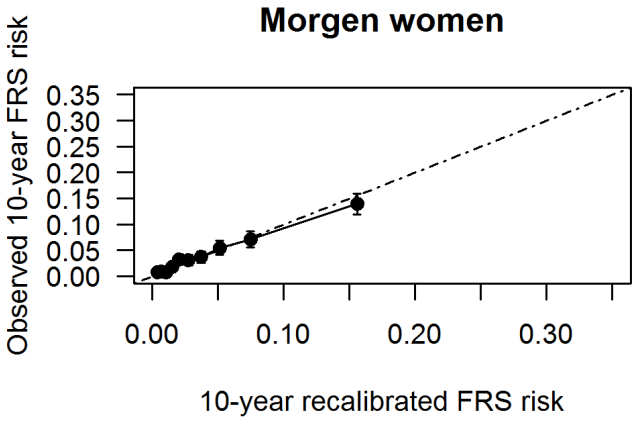


Appendix 2 - Figure 1: Calibration plot for Prospect individuals









Appendix 2 - Figure 2: Calibration plot for Morgen individuals

3. Information on the estimation of CVD burden

The impact ($I_{i,j}$), in terms of QALY loss, when an event predicted by model *j* occurs in individual i is given by

$$I_{i,j} = \left(\sum_{n=age_i}^{age_i+LE_i} QoL_n \right) * \sum_{k=1}^{\Theta} \left(\pi_{i,k,j} * (1 - u_k) \right)$$

with the number of individual components Θ under consideration, average life expectancy LE_i after surviving an event with remaining quality of life QoL_n, utility u_k and probability $\pi_{i,k,j}$ that an event predicted by prediction model j is of a specific type *k*.
Here, the left component represents the remaining life years – adjusted for their quality – in the absence of CVD events. The right component represents the total expected loss in quality of life due to all predicted CVD events in model *j*. Note that $\pi_{i,k,j}$ is zero for any type of event *k* not included in the composite endpoint of model *j*.
The baseline quality of life of individual i with age n is given by [4,5]

$$QoL_n = -0.00425 * n + 1.06$$

The formula for the expected CVD burden of disease ($BD_{i,j}$) is given by

$$BD_{i,j} = I_{i,j} * r_{i,j}$$

where $r_{i,j}$ is the recalibrated predicted risk for individual i and prediction model j.

For example, the CVD burden estimate of a 59 year old man was 0.9 QALYs, resulting from a 20.8% 10-year CVD risk and health related consequences equal to losing 4.2 QALYs when CVD events occurred. Here, the loss of 4.2 QALYs was calculated from a life expectancy of 20.4 years, adjusted for decrease in quality of life with age (first part of the impact equation), multiplied with the expected impact when a CVD event occurred (second part of the equation). This expected impact is the summation of the expected impact of all 14 CVD event types we observed in the data. For each event type, there was a disutility (Appendix 3 - Table 1) and marginal probability, i.e. the probability that a specific event type occurred given occurrence of CVD. All these 14 marginal probabilities summed up to 1 and were determined by dividing the number of observed events (for that event type) with the total number of observed event (all types). The marginal probabilities were determined per cohort and age group, and separate for gender.

Appendix 3 - Table 1: Utility values [6]

Morbidity	Utility	Disutility
Myocardial infarction (MI)	0.88	0.12
Other Coronary heart disease (OCHD)	0.88	0.12
Cardiac arrest	0.81	0.19
Ischemic stroke (CVAI)	0.63	0.37

Hemorrhagic stroke (CVAH)	0.63	0.37
Other stroke (OCVA)	0.63	0.37
Other Cardiovascular diseases (OCVD)	0.68	0.32
Mortality		
All CVD event types	0	1

Side effect of the preventive treatment were chosen as known as the side effects of statins, see Appendix 3 - Table 2 for details.

Appendix 3 - Table 2: Side effects of preventive treatment [7]

Side effect	**Probability**	**Health loss (utility)**
Minor	0.18	2 days of lost life
Major	1/18000	14 days of lost life
Death, given major side effects	0.09	

4. Information of the combined cohort

Appendix 4 - Table 1 shows baseline information of the combined cohort, separately for men and women. Although women were older and had higher total cholesterol, men were less healthy regarding the other risk factors. Men more often had diabetes, smoked more often, used more preventive treatment medication and had a slightly higher blood pressure. The event distribution for men and women varied substantially between men and women, as shown in Appendix 4 - Table 2. The percentage of non-fatal strokes was higher for women whereas men had more myocardial infarctions. Additionally, the percentage of observed fatal events in men was higher than in women.

Appendix 4 - Table 1: Baseline characteristics of the combined cohort

	Men	Women
Number individuals	16241	31228
Age (SD)	49.82 (13.48)	51.9 (11.65)
Total cholesterol (SD)	199.97 (46.42)	222.05 (45.87)
High density lipoprotein (SD)	45.44 (12.14)	57.69 (15.35)
Using preventive treatment	22%	16%
Systolic blood pressure (SD)	132.11 (19.52)	128.67 (21.03)
Smoking	33%	28%
Diabetes	11%	7%
Follow up Time (min-max)	12.07 (0.00-17.97)	13.58 (0.00-17.97)

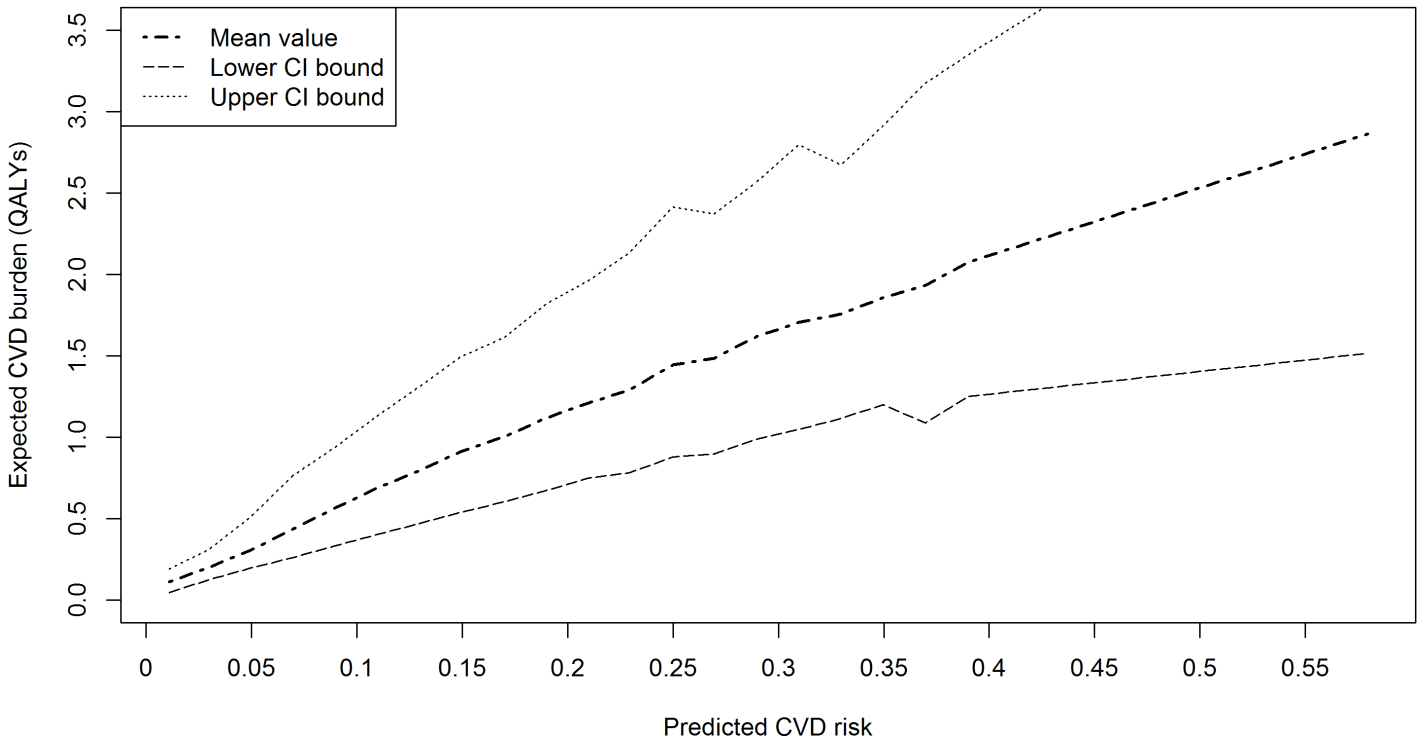
Appendix 4 - Table 2: Observed event distribution for the combined cohort

	Men (n=16241)		Women (n=31228)	
	N	%	N	%
Morbidity				
Myocardial infarction (MI)	451	27	330	16.3
Other Coronary heart disease (OCHD)	290	17.4	613	30.3
Cardiac arrest	10	0.6	9	0.4
Ischemic stroke (CVAI)	304	18.2	352	17.4
Hemorrhagic stroke (CVAH)	13	0.8	84	4.2
Other stroke (OCVA)	29	1.7	51	2.5
Other Cardiovascular diseases (OCVD)	136	8.1	347	17.2
Mortality				
Myocardial infarction (MI)	53	3.2	59	2.9
Other Coronary heart disease (OCHD)	5	0.3	6	0.3
Cardiac arrest, sudden death	148	8.9	54	2.7
Ischemic stroke (CVAI)	20	1.2	11	0.5
Hemorrhagic stroke (CVAH)	2	0.1	13	0.6
Other stroke (OCVA)	1	0.1	23	1.1
Other Cardiovascular diseases (OCVD)	208	12.5	69	3.4

Total number of events (up to 10 years)	1670	2021
Percentage fatal events	26.2%	11.6%
Prevalence events	10.3	6.5

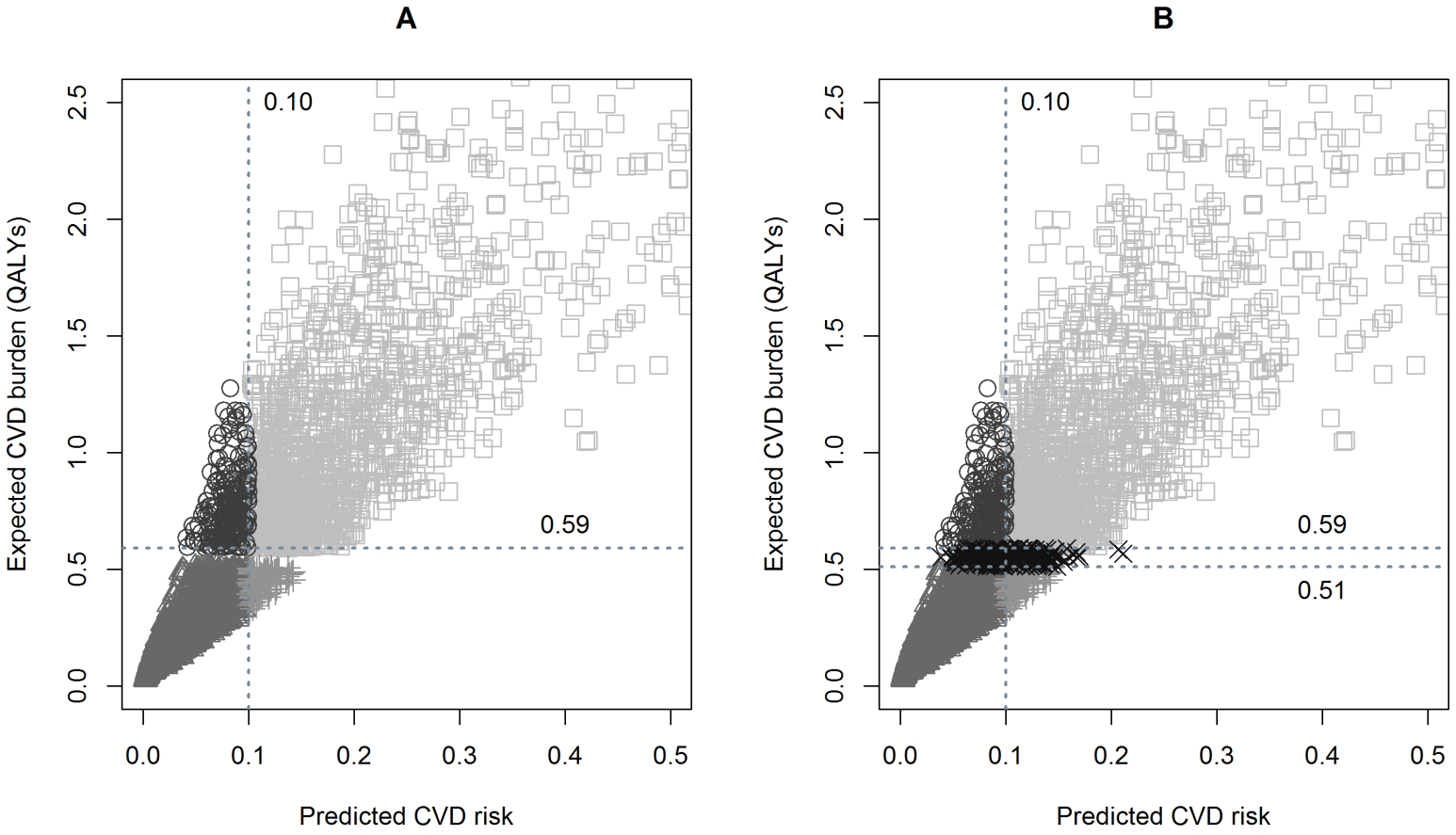
5. CVD risk and CVD burden

The variation in CVD burden increases with CVD risk. Individuals with an absolute small CVD risk are similar, where high risk individuals have a large variation in CVD burden due to the health consequences of CVD events.



Appendix 5 - Figure 1: The average CVD burden estimates per risk group where all predicted risk estimates are divided in groups of 2% and plotted on 1%, 3%, etc. The dotted lines present the 5th- and 95th-percentile values of the burden estimates per risk group risks in each group and not the confidence intervals for the expected mean CVD risk estimates.

6. Investigated scenarios



Appendix 6 - Figure 1: Scatterplot of the predicted CVD risk and expected CVD burden. For clarity, only 10% of the individuals were plotted (random sample). Plot A shows the scenario 1 and 2, with individuals selected according to scenario 1 presented by the plus (+) and squared (□) signs, and individuals selected according to scenario 2 presented by the squared (□) and circle (○) signs (# individuals = 15.263). Plot B shows scenario 3 and 4, with individuals considered for scenario 3 presented by the plus (+), squared (□), and circle (○) signs, and individuals considered for scenario 4 presented by the cross (x), circle (○), and squared (□) signs. The grey dotted lines represent the risk threshold of 10%, and a burden threshold of 0.59 and 0.51 QALYs (only plot B).

7. Gender differences

Results on the selection and impact part, separate for men and women, are shown in Appendix 7 - Table 1 and Appendix 7 - Table 2. The numbers in these tables correspond with **Error! Reference source not found.**, where columns "average risk" and "average CVD burden" corresponds with the values on the y axis of the bars in **Error! Reference source not found.**(upper and lower part). For example, men from the age group "35-45 years" have an average risk and burden of 0.15 and 1.25, based on scenario 1. Moreover, the increase in risk over age, shown in **Error! Reference source not found.**, can also been seen in the tables below, together with the difference in predicted risk for men and women. Men have on average a higher predicted CVD risk and burden for all age groups compared to women. Furthermore, Appendix 7 - Table 1 and Appendix 7 - Table 2 show that the percentage of selected individuals per age group increases with age, hence, selection of high risk individuals in general means selection of older individuals. Additionally, more older men are selected for preventive treatment compared to women from the same age group, for example, 82% vs 33% for age group "55-65" years of the men and women, respectively.

For scenario 2, i.e. burden based selection, the same number of individuals were selected but the percentage of man versus women and the percentages of selected individuals per age groups changes. There is an increase in the proportion of younger individuals and a decrease in the proportion of older individuals selected. The switch in selected individuals results in higher burden estimates for each age group and thus a health gain of 217 QALYs according to scenario 2 compared to scenario 1.

Apart from differences in CVD risk, and in the distribution of CVD event types, experienced by men and women, the reduction in health-related quality of life (i.e. disutility) when experiencing a particular CVD event may also be different for men and women. Technically, it is straightforward to account for different utilities of men and women in models such as the one used here. The same goes for gender-specific burden threshold values. However, the societal acceptance of such gender-specific threshold values for treatment requires further investigation of ethical and social considerations.

Appendix 7 - Table 1:Impact of statin treatment when selecting male individuals based on A) risk threshold of 10% and B) burden threshold of 0.59 QALYs according to FRS.

MEN	Selection			Impact			Selection			Impact	
A: Risk based selection	Total selected individu-als (%)	Average CVD risk	Average estimated CVD burden (QALYs loss)	With preventive treatment (QALYs loss)	Gain in QALYs	**B: Burden based selection**	Total selected individu-als (%)	Average CVD risk	Average estimated CVD burden (QALYs loss)	With preventive treatment (QALYs loss)	Gain in QALYs
15-25	34 (4.9 %)	0.19	1.95	1.27	0.68		51 (7.4%)	0.15	1.57	1.02	0.55
25-35	122 (6.6 %)	0.16	1.42	0.92	0.5		207 (11.2%)	0.13	1.13	0.74	0.4
35-45	485 (15.2 %)	0.15	1.25	0.81	0.44		910 (28.6%)	0.12	1.00	0.65	0.35
45-55	2221 (49.2 %)	0.17	1.13	0.73	0.39		2521 (55.8%)	0.16	1.09	0.71	0.38
55-65	3127 (82.4 %)	0.21	1.26	0.82	0.44		3019 (79.6%)	0.21	1.3	0.85	0.45
65-75	1777 (99.0 %)	0.34	1.78	1.16	0.62		1762 (98.1%)	0.34	1.8	1.17	0.63
75-85	417 (100%)	0.54	2.07	1.34	0.72		417 (100%)	0.54	2.07	1.34	0.72
Total	*8182 (50.4%)*	*0.24*	*11320 (1.38)*	*7362 (0.90)*	*3958 (0.48)*		*8887 (54.7%)*	*0.23*	*11937 (1.34)*	*7764 (0.87)*	*4174 (0.47)*

Appendix 7 - Table 2: Impact of preventive treatment when selecting female individuals based on A) risk threshold of 10% and B) burden threshold of 0.59 QALYs according to FRS.

WOMEN	Selection			Impact			Selection			Impact	
A: Risk based selection	Total selected individu-als (%)	Average CVD risk	Average estimated CVD burden (QALYs loss)	With preven-tive treat-ment (QALYs loss)	Gain in QALYs	**B: Burden based selection**	Total selected individu-als (%)	Average CVD risk	Averag e estimat ed CVD burden (QALYs loss)	With preven-tive treat-ment (QALYs loss)	Gain in QALYs
15-25	30 (3.1%)	0.18	2.1	1.37	0.74		65 (6.7%)	0.12	1.46	0.95	0.51
20-35	59 (2.4%)	0.16	1.55	1.01	0.54		163 (6.5%)	0.11	1.05	0.68	0.37
35-45	154 (4.4%)	0.15	1.95	1.27	0.68		491 (13.9%)	0.10	1.22	0.80	0.43
45-55	12127 (11.3%)	0.16	1.15	0.75	0.4		1586 (14.7%)	0.14	1.08	0.70	0.38
55-65	3249 (33.1%)	0.17	0.95	0.62	0.33		2486 (25.4%)	0.19	1.11	0.72	0.39
65-75	2188 (64.3%)	0.21	0.92	0.6	0.32		1414 (41.5%)	0.26	1.17	0.76	0.41
75-85	184 (99.5%)	0.41	1.19	0.77	0.42		171 (92.4%)	0.43	1.24	0.81	0.43
Total	*7081 (22.7%)*	*0.19*	*7191 (1.02)*	*4675 (0.66)*	*2516 (0.36)*		*6376 (20.4%)*	*0.19*	*7195 (1.13)*	*4678 (0.73)*	*2517 (0.39)*

8. Differences in cohorts

Results on the selection and impact, separate for cohorts, are shown in Appendix 8 - Table 1, Appendix 8 - Table 2, and Appendix 8 - Table 3. The different combined cohorts have a large variation in risk estimates hence we used a relative risk threshold of 10% rather than an absolute risk threshold. In other words, individuals with the highest 10% risk and highest 10% burden estimates were selected and compared among each other.

Across all cohorts, the selection of high risk individuals, i.e. scenario 1, in general means selection of older individuals. Additionally, more men are selected for preventive treatment compared to women.

For scenario 2, i.e. relative burden threshold, exactly the same number of individuals was selected but the percentage of man versus women and the average age of the selected individuals changes. There is an increase in the proportion of younger individuals and women selected resulting in higher burden estimates for each cohort and thus a health gain of 109 (8.6%), 20 (2.6%), and 15 (2.4%) QALYs according to scenario 2 compared to scenario 1, according to the SMART, Morgen, and Prospect cohort.

Appendix 8 - Table 1: Impact of preventive treatment when selecting individuals from SMART cohort based on A) relative risk threshold of 10% and B) relative burden threshold of according to SMART risk score.

A: Scenario 1 - risk based strategy								
	Selection					**Impact**		
	Total selected individuals (%)	Average age (SD)	Average CVD risk	Expected number of events	Estimated CVD burden (QALYs lost)	With preventive treatment (QALYs lost)	Expected number of events	Gain in QALYs
Men	868 (81.5%)	70.6 (7.1)	0.63	545	2698 (3.1)	1754 (2.0)	354	944 (1.1)
Women	197 (18.5%)	70.1 (9.1)	0.61	120	598 (3.0)	389 (2.0)	79	209 (1.1)
Men and Women	1065 (100%)	70.5 (7.5)	0.62	666	3296 (3.1)	2143 (2.0)	433	1153 (1.1)
B: Scenario 2 - burden based selection								
	Selection					**Impact**		
	Total selected individuals (%)	Average age (SD)	Average CVD risk	Expected number of events	Estimated CVD burden (QALYs lost)	With preventive treatment (QALYs lost)	Expected number of events	Gain in QALYs
Men	841 (79.0%)	65.0 (10.2)	0.59	497	2810 (3.3)	1827 (2.1)	323	983 (1.2)
Women	224 (21.0%)	57.7 (12.1)	0.48	107	796 (3.6)	518 (2.3)	69	279 (1.2)
Men and Women	1065 (100%)	63.5 (11.0)	0.53	603	3606 (3.4)	2345 (2.2)	392	1261 (1.2)
Total difference								**109 (8.6%)**

Appendix 8 - Table 2: Impact of preventive treatment when selecting individuals from Morgen cohort based on A) relative risk threshold and B) relative burden threshold according to FRS.

A: Scenario 1 - risk based strategy								
	Selection					**Impact**		
	Total selected individuals	Average age (SD)	Average CVD risk	Expected number of events	Estimated CVD burden (QALYs lost)	With preventive treatment (QALYs lost)	Expected number of events	Gain in QALYs
Men	1558 (76.2%)	55.1 (5.3)	0.23	351	1656 (1.1)	1077 (0.7)	228	580 (0.4)
Women	485 (23.7%)	56.8 (4.7)	0.21	102	500 (1.0)	325 (0.7)	67	175 (0.4)
Men and Women	2043 (100%)	55.5 (5.2)	0.22	454	2156 (1.1)	1402 (0.7)	295	755 (0.4)
B: Scenario 2 - burden based selection								
	Selection					**Impact**		
	Total selected individuals	Average age (SD)	Average CVD risk	Expected number of events	Estimated CVD burden (QALYs lost)	With preventive treatment (QALYs lost)	Expected number of events	Gain in QALYs
Men	1543 (75.5%)	52.6 (6.4)	0.22	340	1687 (1.1)	1096 (0.7)	221	590 (0.4)
Women	500 (24.5%)	54.2 (6.2)	0.20	101	528 (1.1)	343 (0.7)	66	185 (0.4)
Men and Women	2043 (100%)	53.0 (6.3)	0.21	441	2215 (1.1)	1496 (0.7)	287	775 (0.4)
Total difference								**20 (2.6%)**

Appendix 8 - Table 3: Impact of preventive treatment when selecting individuals from Prospect cohort based on A) relative risk threshold and B) relative burden threshold according to FRS.

A: Scenario 1 - risk based strategy								
	Selection					**Impact**		
	Total selected individuals	Average age (SD)	Average CVD risk	Expected number of events	Estimated CVD burden (QALYs lost)	With preventive treatment	Expected number of events	Gain in QALYs
Women	1641 (100%)	62.9 (5.2)	0.24	390	1712 (1.0)	1112 (0.68)	253	599 (0.37)
B: Scenario 2 - burden based selection								
	Selection					**Impact**		
	Total selected individuals	Average age (SD)	Average CVD risk	Expected number of events	Estimated CVD burden (QALYs lost)	With preventive treatment	Expected number of events	Gain in QALYs
Women	1641 (100%)	60.6 (5.7)	0.23	380	1753 (1.1))	1139 (0.69)	247	614 (0.37)
Total difference								**15 (2.4%)**

9. CREW member list

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