

The Viborg Vascular (VIVA) randomised screening trial



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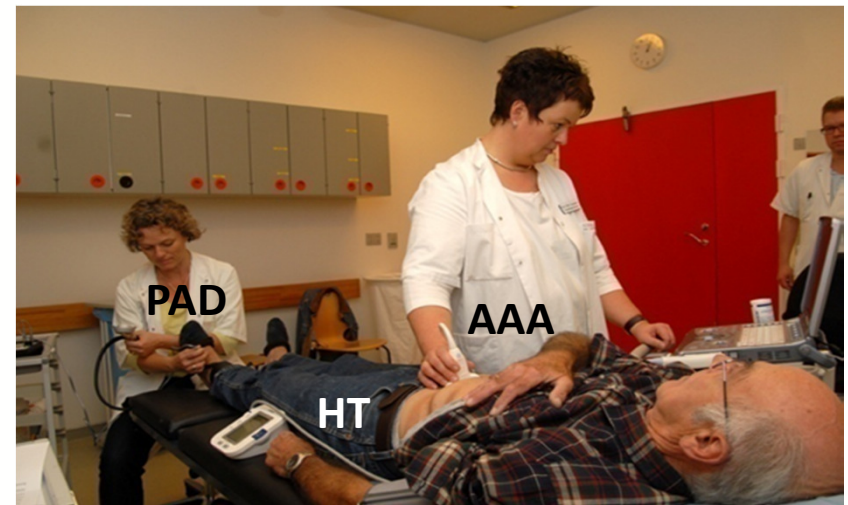
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Primary aim

- Screening for CVD hasn't caught much attention
- Primary to test whether *triple vascular screening* for AAA, PAD and hypertension reduces overall mortality in 65-74 year old men
- Sample size calculation ≈ 50.000
 - RCT 1:1 based upon a relative risk reduction of 5%
 - 2 x 23,604 ($\alpha=5\%$, $\beta=90\%$)



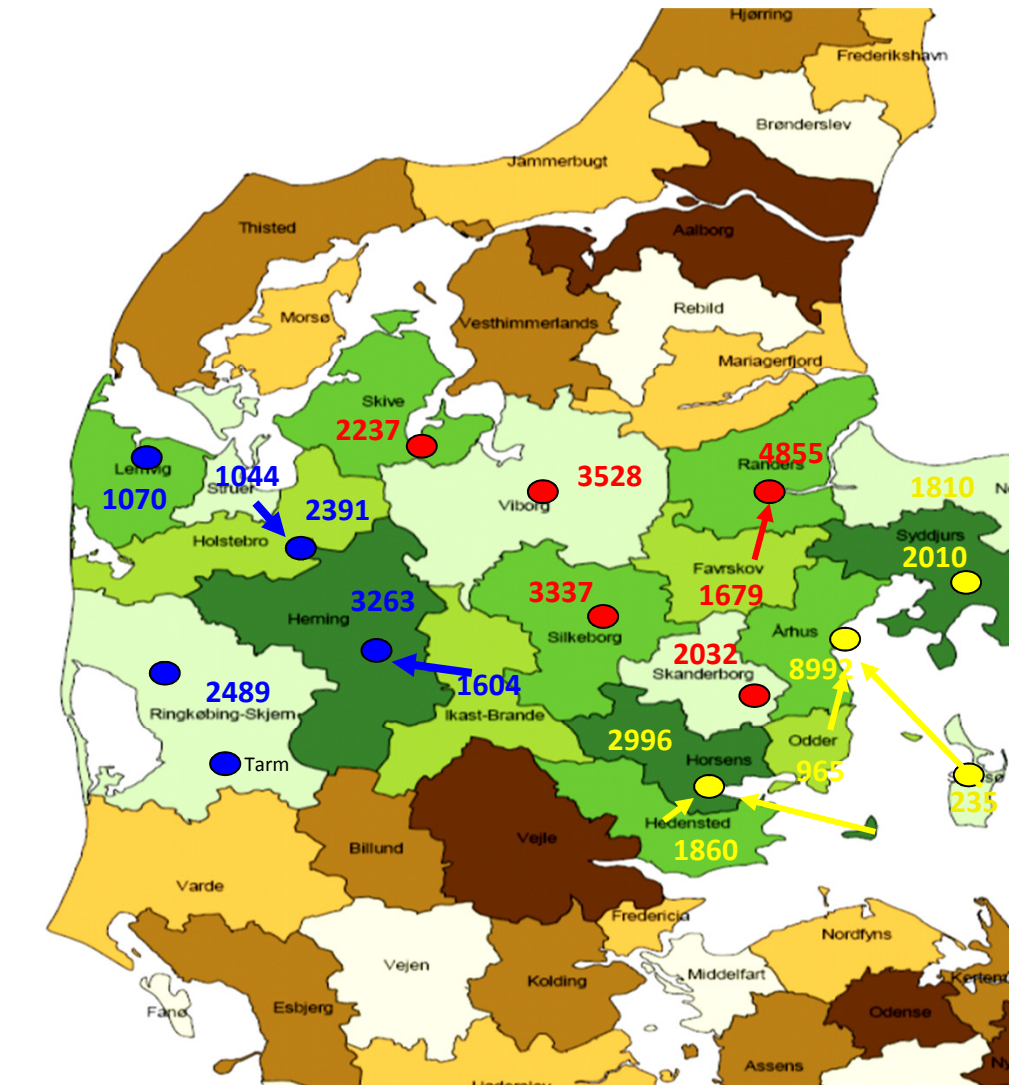
Triple vascular screening

Protocol: Grondal N, Sogaard R, Henneberg EW, Lindholt JS. The Viborg Vascular (VIVA) screening trial of 65-74 year old men in the central region of Denmark: study protocol. *Trials* 2010; **11**: 67.

Secondary aims

- Many, but particular for health policy makers
 - Cost effectiveness
 - QoL consequences (EQ-5D)
 - Harms (diabetes, intracerebral haemorrhage, renal failure, cancer, and 30 d postoperative mortality after cardiovascular procedures)





Enrollment 2008-2011

- *Central Region of Denmark* – 1.2 million inhabitant (>1/5 of the Danish population)
- No exclusions: **All 50,168 men randomised**
- Computerbased randomisation secured consent - stratified by the 16 municipalities
- The control group was masked
- Authors had no influence on- and were blinded for outcomes to date of analysis

- : Team East; 17,668
- : Team Mid; 17,636
- : Team West; 14,864

Organisation

- at 14 local hospitals/Health centres
- by 6 special-trained nurses
- in 3 mobile teams
- Abdominal US and Doppler-based ABI (Pic) + consultations of positive findings + controls
- Assisted by a secretary

Interventions of positive findings

- Men with an AAA (+30 mm)
- Men with PAD (ABI < 0.90 or > 1.4)



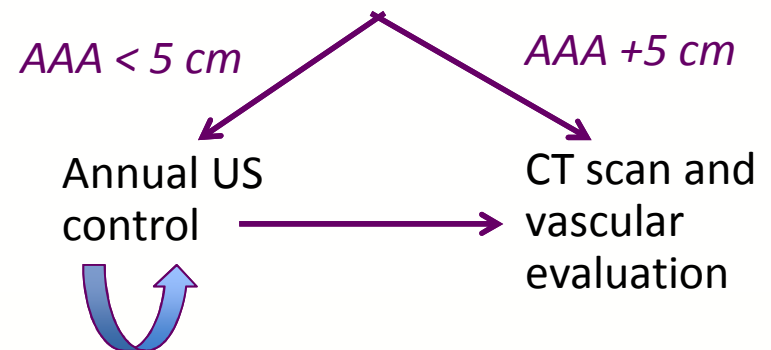
Nurse driven consultation for confirmation and initiation of preventive actions

- 75 mg Low dose aspirin
- 40 mg Simvastatin
- Instructions on diet, smoking cessation, and exercise.

Men with suspected moderate to severe hypertension (BP > 160/100 mmHG)



Referred for confirmation and treatment at G.P.



Attendance and prevalences

Attendance rate: 75%

Prevalence of positive findings

Abdominal aortic aneurysm

- 619 AAAs (3.3 %)
- 61 > 55 mm (10%) → 307 (49.6%) had repair within five years.

Peripheral arterial disease

- 2,073 with PAD (11 %) → 80 (4%) had repair for IC within five years.
- 1229 impaired walking distance (60 %)

33% with AAA/PAD (4% of all) initiated statin and/or aspirin

Possible hypertension

- 1,963 (10 %) with possible hypertension

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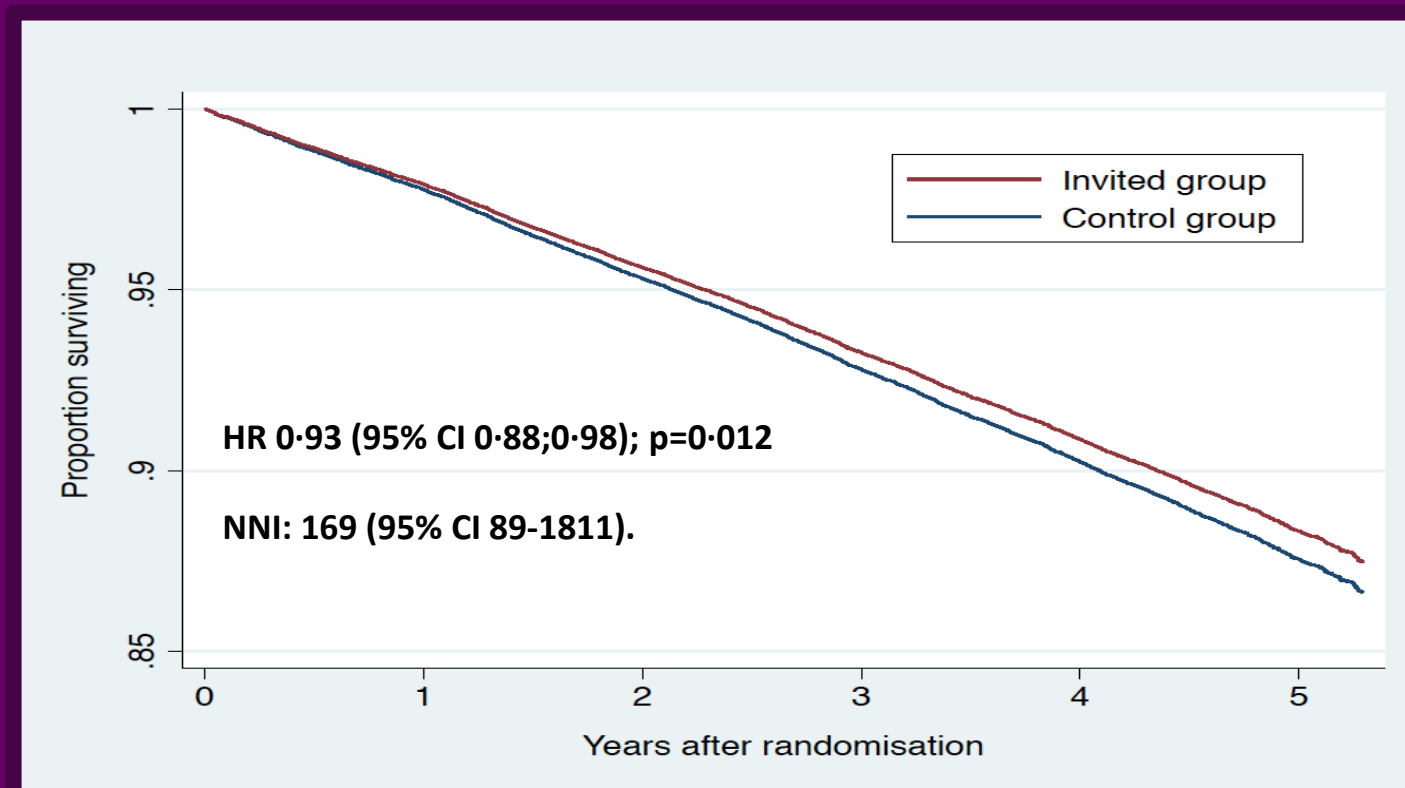
Baseline characteristics

Table 1: Baseline characteristics

	Control group	Invited group
Age (years)	69 (64-75)	69 (64-75)
Prescription medication during last year		
Antithrombotic agents	7426 (30%)	7479 (30%)
Lipid modifying agents	8863 (35%)	8904 (36%)
Antihypertensives and beta blocking agents	5635 (22%)	5475 (22%)
Drugs used in diabetes	2534 (10%)	2445 (10%)
Hospital admission during last 5 years		
Arterial hypertension	760 (3%)	744 (3%)
AMI	650 (3%)	685 (3%)
Ischemic heart disease ex. AMI	1638 (7%)	1643 (7%)
Peripheral occlusive arterial disease	269 (1%)	247 (1%)
Stroke or transient ischemic attack	753 (3%)	734 (3%)
Chronic obstructive pulmonary disease	692 (3%)	718 (3%)

Data are n (%) or mean (range). AMI=acute myocardial infarction.

Overall mortality



Cost effectiveness

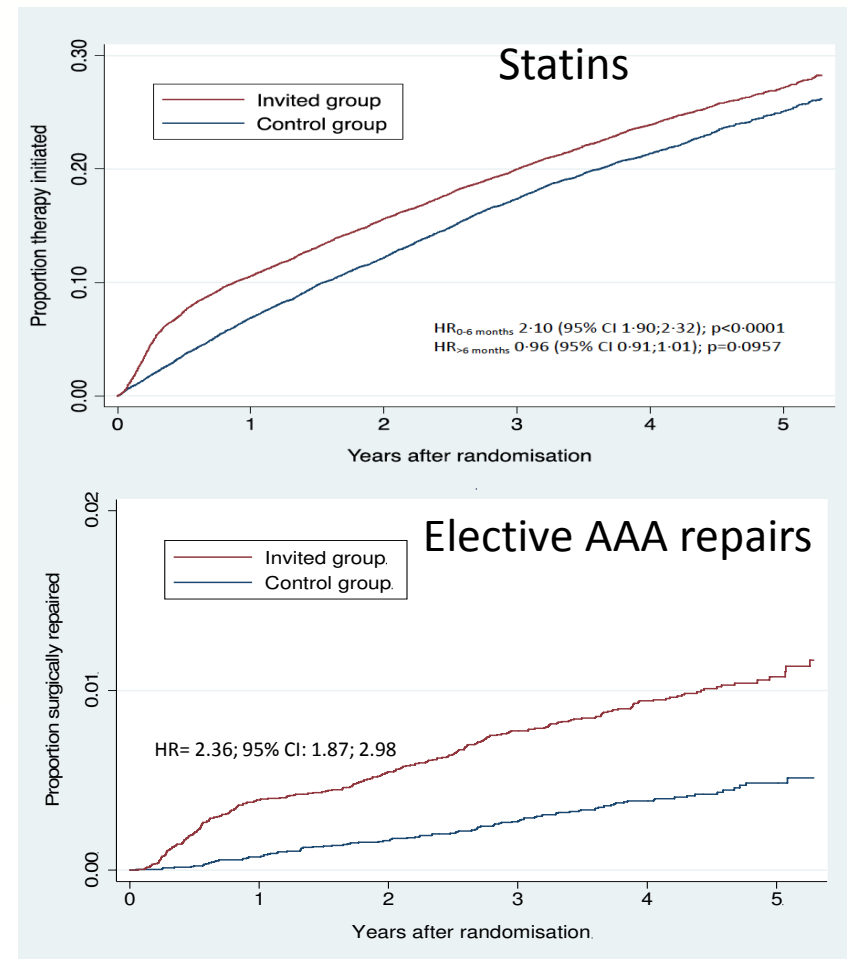
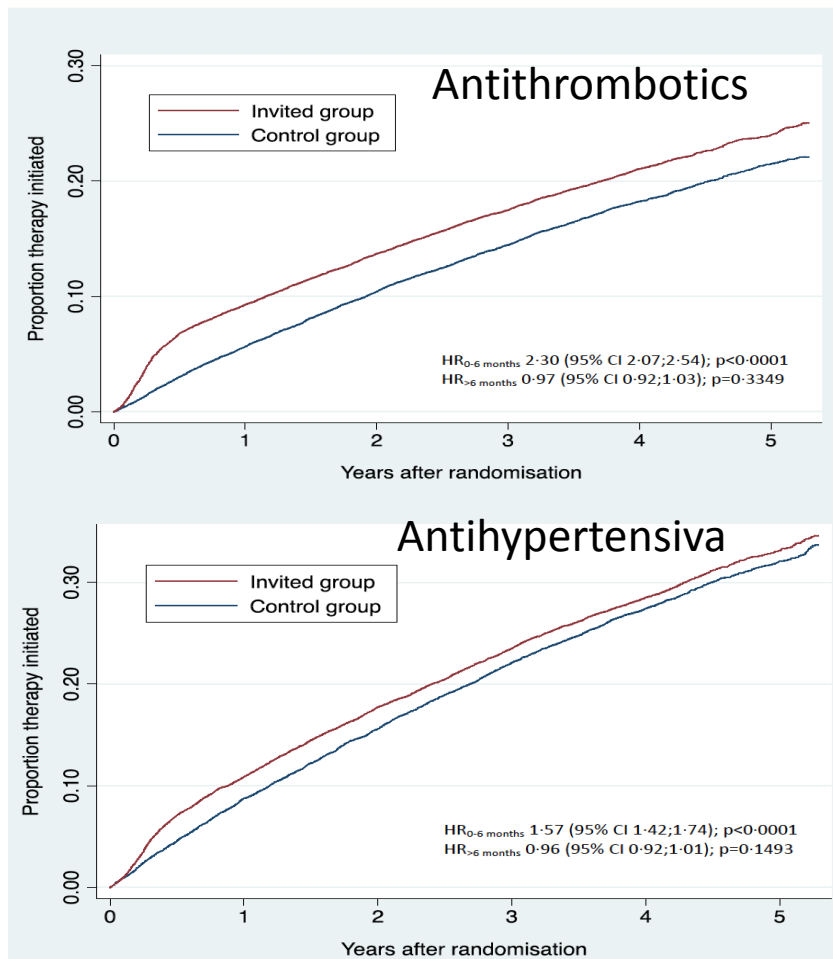
- Cost of screening: **€32** per invitee
incl. the invitation procedure, transportation costs, utensils, overhead costs, 75% work load and equipment
- Incremental cost of screening: **€148** (95% CI, -215 to 512) per invitee.
incl. screening, medication, GP consultations, out-and in-hospital contacts (incl. CVD surgery)

*Costs of a LY and a QALY gain were respectively
€6872 and €2148.*

- At a threshold for willingness to pay of €40 000, the probabilities for cost effectiveness were estimated at **98% and 99%**, respectively.

All based 2014 price year and 3.5% discounting

Initiation of preventive medication and surgery



No significant serious harms

Table 4: Adverse events

	Control group			Invited group			HR (95% CI)
	Person years	Number of events	Rate per 100000 person years (95% CI)	Person years	Number of events	Rate per 100000 person years (95% CI)	
Pharmacological therapy for diabetes							
Use initiated after baseline	91154	1376	1510 (1432 to 1591)	92503	1395	1508 (1431 to 1589)	1.00 (0.93 to 1.08)
Any use	91525	3779	4129 (3999 to 4263)	92836	3709	3995 (3869 to 4126)	0.98 (0.93 to 1.02)
Intracerebral haemorrhage	104028	146	140 (119 to 165)	105259	154	146 (125 to 171)	1.04 (0.83 to 1.31)
Renal failure	103006	668	649 (601 to 670)	104295	638	612 (566 to 661)	0.94 (0.85 to 1.05)
Cancer	9771	3637	3719 (3601 to 3842)	99142	3543	3578 (3457 to 3693)	0.96 (0.92 to 1.01)
Death within 30 days after surgery							
AAA repair	104245	10	9.59 (5.16 to 17.83)	105448	12	11.38 (6.46 to 20.04)	1.19 (0.51 to 2.75)
PAD repair	104245	3	2.88 (0.93 to 8.92)	105448	8	7.59 (3.79 to 15.17)	2.63 (0.70 to 9.93)
CABG	104245	4	3.84 (1.44 to 10.22)	105448	7	6.64 (3.16 to 13.92)	1.73 (0.51 to 5.90)
PCI	104245	28	26.86 (18.55 to 38.90)	105448	22	20.86 (13.74 to 31.69)	0.78 (0.44 to 1.36)
Total	104245	41	39.33 (28.96 to 53.42)	105448	47	44.57 (33.49 to 50.32)	1.13 (0.75 to 1.72)

NA=not applicable, AAA=abdominal aortic aneurysm, PAD=peripheral artery disease, CABG=coronary artery bypass graft, PCI=percutaneous coronary intervention, CVD=cardiovascular disease.

Quality of life

Baseline survey	All			Positive screening test					
				PAD (n=1963)			AAA (n=591)		
	Mean	SD	P-value	Mean	SD	P-value	Mean	SD	P-value
General index									
Attenders (n=18245)	·891	·001	<·001	·823	·182	<·001*	·859	·163	<·001*
Controls (n=821)	·870	·005							
Difference	·020	·005							
Anxiety/depression									
Attenders (n=18506)	·109	·002	·283	·157	·364	<·001*	·139	·346	·016*
Controls (n=828)	·121	·011							
Difference	·012	·011							
Longitudinal survey	Followed after positive screening test								
	All			PAD (n=1261/n=1306)			AAA (n=445/n=460)		
	Mean	SD	P-value	Mean	SD	P-value	Mean	SD	P-value
General index (n=1590)									
Before screening	·846	·004	<·001	·836	·005	<·001	·868	·007	·275
Before control	·862	·004							
Difference	·016	·003							
Anxiety/depression (n=1648)									
Before screening	·142	·009	·063	·146	·010	·046	·128	·016	·782
Before control	·127	·008							
Difference	·015	·063							

PAD= Peripheral artery disease, AAA=abdominal aortic aneurysm, SD=standard deviation.
 *=compared with attenders tested negative.

Overdiagnosing

Def.: not offered or do not accept prophylactic therapy causing net benefit in life expectancy

Of the 168 out of 169 invited men whose life will not be saved,
42 (25%) will decide not to participate in screening,
98 (58%) will be tested negative,
10 (6%) will be diagnosed and accept prophylactic therapy

18 (11%) will be potentially overdiagnosed



In breast cancer screening, between **19% and 57%** are estimated to be overdiagnosed

Ref. : Carter JL, Coletti RJ, Harris RP. Quantifying and monitoring overdiagnosis in cancer screening: a systematic review of methods. *Bmj* 2015; **350**: g7773

Overtreatment

Def.: undergoing treatment not causing a net benefit in life expectancy

10 out of the 169 men accepts prophylactic action,

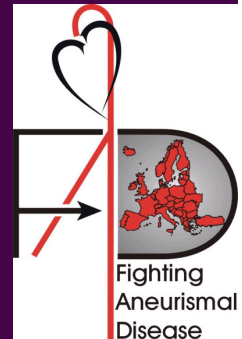
- 1 out of the 2 (**52%**) who undergo surgery
- or 8 out of the 9 (**88%**) who are treated pharmacologically will be overtreated.

For comparison, 5-7 preventive carotid TEAs are needed to save one life from death or major stroke in patients with symptomatic carotid stenosis.

Ref.: Orrapin S, Rerkasem K. Carotid endarterectomy for symptomatic carotid stenosis. *Cochrane Database Syst Rev* 2017; **6**: CD001081.

Vascular triple screening for 65-74 year old men

- 7% lower overall mortality
- 169 NNI
- € 2148 per gained QALY
- No serious negative side effects
(Postop deaths, CNS bleeding, DM, cancer, uraemia, QoL, overdiagnosing & overtreatment)
- *For clinicians:*
 - AAA & PAD patients ought to receive statins & antiplatelets
- *For health policy makers:*
 - Implement triple vascular screening of 65-74 year old men



Thanks for the attention

Details available online at *The Lancet*



The VIVA screening trial team 2008

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