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Adherence to Prescribed Drugs Among 65–74 Year Old Men Diagnosed with Abdominal Aortic Aneurysm or Peripheral Arterial Disease in a Screening Trial: A VIVA Substudy

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WHAT THIS PAPER ADDS

This is the first study to report adherence to preventive cardiovascular medication among 65–74 year old men diagnosed with abdominal aortic aneurysm or peripheral arterial disease in a multifaceted screening trial for cardiovascular disease. At the five year follow up, drug initiation and adherence to recommended cardiovascular preventive treatments were low among non-users of antiplatelet and statin treatment at screening. Drug adherence among users at screening exceeded 80%. The effectiveness of screening is, to some extent, offset by the poor fulfilment of preventive treatment. Research initiatives in future trials are required to increase initiation and persistence, especially among non-users at baseline.

Objective: Adherence to antiplatelet and statin therapy in participants diagnosed with abdominal aortic aneurysm (AAA) or peripheral arterial disease (PAD) was examined in a vascular screening trial.

Methods: This was a population based cohort study. The study population consisted of 65–74 year old men diagnosed with AAA or PAD in the Viborg Vascular (VIVA) multifaceted screening trial for CVD. Data from the VIVA screening cohort were linked to data from Danish registers from 2007 to 2016. Initiation of antiplatelet and statin treatment was measured within 120 days after screening. Persistence was defined as no treatment gap >100 days between two prescription renewals after screening. A proportion of days covered ≥80% over five years of follow up was used as a categorical cut off for adherence.

Results: Among the 18,748 screened participants, 618 with AAA and 2051 with PAD were identified. Among non-users at baseline, 65% and 62% initiated antiplatelet and statin treatment, 57% and 59% persisted with antiplatelet and statin use, and 60% and 57% were adherent, respectively. Among users at baseline, 73% and 69% had filled an antiplatelet or statin prescription, respectively, within 120 days after screening. Further, 79% and 73% persisted with their antiplatelet and statin treatment, and 89% and 83% were adherent, respectively.

Conclusion: In a vascular screening trial, six of every 10 non-users initiated preventive treatment; among these, the adherence rate was 57–60%. Among users at baseline, the five year adherence to antiplatelet and statin treatment exceeded 80%. The effectiveness of screening initiatives might be improved by measures to improve the fulfilment of preventive medication.

Keywords: Cardiovascular diseases, Medication adherence, Medication persistence, Registers, Screening, Secondary prevention
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INTRODUCTION

The prevalence and incidence of cardiovascular disease (CVD) have decreased over the last 20 years.[1,2] A contributing factor to the declining incidence is preventive pharmacological treatment, such as the use of antiplatelet and statin drugs, which reduces the risk of developing CVD in

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people with subclinical manifestations.[3–6] Screening for CVD is still controversial, and the benefits of such screening programs have been discussed intensively.[7–10] Recently, the Viborg Vascular (VIVA) multifaceted screening trial for CVD reported in *The Lancet* that screening for abdominal aortic aneurysm (AAA), peripheral arterial disease (PAD), and hypertension gave an absolute mortality risk reduction of 0.6% in favour of screening and a corresponding hazard ratio of 0.93 (95% confidence interval [CI] 0.88—0.99) after a median follow up of 4.4 years. The number needed to invite to screening to avoid one death was 169.[11] The incremental cost of a quality adjusted life years was estimated at €2148.[12] This could be linked to the initiation of preventive pharmacological treatment.[11] However, it is well established that adherence to preventive cardiovascular medication is suboptimal.[13] It is highly conceivable that some of the effects of cardiovascular screening trials are offset by suboptimal adherence among participants, which could affect the effectiveness of screening.

The aim of this study was to examine the initiation, persistence, and adherence to antiplatelet and statin therapy in patients with AAA and PAD diagnosed by population based screening in the VIVA trial.

MATERIALS AND METHODS

This population based cohort study was conducted using data from a randomised screening study carried out in the Central Denmark Region, Denmark (The VIVA screening trial conducted from October 2008 to January 2011)[11] and from several Danish registers and databases provided by The Health Data Board. The VIVA trial is registered at Clinical Trials.gov (NCT00662480, Biomedical Research), at the Ethics Committee of Central Denmark Region (journal number: M-20080028), and at the Danish Data Protection Agency (journal number: 1-16-02-1-08). All participants provided informed consent. Data from Statistics Denmark were anonymous, so individuals could not be identified.

Study population

The study population consisted of all participants diagnosed with AAA and PAD in the screening arm of the VIVA screening trial (2504 participants).[11] VIVA included all men from the Central Denmark Region aged 65—74 years who were randomised (1:1) to screening or no screening for vascular disease from 2008 to 2011. The screening included ankle brachial pressure index (ABI) and an ultrasound scan of the abdominal aorta performed by trained nurses. Participants who were diagnosed with AAA or PAD were offered a control measurement within one week to confirm the findings. The study nurse informed the participants about the findings, disease progression, and treatment, and about risk factors and suggestions for lifestyle changes. A prescription for statin and acetylsalicylic acid or clopidogrel was provided for three months of treatment, and participants were advised to renew the prescription via their general practitioner. Men with AAA were rescanned once a year, and men with PAD were checked for ABI one year after the screening session.

Self reported data

Participants completed a questionnaire at screening in order to provide information about their family history of CVD, diabetes mellitus (DM), hypertension, claudication, smoking, medication, and state of health using the generic health measurement tool, EuroQol-5D. The EuroQol-5D utility score captures five dimensions, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and gives a value on a visual analogue scale. Each question captures a three level score, weighted to Danish preferences, that increases with poorer quality of life.[14] Height and weight were self reported at screening.

Register data

The baseline data were linked, using the Central Person Register number for each person, to register data from the Central Person Registry and the Danish National Prescription Register (DNPR).[15,16] Information on vital and emigration status, including date of death or emigration, and socioeconomic and demographic information, was obtained via linkage with Statistics Denmark.[17] The DNPR contains information on all prescription drugs dispensed from all community pharmacies in Denmark since 1995.[18] All citizens in Denmark are covered by the national health insurance plan, and the cost of drugs is partially reimbursed. Pharmacies are required by law to register all prescriptions redeemed, including the strength of the drug unit, the package size, and the date of prescription redemption. All filled prescriptions are classified according to the Anatomical Therapeutic Chemical system and the defined daily dose. Statins were identified by the code C10AA. To accommodate switching between blood thinners without reclassification of exposure status, anti-thrombotic drugs were assigned the following code, which included antiplatelets and oral anticoagulants: acetylsalicylic acid B01AC06, clopidogrel B01AC04, dipyridamole B01AC07, prasugrel B01AC22, ticagrelor B01AC24, Asasantin SR B01AC30 and anticoagulants by Vitamin K antagonist B01AA, dabigatran etexilate B01AE07, rivaroxaban B01AF01, apixaban B01AF02, and edoxaban B01AF03. All antiplatelets and oral anticoagulants were grouped under “anti-thrombotic”. All prescription redemptions were identified from one year before screening and up to five years after screening, death, or emigration, whichever came first. Drugs that were bought over the counter or dispensed during a hospital stay are not included in the DNPR and were not included in the analysis.

Analysis of medicine adherence assumed a prescribed daily dose of one tablet per day for statins, acetylsalicylic acid, clopidogrel, warfarin, phenprocoumon, rivaroxaban, and edoxaban. Exposure to dipyridamole, dabigatran etexilate, apixaban, and ticagrelor was based on the assumption of two tablets prescribed per day. The end of follow up was five years after screening date, death, or emigration, whichever came first.

Data retrieved from Statistics Denmark included the participants' highest attained educational level, marital status, labour market status, and municipality.[15,17,19,20]

Socioeconomic indicators

Highest attained education was categorised into three groups: < 10 years, 10–12 years, and >12 years. Two groups, 12–14 years (bachelor level) and >14 years of education (master level), were merged owing to the low number of people having > 14 years of education. Employment was classified into three groups: working, early retirement, and age pension. Residential address was classified as rural or village area <1000 citizens, small provincial town 1000–9,999, and provincial town >10,000. Baseline variables included from the screening program were the participants' health state (EQ5-D0), body mass index, pain on walking, smoking (never, ex-, and current), comorbidity (history of diabetes, hypertension, acute myocardial infarction [AMI], angina), and user status at baseline of statins or antiplatelet/oral anticoagulant.

Outcome

For the fulfilment of medication, anti-thrombotics and statins were examined separately, stratified for user status at screening. Users were defined as having filled one or more prescriptions of the drug in question in the year before

Table 1. Baseline patient characteristics according to use of antithrombotic and statin treatment at baseline (n = 2504, all men)

Parameter	Antithrombotic treatment based on registry data on prescription redemptions			Statin treatment based on registry data on prescription redemptions		
	Non-users n = 851 (34)	Users n = 1653 (66)	p-value	Non-users n = 883 (33)	Users n = 1621 (68)	p-value
Mean ± SD age (y)	69 ± 2.8	70 ± 2.9	0.999	70 ± 2.8	70 ± 2.9	0.880
Body mass index (kg/m^2)[a,b]			<0.001			<0.001
<25	326 (39)	488 (30)		336 (39)	478 (30)	
25–30	378 (44)	763 (46)		386 (44)	755 (48)	
>30	132 (16)	372 (23)		148 (17)	356 (22)	
Smoking status[b]			<0.001			<0.001
Never smoker	113 (13)	183 (11)		127 (15)	169 (10)	
Ex-smoker	341 (40)	879 (53)		346 (39)	874 (54)	
Current smoker	394 (46)	590 (36)		407 (46)	577 (36)	
Screening detected diagnosis						
Abdominal aortic aneurysm	251 (29)	367 (22)	<0.001	244 (28)	374 (23)	0.013
Peripheral arterial disease	654 (77)	1397 (85)	<0.001	690 (78)	1361 (84)	<0.001
Comorbidity[b]						
Diabetes	73 (9)	344 (21)	<0.001	55 (6)	362 (22)	<0.001
Hypertension	335 (39)	1045 (63)	<0.001	349 (40)	1031 (64)	<0.001
Acute myocardial infarction[a]	17 (2)	430 (29)	<0.001	44 (6)	403 (28)	<0.001
Angina[a]	35 (4)	330 (22)	<0.001	59 (8)	307 (21)	<0.001
Present pain on walking	370 (43)	1000 (61)	<0.001	400 (46)	970 (60)	<0.001
Self-declared use of medication for cardiovascular disease[b]						
Antiplatelet[a]	83 (10)	1322 (85)	<0.001	229 (26)	1176 (78)	<0.001
Warfarin[a]	2 (0)	216 (14)	<0.001	60 (7)	158 (10)	<0.001
Statins[a]	193 (23)	1251 (77)	<0.001	23 (3)	1432 (89)	<0.001
Mean ± SD QoL[a,b]	0.85 ± 0.20	0.78 ± 0.24	<0.001	0.84 ± 0.20	0.78 ± 0.24	<0.001
Highest attained education (y)			0.069			0.418
<10	333 (39)	683 (41)		365 (41)	651 (40)	
10–12	411 (48)	811 (49)		417 (47)	805 (50)	
>12	107 (13)	159 (10)		101 (12)	165 (10)	
Employment			<0.001			0.003
Working	120 (14)	149 (9)		118 (13)	151 (9)	
Early retirement	67 (8)	127 (8)		75 (9)	119 (7)	
Age pension	664 (78)	1377 (83)		690 (78)	1351 (84)	
Home ownership	619 (73)	1054 (64)	<0.001	635 (72)	1038 (64)	<0.001
Living alone	161 (19)	361 (22)	0.094	184 (21)	338 (21)	0.984
Residential area (no. of inhabitants)			0.027			0.010
<1000	238 (28)	394 (24)		251 (29)	381 (23)	
1000–9999	250 (29)	472 (28)		256 (29)	466 (29)	
≥10,000	361 (42)	787 (48)		374 (42)	774 (48)	

User status was defined by prescription redemptions one year prior to screening, although the participant had self-reported use of the drug in question. Values are n (%) unless otherwise stated. AMI = acute myocardial infarction; BMI = body mass index; QoL = quality of life; SD = standard deviation; y = years.

[a] Valid observations <100%: BMI 98%, smoking status 99.8%, diabetes mellitus 99.5%, hypertension 99.6%, AMI 87%, angina 87%, pain present on walking 99.6%, antiplatelet 94%, warfarin 95%, statins 98%, QoL 96%, home ownership 99.9%, residential area 99.8%.

[b] Self-reported data.

screening, and non-users were defined as not having filled prescriptions the year prior the screening date: initiation was taken as the time from the date of screening to filling a prescription using the Aalen-Johansen method and accounting for competing risk of death. As the measure of initiation, the estimated probability of filling a prescription $\leq$120 days from the date of screening was used, accounting for a competing risk of death.

A supplementary analysis was performed for initiation within 90 days after the screening date.

For participants who initiated the drug in question, persistence was calculated as the time from the date of screening to the date on which the patient failed to refill a new prescription, which was defined as $>$ 100 days after the day on which the patient was expected to refill. As the measure of non-persistence, the estimated probability of having a medication gap of $>$100 days after the date of screening until death or end of follow up, whichever came first, was used. Proportional persistence was calculated by subtracting the proportion of non-persistence from 1.

For participants who initiated the drug in question, adherence was calculated as the proportion of days covered (PDC) and was measured from the date of screening for non-users and the date of the last redeemed prescription before screening for users at baseline, until death or end of follow up. As measures of adherence, the proportion of days covered among those who initiated treatment was reported. A PDC of $\geq$80% was considered good adherence.[21,22] Adherence for the whole cohort was also measured, assigning those who never initiated treatment a PDC of 0.

Statistical analysis

Frequency distributions for categorical variables and mean $\pm$ SD for continuous variables are reported. The binary outcomes were compared using Pearson's chi-square test and continuous outcomes were compared using an unpaired *t* test. Cumulative incidence proportions, adjusted for a competing risk of death, were estimated by the Aalen-Johansen method. Logistic regression models were used to identify predictors of initiation and adherence. Cox proportional hazard regression models were used to identify predictors of non-persistence. A 5% significance level and 95% CIs were used. Statistical analyses were performed using Stata MP 14.1 (StataCorp. College Station, TX, USA).

RESULTS

Among 18,748 screened participants in the VIVA screening arm, 618 participants with AAA and 2051 with PAD were identified, resulting in a total of 2504 participants with AAA and/or PAD. The distribution of baseline characteristics among participants is presented in Table 1.

Initiation

Fig. 1 shows the cumulative distribution of first prescriptions of anti-thrombotic and statin treatment after screening, stratified by non-user and user status of the drug in question at baseline. Among non-users at baseline, 65% (n = 554) redeemed an anti-thrombotic prescription within 120 days after screening, and 62% (n = 542) redeemed a statin prescription. Among users at baseline, 73% (n = 1204) redeemed an anti-thrombotic prescription, and 69% (n = 1116) redeemed a statin prescription within 120 days after screening (Table 2). Participants diagnosed with AAA had a higher proportion of initiators at baseline than participants diagnosed with PAD for anti-thrombotic treatment 82% (n = 251) vs. 60% (n = 654) and for statin treatment 75% (n = 244) vs. 58% (n = 690) (Table 2).

Persistence

Fig. 2 shows the cumulative distribution of persistence, stratified by treatment user status at screening. Among non-users at screening, 57% were persistent to anti-

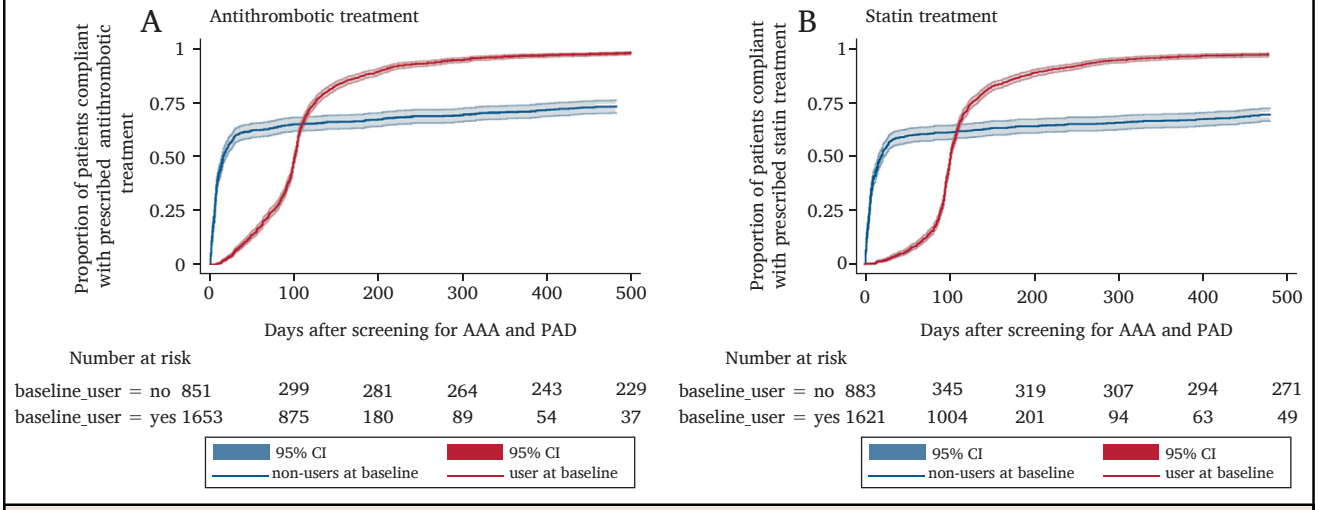

Figure 1. Time to first prescription fulfilment of anti-thrombotic (Panel A) and statin (Panel B) treatment after screening, stratified by users and non-users of the drug in question at baseline. CI = confidence interval; AAA = abdominal aortic aneurysm; PAD = peripheral arterial disease.

Table 2. Compliance with treatment across stages of prescription redemption for 2504 participants who were diagnosed with abdominal aortic aneurysm (AAA) or peripheral arterial disease (PAD) in a cardiovascular screening trial, stratified for user status at baseline

Assessment of compliance	Compliance with Antithrombotic treatment, % (95% CI)			Compliance with Statin treatment, % (95% CI)		
	Non-users at baseline $n = 851$	Users at baseline $n = 1653$	*p*-value	Non-users at baseline $n = 883$	Users at baseline $n = 1621$	*p*-value
Initiation ≤ 120 days	$n = 554$	$n = 1204$		$n = 542$	$n = 1116$	
Percentage of initiation ≤120 days	65 (62–68)	73 (71–75)	<0.001	62 (58–65)	69 (67–72)	<0.001
No. of screening detected AAA	$n = 251$	$n = 367$		$n = 244$	$n = 374$	
Percentage of initiation ≤120 days for AAA	82 (76–86) ($n = 205$)	71 (67–76) ($n = 262$)	0.003	75 (67–80) ($n = 182$)	68 (64–73) ($n = 256$)	0.100
No. of screening detected PAD	$n = 654$	$n = 1397$		$n = 690$	$n = 1361$	
Percentage of initiation ≤120 days for PAD	60 (56–64) ($n = 392$)	73 (70–75) ($n = 1015$)	<0.001	58 (55–62) ($n = 402$)	70 (67–72) ($n = 949$)	<0.001
Persistence[a] of initiation ≤ 120 days	$n = 554$	$n = 1204$		$n = 542$	$n = 1116$	
Percentage of persistence	57 (53–61) ($n = 316$)	79 (76–81) ($n = 950$)	<0.001	59 (55–63) ($n = 320$)	73 (70–75) ($n = 814$)	<0.001
No. of AAA initiators ≤120 days	n = 205	n = 262		n = 182	n = 254	
Percentage of persistence for AAA	60 (53–67) ($n = 123$)	77 (71–81) ($n = 201$)	<0.001	58 (50–65) ($n = 105$)	72 (67–78) ($n = 184$)	<0.001
No. of PAD initiators ≤120 days	$n = 392$	$n = 1015$		$n = 392$	$n = 1015$	
Percentage of persistence for PAD	56 (51–61) ($n = 220$)	80 (76–82) ($n = 813$)	<0.001	56 (51–61) ($n = 220$)	80 (76–82) ($n = 813$)	<0.001
Adherence (PDC ≥ 80%) of initiation ≤ 120 days	$n = 554$	$n = 1204$		$n = 542$	$n = 1116$	
Percentage of adherence	60 (56–65) ($n = 336$)	89 (87–90) ($n = 1069$)	<0.001	57 (53–61) ($n = 310$)	83 (81–85) ($n = 931$)	<0.001
No. of AAA initiators ≤120 days	$n = 205$	$n = 262$		$n = 182$	$n = 254$	
Percentage of adherence for AAA	66 (59–72) ($n = 135$)	88 (84–91) ($n = 231$)	<0.001	62 (54–68) ($n = 112$)	80 (75–84) ($n = 203$)	<0.001
No. of PAD initiators ≤120 days	$n = 392$	$n = 1015$		$n = 400$	$n = 941$	
Percentage of adherence for PAD	58 (53–63) ($n = 229$)	89 (87–91) ($n = 903$)	<0.001	56 (51–60) ($n = 222$)	84 (82–86) ($n = 791$)	<0.001
Adherence including non-initiators and non-persistence (PDC ≥ 80%)	$n = 851$	$n = 1653$		$n = 883$	$n = 1621$	
Percentage of adherence for all	43 (40–47) ($n = 368$)	80 (78–82) ($n = 1326$)	<0.001	38 (35–42) ($n = 338$)	73 (71–76) ($n = 1191$)	<0.001
No. of screening detected AAA	$n = 251$	$n = 367$		$n = 244$	$n = 374$	
Percentage of adherence for all AAA	58 (50–62) ($n = 140$)	80 (76–84) ($n = 294$)	<0.001	50 (43–56) ($n = 121$)	73 (69–78) ($n = 274$)	<0.001
No. of screening detected PAD	$n = 654$	$n = 1397$		$n = 690$	$n = 1.361$	
Percentage of adherence for all PAD	39 (36–43) ($n = 258$)	80 (75–82) ($n = 1115$)	<0.001	35 (32–39) ($n = 243$)	73 (71–76) ($n = 1000$)	<0.001

Follow-up ended five years after screen date, death or emigration whichever came first. Values are percentage (95% CI). PDC = proportion of days covered. CI = confidence interval.
[a] Percentage of initiation ≤120 days.

thrombotics, and 59% were persistent to statins. For users at baseline, the corresponding persistence levels were 79% and 73%, respectively (Table 2).

Adherence

Among non-users at baseline, adherence (PDC ≥ 80%) to anti-thrombotic treatment was 60% and to statin treatment 57% over the five years of follow up (Table 2). The corresponding figures for users at baseline were 89% and 83%, respectively (Table 2). Adherence for all participants, including non-initiators, was 43% to anti-thrombotics and 38% to statin treatment among non-users at baseline and was 80% and 73%, respectively, among users at baseline (Table 2).

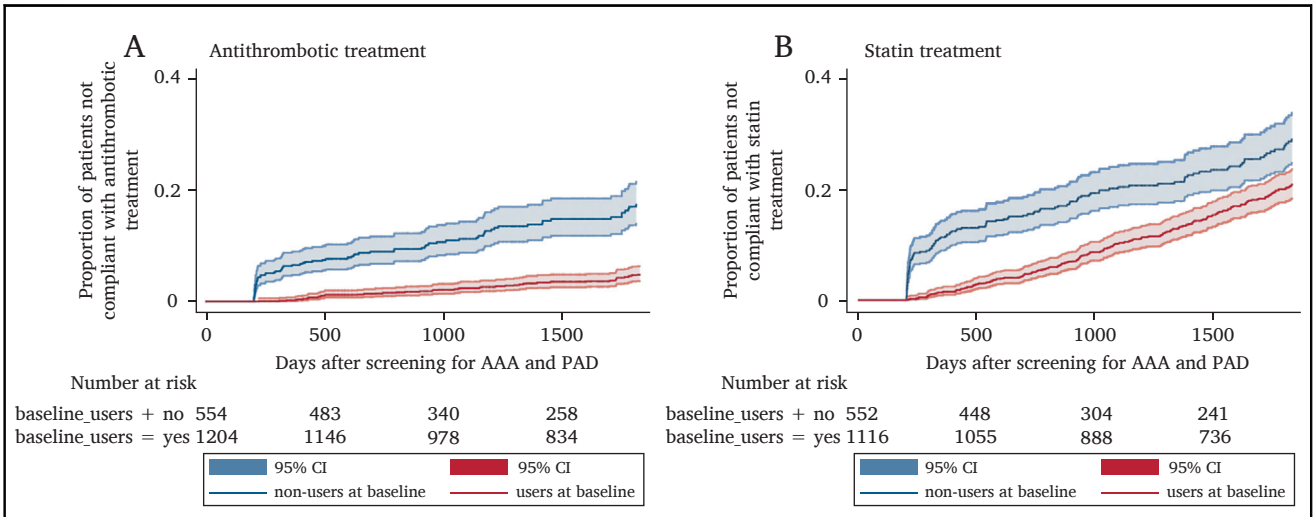

Figure 2. Proportion of non-persistence to anti-thrombotic (Panel A) and statin (Panel B) treatment after screening, stratified by users and non-users of the drug in question at baseline. Non-persistence was defined as a gap in medication use of more than 100 days. CI = confidence interval; AAA = abdominal aortic aneurysm; PAD = peripheral arterial disease.

Predictors of initiation

Predictors for initiation of anti-thrombotic treatment among non-users at screening were employment status (age pension group vs. the working group: adjusted odds ratio [aOR] 1.84, 95% CI 1.06—3.19) and living in a residential area (≥10,000 inhabitants vs. those living in rural settings: aOR 1.82, 95% CI 1.10—3.01).

Initiation of statin therapy was more likely among ex- and current smokers vs. never smokers (ex-smoker: aOR 2.15, 95% CI 1.22—3.77; present smoker: aOR 2.42, 95% CI 1.38—4.26) and for participants with self reported pain on walking at baseline (aOR 1.92; 95% CI 1.25—2.95). Non-users at baseline with DM were less likely to redeem the first statin prescription <120 days after screening (DM: aOR 0.27; 95% CI 0.13—0.55) (Table 3).

In a sensitivity analysis, the time window for initiation was shortened to 90 days (Table S1), but this did not substantially change any predictors (Table S2; see Supplementary Material).

Among users at baseline, current smokers, those with self reported pain on walking, and those with an education of 10—12 years were less likely to redeem the first statin prescription within 120 days (current smoker: aOR 0.52, 95% CI 0.31—0.87; pain at walking: aOR 0.70, 95% CI 0.52—0.94; education 10—12 years: aOR 0.66, 95% CI 0.50—0.87). No predictors of anti-thrombotics were found among users at baseline (data not shown).

Predictors of persistence

No predictors for persistence were found for non-users at baseline (Table S3; see Supplementary Material) or for users at baseline (data not shown).

Predictors of adherence

Non-users at screening with <10 years of education had better adherence to anti-thrombotics than did those with >12 years of education (education > 12 years: aOR 0.48, 95% CI 0.26—0.87) and people living in a provincial town with ≥10,000 inhabitants had a higher adherence to statins than did those living in rural settings (aOR 1.66, 95% CI 1.02—2.69) (Table 4).

For users at baseline, predictors of adherence to anti-thrombotic treatment within 120 days were history of AMI and current use of statin treatment (AMI: aOR 1.62, 95% CI 1.14—2.31; statin: aOR 1.98, 95% CI 1.44—2.71). The predictor of adherence to statin treatment was living in a provincial town with ≥10.000 inhabitants (aOR 1.70, 95% CI 1.05—2.75) (data not shown).

DISCUSSION

In this study, based on participants who were diagnosed with PAD or/and AAA at screening, six of every 10 non-users initiated preventive treatment, and among those adherence was 57—60%. Among users at baseline, the 5 year adherence to antiplatelet and statin treatment exceeded 80%.

A Swedish study, involving both women and men, aged 65—74 years, showed that adherence to statin treatment (PDC ≥ 80%) after a stroke was 77% over 2 years of follow up.[23] It was also reported that users of statins before the stroke were more adherent than new users (aOR 1.75, 95% CI 1.58—1.93). A Danish study among men aged 64—84 years who received treatment for hypertension and were without CVD or diabetes showed 81% persistence to statin treatment in a four year follow up, and 67.9% had PDC ≥80%.[24]

In the present study, the major characteristics associated with adherence were use of anti-thrombotic and statin treatment at baseline. Participants with a history of myocardial infarction were more likely to be adherent to anti-thrombotic treatment, which is in clear accordance with previous findings.[25] Non-users with DM at baseline initiated statin treatment less often. A likely reason for this

Table 3. Characteristics associated with initiation of anti-thrombotic and statin treatment within 120 days after screening among non-users at baseline

Characteristics at time of screening	Initiation of anti-thrombotic treatment within 120 days of screening among non-users at baseline (n = 851)		Initiation of statin treatment within 120 days of screening among non-users at baseline (n = 883)	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]
Each additional year after screening	0.98 (0.93–1.03)	0.96 (0.89–1.04)	0.99 (0.94–1.04)	0.98 (0.91–1.06)
Body mass index (kg/m^2)				
<25	Ref.	Ref.	Ref.	Ref.
≥25–30	0.96 (0.71–1.32)	1.03 (0.67–1.57)	1.00 (0.74–1.35)	1.16 (0.76–1.76)
>30	1.05 (0.68–1.61)	1.54 (0.81–2.93)	0.87 (0.58–1.28)	1.19 (0.66–2.14)
Smoking				
Never smoker	Ref.	Ref.	Ref.	Ref.
Ex-smoker	1.63 (1.06–2.50)	0.90 (0.46–1.71)	2.25 (1.48–3.40)	2.15 (1.22–3.77)
Current smoker	1.97 (1.28–3.02)	1.09 (0.58–2.07)	2.75 (1.83–4.14)	2.42 (1.38–4.26)
Screening detected diagnose				
Abdominal aortic aneurysm	3.21 (2.25–4.60)	1.67 (0.76–3.71)	2.25 (1.62–3.06)	1.65 (0.72–3.80)
Peripheral arterial disease	0.32 (0.21–0.47)	0.98 (0.41–2.35)	0.50 (0.35–0.71)	1.08 (0.44–2.67)
Comorbidity				
Diabetes	0.58 (0.36–0.94)	0.63 (0.31–1.25)	0.33 (0.19–0.58)	0.27 (0.13–0.55)
Hypertension	1.18 (0.88–1.57)	1.08 (0.71–1.63)	1.09 (0.82–1.44)	1.09 (0.73–1.64)
Acute myocardial infarction	0.45 (0.17–1.21)	0.43 (0.15–1.24)	0.40 (0.21–0.73)	0.67 (0.32–1.40)
Angina	1.60 (0.65–3.91)	2.05 (0.73–5.77)	0.49 (0.28–0.85)	0.78 (0.41–1.55)
Present pain on walking	1.03 (0.77–1.38)	1.38 (0.90–2.13)	1.55 (1.17–2.04)	1.92 (1.25–2.95)
Use of medication for cardiovascular disease				
Antiplatelet			0.59 (0.44; 0.81)	0.51 (0.32; 0.79)
Warfarin			0.64 (0.38; 1.08)	0.53 (0.26; 1.05)
Statins	1.06 (0.76–1.48)	0.90 (0.56–1.46)		
Quality of Life (per increment of 1)	2.95 (1.46–5.97)	4.20 (1.47–12.0)	2.53 (1.26–5.06)	2.63 (0.87–7.94)
Highest attained education (y)				
<10	Ref.	Ref.	Ref.	Ref.
10–12	0.98 (0.72–1.34)	0.86 (0.56–1.31)	1.00 (0.74–1.34)	0.80 (0.53–1.21)
>12	1.25 (0.78–2.00)	1.00 (0.54–1.85)	0.82 (0.53–1.29)	0.58 (0.32–1.04)
Employment				
Working	Ref.	Ref.	Ref.	Ref.
Early retirement	1.41 (0.76–2.63)	1.78 (0.70–4.50)	1.03 (0.57–1.86)	0.88 (0.37–2.09)
Age pension	1.46 (0.98–2.17)	1.84 (1.06–3.19)	1.23 (0.76–1.68)	1.04 (0.58–1.90)
Home ownership	1.11 (0.81–1.52)	0.96 (0.60–1.54)	1.15 (0.85–1.55)	1.13 (0.73–1.77)
Living alone	1.00 (0.70–1.43)	0.98 (0.59–1.64)	0.80 (0.58–1.12)	0.89 (0.54–1.46)
Residential area no. of inhabitants				
<1000	Ref.	Ref.	Ref.	Ref.
1000–9999	1.03 (0.71–1.48)	0.90 (0.54–1.49)	0.83 (0.58–1.19)	0.73 (0.44–1,21)
≥10,000	1.35 (0.96–1.91)	1.82 (1.10–3.01)	0.93 (0.67–1.29)	0.87 (0.53–1.42)

OR = odds ratio; CI = confidence interval; y = years.
[a] Mutually adjusted for all variables.

lack of adherence could be previous exposure to statin and refusal of re exposure because of a history of side effects or fear of side effects influenced by negative information about statins from the media.[26]

The study findings concur with previous reports that socioeconomic status does not predict adherence.[23,27,28]

The major strength of this study is its population based design, which increases its external validity. Death and emigration status are linked to the civil person registration number, which secures a complete follow up.[15] The Danish National Prescription Register has complete capture of all prescriptions of reimbursed drugs.[18]

There was no information on participants' attitudes to being medicated and there was no history of medication side effects before the screening session. Low dose acetylsalicylic acid is available over the counter, and over the counter deliveries are not reported to the data sources used herein. However, according to the Danish Medicines Agency, only 9% of low dose acetylsalicylic acid is sold over the counter without a prescription (www.medstat.dk). For most anti-thrombotic treatment, treatment is planned with standard doses, so the treatment period from the dispensed quantity could be inferred. Participants with AMI or undergoing coronary revascularisation in the follow up period may have received dual or triple anti-thrombotic treatment, which may inflate the PDC level. Therefore it is possible that some participants were misclassified with respect to PDC.

Table 4. Characteristics associated with five year adherence (proportion of days covered [PDC] ≥ 80%) to anti-thrombotic and statin treatment among non-users at baseline who initiated treatment ≤ 120 days after date of screening

Characteristics at time of screening	Characteristics of adherence to anti-thrombotic treatment among non-users at baseline (n = 554)[b]		Characteristics of adherence to statin treatment among non-users at baseline (n = 542)[b]	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]
Each additional year after screening	1.02 (0.96–1.09)	1.03 (0.95–1.11)	0.97 (0.92–1.04)	0.94 (0.87–1.01)
Body mass index (kg/m^2)				
<25	Ref.	Ref.	Ref.	Ref.
≥25–30	1.30 (0.90–1.89)	1.14 (0.74–1.76)	1.24 (0.85–1.80)	1.08 (0.71–1.65)
>30	1.44 (0.86–2.41)	1.03 (0.56–1.89)	1.47 (0.88–2.47)	1.25 (0.69–2.27)
Smoking				
Never smoker	Ref.	Ref.	Ref.	Ref.
Ex-smoker	1.59 (0.89–2.84)	1.21 (0.62–2.35)	1.47 (0.80–2.68)	1.37 (0.69–2.71)
Current smoker	1.10 (0.63–1.93)	0.94 (0.49–1.51)	0.99 (0.55–1.78)	1.11 (0.57–2.18)
Screening detected diagnose				
Abdominal aortic aneurysm	1.41 (0.98–2.01)	1.57 (0.74–3.34)	1.29 (0.89–1.85)	1.40 (0.68–2.89)
Peripheral arterial disease	0.73 (0.50–1.08)	0.94 (0.42–3.34)	0.77 (0.52–1.14)	1.09 (0.50–2.41)
Known comorbidities				
Diabetes	1.51 (0.74–3.05)	1.01 (0.46–2.22)	3.10 (1.01–9.41)	3.59 (0.97–13.26)
Hypertension	1.68 (1.18–2.39)	1.46 (0.97–2.21)	1.25 (0.88–1.77)	0.98 (0.66–1.47)
Acute myocardial infarction	0.63 (0.18–2.22)	0.49 (0.11–1.77)	1.18 (0.50–2.78)	0.89 (0.34–2.34)
Angina	1.45 (0.65–3.26)	1.61 (0.66–3.94)	1.45 (0.72–2.93)	1.49 (0.65–3.40)
Present pain on walking	0.75 (0.53–1.05)	0.81 (0.52–1.24)	0.70 (0.50–0.98)	0.68 (0.45–1.05)
Use of medication for cardiovascular disease				
Antiplatelet			1.17 (0.77–1.77)	1.33 (0.82–2.18)
Warfarin			1.40 (0.66–2.99)	1.14 (0.48–2.75)
Statins	1.66 (1.09–2.53)	1.46 (0.89–2.39)		
Quality of Life (per increment of 1)	1.33 (0.50 ± 3.57)	0.99 (0.30 ± 3.22)	1.55 (0.56 ± 4.32)	1.44 (0.42 ± 4.99)
Highest attained education (y)				
<10	Ref.	Ref.	Ref.	Ref.
10–12	0.89 (0.61–1.30)	0.84 (0.54–1.28)	1.26 (0.87–1.81)	1.17 (0.77–1.76)
>12	0.52 (0.30–0.88)	0.48 (0.26–0.87)	0.91 (0.52–1.62)	0.71 (0.37–1.36)
Employment				
Working	Ref.	Ref.	Ref.	Ref.
Early retirement	0.77 (0.34–1.62)	0.86 (0.34–2.18)	0.60 (0.28–1.28)	0.50 (0.20–1.22)
Age pension	0.87 (0.51–1.48)	0.80 (0.43–1.51)	0.68 (0.40–1.15)	0.78 (0.42–1.43)
Home ownership	0.98 (0.67–1.44)	1.10 (0.70–1.73)	0.95 (0.65–1.40)	1.18 (0.76–1.86)
Living alone	1.18 (0.76–1.83)	1.42 (0.84–2.41)	1.29 (0.83–1.99)	1.34 (0.80–2.22)
Residential area no. of inhabitants				
<1000	Ref.	Ref.	Ref.	Ref.
1000–9999	0.71 (0.45–1.13)	0.85 (0.49–1.45)	1.09 (0.70–1.70)	1.00 (0.60–1.66)
≥10,000	0.95 (0.62–1.44)	1.16 (0.70–1.91)	1.60 (1.06–2.42)	1.66 (1.02–2.69)

OR = odds ratio; CI = confidence interval; y = years.
[a] Mutually adjusted for all variables.
[b] Non-users at baseline who initiated treatment ≤120 days after date of screening (refers to Table 2).

CONCLUSION

Initiation, persistence, and adherence to antiplatelet and statin therapy, among participants in the VIVA screening trial for CVD diagnosed with PAD and AAA, were suboptimal, especially in the group of non-users at baseline. No strong and consistent predictors of adherence were identified. The effectiveness of screening is, to some extent, offset by the poor fulfilment of preventive treatment.

CONFLICT OF INTEREST

Ina Qvist has received speaker's fees from Bayer, Boehringer Ingelheim, BMS, and Pfizer. Lars Frost has been a member of advisory boards for BMS and Pfizer, and has received speaker's fees from Bayer, MSD, Boehringer Ingelheim, BMS, and Pfizer.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2018.09.023.

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