

Identification of Cardiovascular Patient Groups at Risk for Poor Medication Adherence

A Cluster Analysis

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Background: Poor medication adherence limits the secondary prevention of cardiovascular diseases (CVDs) and leads to increased morbidity, mortality, and costs. Identifying groups of patients at risk of poor adherence behavior could enable an intervention to be developed and target patients appropriately. **Objective:** The first aim of this study was to identify homogeneous subgroups of cardiovascular outpatients based on their cardiovascular risk factors. Subsequently, differences in medication adherence between these groups were examined. **Methods:** In this retrospective, observational study, patients with an established CVD were included. Well-known cardiovascular risk factors such as smoking, diet, exercise, blood lipid levels, blood pressure, and body mass index were collected. To identify patient subgroups, a 2-step cluster analytic procedure was performed. Differences between the groups on medication adherence were determined on the outcome of the Modified Morisky Scale. Data collection took place between October 2011 and January 2013. **Results:** Cardiovascular risk factors of 530 patients were included in the cluster analysis. Three groups were identified. Compared with other clusters (clusters 1 and 2), cluster 3 contained significantly fewer patients who could be classified as highly adherent and more patients classified as medium adherent (23% and 57%, respectively; $P = .024$). This group was characterized by a younger age (53% were <55 years old) and using a relatively low number of different medications (41% used <4 different medications). Besides, in this subgroup the most smokers (37%), unhealthy alcohol users (27%), and patients with unhealthy eating habits (14%) were present. **Conclusion:** This study showed that cardiovascular patients who are relatively young and have an unhealthy lifestyle are at risk for nonadherent behavior.

KEY WORDS: cardiovascular nursing, cluster analysis, lifestyle, medication adherence, secondary prevention

Cardiovascular disease (CVD) remains a major cause of death worldwide. In 2015, 17.9 million people died of the disease.¹ Twenty-five percent of these CVD events occur in individuals with a previously established CVD.² The risk for CVDs can be reduced by improving

the behavioral risk factors associated with CVD, such as smoking, an unhealthy diet, obesity, physical inactivity, and harmful use of alcohol.³ In addition to

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these behavioral interventions, pharmaceutical treatment with aspirin, statins, and blood pressure (BP)-lowering medication significantly reduces morbidity and mortality in patients with established CVD.^{4,5} Unfortunately, a substantial proportion of people do not adhere adequately to cardiovascular medications. A recent review showed that only 60% of people who use cardiovascular medication were adherent to their cardiovascular medication.⁶ About 10% of all CVD events may even be attributed to poor adherence to medications alone.⁷ Barriers contributing to suboptimal medication adherence can be distinguished in objective factors, such as socio-demographic and clinical variables, and more subjective factors, such as patients' personal beliefs about medication.⁸ Such determinants for nonadherent behavior are mostly difficult to change and influence each other.⁹

Even though there are numerous interventions to improve medication adherence in cardiovascular patients, they often show only small effects.¹⁰ Besides, these interventions are often complex, which make adaptation, implementation, scalability, and sustainability difficult in cardiovascular risk management (CVRM).² To adequately target interventions to patients who are at risk of nonadherent behavior, we need to have a better understanding of who should be targeted through what interventions.

According to the European guidelines in CVRM, in all patients who have had a cardiovascular event, risk factors of CVD (high BP, high cholesterol levels, and unhealthy lifestyle behaviors) should be identified and preventive therapies (medication and lifestyle interventions) should be taken.¹¹ It is known that multiple barriers can influence adherence.¹² Therefore, these risk factors, together with baseline characteristics (such as age and occupation), may also be used to identify patients with CVD who are at risk of nonadherent behavior. Other studies applying cluster analysis to medication adherence indicate that these homogeneous groups can be identified.^{13–15} By combining and clustering the risk factors of CVD, patient groups who are at risk of nonadherent behavior might be better determined. Consequently, an intervention to improve medication adherence can be better targeted. The present study applies the well-known CVD risk factors of individual patients to a subgroup of patients with suboptimal adherence levels. The discriminative power of these subgroups might be enhanced by incorporating data about patients' beliefs about medication. Building on results of previous research,¹⁶ the first aim of this study is to identify homogeneous subgroups of cardiovascular patients based on their potential cardiovascular risk factors and beliefs about their medication. The second aim of this study is to examine whether these subgroups of patients differ in the level of medication adherence. Identifying these high-risk groups could enable an intervention to be developed and patients to be targeted more appropriately.¹³

METHODS

Setting and Sample

All patients referred to the Radboud University Medical Center with a new diagnosis of 1 of the following conditions are included in the hospital CVD screening program: acute coronary syndrome, myocardial infarction, peripheral arterial disease, an aneurysm of the aorta, or transient ischemic attacks or ischemic stroke.

This regular screening program aims to identify cardiovascular risk factors and consists of a screening of lifestyle (smoking, diet, and exercise), blood lipid levels, BP, and body mass index (BMI). If indicated, preventive therapies (medication and lifestyle interventions) are structurally initiated and followed over time.¹¹ For the sample size, all the patients who participated in this hospital screening program between 2012 and 2013 (530) were included in the analysis. Seven percent of the patients did not fill out the Modified Morisky Scale (MMS) document and therefore were excluded.

Data Collection and Timeline

Data were derived from the screening program and captured in a secured website that could be accessed only by the nurses involved in the screening program by entering a security code. Within, on average, 6 weeks after the CVD event, baseline characteristics and the questionnaires were collected for all patients as part of the screening program. The data used to identify patients at risk for nonadherent behavior were organized using the World Health Organization (WHO) Multidimensional Adherence Model. This conceptual framework allows the construction of poor adherence profiles in patients with chronic diseases.¹⁷ The WHO organizes adherence barriers into 5 dimensions; healthcare/health system-, therapy-, condition-, social/economic-, and patient-related barriers.¹⁸ Data from the regular screening program and from an additional questionnaire used in a previous study were classified according this framework.

Healthcare System–Related Factors

Major components of the healthcare system dimension are patients' perceptions about the healthcare system, satisfaction with pharmacy services, and availability of financial compensation for the medication.¹² In our population, all patients were drawn from the same hospital-wide screening program and were already discharged from the hospital. The hospital care and drugs for all these patients are reimbursed according to the national healthcare insurance terms. As a result, healthcare-system characteristics do not vary among eligible patients and were therefore not considered as a separate dimension in the present study.

Therapy-Related Factors

Examples of barriers identified in this dimension are occurrence of side effects, complexity of drug regimens, and interference of medication taking with daily routines.¹² Collected data from the regular screening program for this dimension were the number of doses of all medication and the type of cardiovascular drugs (platelet aggregation inhibitors, lipid-modifying agents, and antihypertensive drugs) prescribed. All data included the names of the medication arranged by the Anatomic Therapeutic Chemical code. The Anatomic Therapeutic Chemical classification system is a measuring unit for international drug utilization monitoring and research.¹⁹ For the cluster analysis, the number of prescribed medications was categorized by the researchers into small (<4 different drugs), medium (4–8 different drugs), and large (using ≥ 9 different drugs).

Condition-Related Factors

Absence of symptoms in the years after an event may result in the perception that the illness is benign. This may lead to doubts about the necessity of continuous treatment.²⁰ All different CVDs were recorded in our sample. Although a high BMI and especially hypertension and hyperlipidemia are clinical outcomes, they can also be considered as an indicator for (non)adherent behavior.²¹ In conformity with the hospital screening program, blood was drawn from all patients to determine low-density lipoprotein (LDL) cholesterol levels. Blood pressure was measured according to the recommendations of the European Society of Hypertension²² with a validated automated device and based on a mean of 4 office measurements. The BMI was calculated for each patient. All variables were dichotomized for the cluster analysis (within target levels or not). Target BP levels were set according to the European Society of Hypertension recommendations (ie, a systolic BP level of <140 mm Hg). Target LDL cholesterol level should be 1.8 mmol/L (70 mg/dL). Overweight (yes or no) was defined by a BMI ranging greater than 25 kg/m².

Social/Economic Factors

Barriers identified from this dimension can be a lack of social support, financial burden of medications, and health literacy.^{12,23} It is also generally assumed that older (≥ 65 years) patients with CVD usually have worse medication adherence compared with younger (<55 years) patients.^{23,24} The following social economic characteristics were collected as part of the usual screening program: age, level of education, and employment status. Age was divided into 3 groups: young (<55 years), middle-aged (55–75 years), and aged (>75 years).

Patient-Related Factors

An unhealthy lifestyle (smoking, unhealthy diet, and a lack of physical exercise) is associated with an increased risk of cardiovascular events.²² It is questionable whether

poor medication adherence directly causes worse health outcomes or whether there are concomitant factors. It has been speculated that medication adherence is a marker for other health choices, the so-called “healthy adherer effect.”²⁵ Indeed, adherence to lifestyle modification was significantly associated with medication adherence in patients with post-acute myocardial infarction, suggesting that patients with low medication adherence may have an unhealthy lifestyle.²⁶ If this hypothesis is correct, an (un)healthy lifestyle could be a marker for (non)adherent behavior.²⁷ The hospital CVRM program includes a lifestyle risk assessment for smoking, alcohol use, physical activity, and eating habits. Lifestyle is evaluated through self-report using a computerized lifestyle questionnaire and covers smoking, alcohol use, physical activity, and eating habits, based on validated questionnaires. They comprise the following sections.²⁸

- Questions regarding smoking status using questions from the Fagerström questionnaire, with 11 questions about current smoking status, smoking history, smoking patterns, and smoking addiction.²⁹ If a patient smoked at the time the questionnaire was completed, he/she was identified as having a risky smoking lifestyle.
- Ten questions from the Alcohol Use Disorders Identification Tests were used to measure the quantity and frequency of alcohol consumption and problems associated with it.^{30–32} Three questions ask about the frequency and amount of use, 3 questions ask about alcohol dependency, and 4 questions ask about drinking-related problems. Risky alcohol consumption was defined by the Dutch College of General Practitioners as men drinking more than 3 (standard Dutch glass) units a day and women drinking more than 2 units a day³³ and concerned a score of 6 or more on the Alcohol Use Disorders Identification Tests.
- Three questionnaires, with in total 28 questions, measured eating habits. These questionnaires have been validated in a Dutch eating-habits study about fat, fiber, fruit, and vegetable intake.^{34–37} Fourteen questions measured total and saturated fat intake as a percentage of total caloric intake. Eight questions measured fiber intake in grams/kilocalories, and 6 questions measured fruit and vegetable intake in grams per day. Having an unhealthy diet was based on 4 criteria: more than 35% of the total caloric intake as fat, less than 3 g of fiber per day, more than 200 g of vegetables per day, and less than 2 servings of fruit per day. These criteria fit the Dutch standards of healthy diet.
- Finally, 7 questions assessed habitual physical activity. These questions were taken from the short version of the International Physical Activity Questionnaire.^{38,39} The questions asked about the frequency and intensity of physical activity each week. Patients who had fewer than 30 minutes of moderate exercise per day were placed into the “risky lifestyle” category.

Central to patients' medication adherence is their judgment of their personal needs for taking medication.^{9,40,41} One possible explanatory determinant for (non)adherence behavior comprises the beliefs about medication. Personal beliefs about needs for treatment (necessity beliefs) and concerns about several potential adverse consequences (concern beliefs) could explain a large part

of (non)adherent behavior.^{9,40,41} If patients perceive that the need for medication outweighs the concerns, they are more likely to be adherent to their medication.⁴² To evaluate these patients' beliefs and perceptions about their medication, the Beliefs About Medicine Questionnaire (BMQ)⁴³ was used. This questionnaire was completed as part of the parent study.¹⁶ Respondents stated their degree of agreement with each individual statement about medicines on a 5-point Likert scale. To separate patients based on their beliefs about the necessity of their medication and their concerns about taking medication, the total necessity and concern scores (5–25) were split at midpoint (thus, 5–12 was considered as low and 13–25 was considered as high). Patients were then classified into 4 different categories according to the guideline: accepting (high necessity and low concerns), ambivalent (high necessity and high concerns), skeptical (high concerns and low necessity), and indifferent (low concerns and low necessity).^{44–46} Adherence was measured using the MMS,^{47–49} a validated questionnaire consisting of 8 items aimed at measuring adherence. Each item accounts for 0 or 1 when questions are answered by no or yes, respectively. Consequently, total MMS scores range between 0 and 8. These scores were divided into 3 levels of adherence: low adherence (sum score <6), medium adherence (sum score 6 or 7), and high adherence (sum score of 8).

Statistical Analysis

Cluster analysis was used to identify groups of patients at risk for nonadherence.

To identify patient subgroups with different adherence behavior, a 2-step cluster analytic procedure was performed.¹³ First, a hierarchical cluster analysis (the Ward method) was performed to determine the number of clusters. The dendrogram obtained with the Ward procedure was inspected to identify the best cluster solution. Then, a K-means cluster analysis was undertaken to specify the cluster number derived from the Ward method. To establish the difference between the groups on medication adherence, the groups (clusters) were compared by a χ^2 test (all variables were categorical) on the outcome of the MMS. SPSS version 25 was used to perform the analyses.

RESULTS

Study Sample

A total of 530 patients participated in this hospital screening program between 2012 and 2013. Thirty-eight (7%) patients did not fill out the MMS, so 492 patients were included in the analysis. For the demographics of the total sample, see Table 1. On average, most patients used a medium amount of medication (n = 325 [66%]) and almost all used a plated aggregation inhibitor

TABLE 1 Demographics Total Sample

	n (%) or Mean \pm SD
Gender	
Male	324 (66)
Age, y	61 \pm 11
Young (<55)	150 (31)
Middle-age (56–75)	296 (60)
Aged (>75)	46 (9)
Education level	
Primary	109 (22)
Secondary	223 (45)
University	160 (33)
Employment status	
Employed	162 (33)
Unemployed	15 (3)
Incapacitate	82 (17)
Retired	192 (39)
Housewife/-men	41 (8)

(n = 485 [99%]). Lipid-modifying medication was also used by a large number of patients (n = 453 [92%]). The least frequently used medication was cardiac therapy (n = 65 [13%]). Blood pressure and LDL were within target level for 294 (60%) and 281 (57%) of the patients, respectively. Most patients were middle-aged (n = 296 [60%]) and retired (n = 192 [39%]) and had completed secondary education (n = 223 [45%]). Based on the BMQ, we could differentiate between 4 belief groups. In total, 134 patients (27%) were in the accepting group and 324 (66%) in the ambivalent group. Concerning their lifestyle, 117 patients (24%) were smokers, 77 patients (15%) had unhealthy alcohol consumption, 175 patients (36%) had an unhealthy physical activity, and 54 patients (11%) had unhealthy eating habits. The sample characteristics regarding the variables as addressed in the Methods section are presented in Table 2.

Clusters of Patients

Cluster analysis using the Ward method led us to the selection of a 3-cluster solution. This was followed by a K-means cluster analysis where the number of clusters was defined in advance. Table 3 shows the validity of the cluster solutions. Some of the used medication, LDL, level of education, and the belief groups showed no significant difference between the clusters. According to the variables on which the clusters significantly differed, the cluster profiles are described as follows.

Cluster 1

This cluster comprised 212 patients (43% of the total population). Compared with other clusters, patients were of higher age (n = 36 [17%] were >75 years), used more medication (n = 38 [18%] used >9 different medications), and reached target BP the least (n = 95 [55%] did not reach target BP). On the other hand, patients were more likely to have a healthy lifestyle, as reflected

TABLE 2 Medication Details, Clinical Outcomes, Lifestyle Characteristics, and the Belief Groups; Total Sample

Total Sample (N = 402)	n (%) or Mean ± SD
Number of used medication	
Small (<4)	99 (20)
Medium (4–8)	325 (66)
Large (>9)	68 (14)
Used medication	
Platelet aggregation	485 (99)
Lipid modifying	453 (92)
Antihypertensive	
Cardiac therapy	65 (13)
Diuretics	120 (24)
β-Blockers	269 (55)
Calcium channel blockers	70 (14)
RAAS inhibitors	268 (55)
Blood pressure, mm Hg	138.3 ± 19.4
Blood pressure at target level	294 (60)
LDL, mmol/L	2.5 ± 0.9
LDL at target level	281 (57)
BMI, mean ± SD	26.9 ± 4.3
BMI at target level	181 (37)
Currently smoking	117 (24)
Alcohol use	
Healthy	318 (65)
Could be improved	97 (20)
Unhealthy	77 (15)
Physical activity	
Healthy	265 (54)
Could be improved	52 (11)
Unhealthy	175 (36)
Eating habits	
Healthy	118 (24)
Could be improved	320 (65)
Unhealthy	54 (11)
Belief group	
Accepting	134 (27)
Ambivalent	324 (66)
Skeptical	15 (3)
Indifferent	19 (4)

Abbreviations: BMI, body mass index; LDL, low-density lipoprotein; RAAS, Renin-angiotensin-aldosterone system inhibitors.

by healthy eating habits (n = 64 [31%]) and healthy alcohol use (n = 153 [72%]).

Cluster 2

This cluster comprised 174 patients (35% of the total population). Compared with the other clusters, the highest number of patients reached target BP (n = 133 [76%]) and were mostly overweight (n = 134 [77%]). In this cluster, patients used the lowest number of medications (n = 4 [2%] used <4 medications). Most used a medium number of drugs, of which β-blockers (n = 164 [94%]), Renin-angiotensin-aldosterone system inhibitors (n = 147 [85%]), cardiac therapy (n = 45 [26%]), and lipid-modifying medication (n = 168 [97%]) were highest when compared with those in the other groups. According to their lifestyles, most patients were unhealthy with respect to physical activity (n = 86 [49%]) and healthy

eating habits (n = 32 [18%]). On the other hand, non-smokers were highly present in this group (n = 151 [87%]).

Cluster 3

This cluster comprised 106 patients (22% of the total population). Compared with other clusters, patients were relatively young (n = 56 [53%] were younger than 55 years) and were employed (n = 100 [94%]). This group contained the highest number of patients who used a small amount of medication (n = 44 [41%]) and represented a low use of β-blockers (n = 23 [22%]), RAAS inhibitors (n = 35 [33%]), and cardiac therapy (n = 1 [1%]). On the other hand, compared with other clusters, most of these patients used more than 3 units of alcohol a day (n = 29 [27%]), smoked (n = 39 [37%]), and had unhealthy eating habits (n = 15 [14%]).

Table 4 presents the demographics, medication details, clinical outcomes, lifestyle characteristics, and the belief groups for all clusters.

Medication Adherence

Eighteen percent (n = 90) of all patients had a suboptimal level of adherence. Forty-six percent (n = 225) were medium adherent and 36% (n = 177) were highly adherent. Among the 3 clusters, patients in cluster 3 were significantly less highly adherent (n = 38 [23%]). In addition, 57% (n = 60) of the patients in cluster 3 were classified as medium adherent. Differences among the 3 clusters were significantly different (P = .024).

Table 5 presents the differences in level of adherence based on the MMS, by cluster.

DISCUSSION

In this study, we identified homogeneous subgroups of cardiovascular patients based on their cardiovascular risk factors and beliefs about medication. We determined 3 different clusters, in which we were able to identify patients' profiles associated with adherence levels. The WHO model in which the 5 dimensions of adherence are classified¹⁸ was used to organize the classical cardiovascular risk factors that might influence adherence behavior. Three different groups of patients with CVD could be distinguished in level of medication adherence. Consistent with the conclusions found in other research, isolated established predictors of adherence

TABLE 3 Cross tabulation of the 3-cluster solutions using Ward and K-Means Methods (Cohen κ = 0.42)

Ward	K-Means			Total
	Cluster 1	Cluster 2	Cluster 3	
Cluster 1	200	11	1	212
Cluster 2	108	1	65	174
Cluster 3	0	0	106	106

TABLE 4 Demographics, Medication Details, Clinical Outcomes, Lifestyle Characteristics, and the Belief Groups for All Clusters

	Cluster 1 (n = 212)	Cluster 2 (n = 174)	Cluster 3 (n = 106)	P
Number of used medication				<.001
Small (<4)	51 (24)	4 (2)	44 (41)	
Medium (4–8)	123 (58)	145 (84)	57 (54)	
Large (>9)	38 (18)	25 (14)	5 (5)	
Used medication				
Platelet aggregation	209 (99)	171 (98)	105 (99)	.87
Lipid modifying	189 (89)	168 (97)	96 (91)	.02
Antihypertensive				
Cardiac therapy	19 (9)	45 (26)	1 (1)	<.001
Diuretics	58 (27)	33 (19)	29 (27)	.12
β-Blockers	82 (39)	164 (94)	23 (22)	<.001
Calcium channel blockers	34 (16)	28 (16)	8 (8)	.08
RAAS inhibitors	86 (40)	147 (85)	35 (33)	<.001
Blood pressure at target level	95 (45)	133 (76)	66 (62)	<.001
LDL at target level	111 (52)	112 (64)	58 (55)	.051
BMI at target level	95 (45)	40 (23)	46 (43)	<.001
Age				<.001
Young (<55)	33 (16)	61 (35)	56 (53)	
Middle-age (56–75)	143 (67)	103 (59)	50 (47)	
Aged (>75)	36 (17)	10 (6)	0 (0)	
Level of education				.09
Primary	55 (26)	40 (23)	14 (13)	
Secondary	96 (45)	77 (44)	50 (47)	
University	61 (29)	57 (33)	42 (40)	
Employment status				<.001
Employed	0 (0)	62 (36)	100 (94)	
Unemployed	3 (1)	6 (3)	6 (6)	
Incapacitate	51 (24)	31 (18)	0 (0)	
Retired	122 (58)	70 (40)	0 (0)	
Housewife/-men	36 (17)	5 (3)	0 (0)	
Belief group				.18
Accepting	62 (29)	40 (23)	32 (30)	
Ambivalent	136 (64)	125 (72)	63 (59)	
Skeptical	4 (2)	6 (3)	5 (5)	
Indifferent	10 (5)	3 (2)	6 (6)	
Currently smoking	55 (26)	23 (13)	39 (37)	<.001
Alcohol use				<.001
Healthy	153 (72)	109 (63)	56 (53)	
Could be improved	38 (18)	38 (22)	21 (20)	
Unhealthy	21 (10)	27 (15)	29 (27)	
Physical activity				<.001
Healthy	116 (63)	71 (41)	78 (74)	
Could be improved	26 (12)	17 (10)	9 (9)	
Unhealthy	70 (33)	86 (49)	19 (18)	
Eating habits				.05
Healthy	64 (31)	32 (18)	22 (21)	
Could be improved	130 (61)	121 (70)	69 (65)	
Unhealthy	18 (8)	21 (12)	15 (14)	
Belief group				.18
Accepting	62 (29)	40 (23)	32 (30)	
Ambivalent	136 (64)	125 (72)	63 (59)	
Skeptical	4 (2)	6 (3)	5 (5)	
Indifferent	10 (5)	3 (2)	6 (6)	

Data are presented as n (%) of patients.

Abbreviations: BMI, body mass index; LDL, low-density lipoprotein; RAAS, Renin-angiotensin-aldosterone system inhibitors.

are often insufficient to identify individual patients who are likely to be nonadherent.²⁷

Compared with clusters 1 and 2, patients in cluster 3 had a significantly poorer medication adherence. This

patient group was characterized by those of a relatively young age, using a limited number of medication, and an unhealthy lifestyle. As older age has previously been identified as a major determinant for nonadherence,^{23,24}

TABLE 5 Differences in Level of Adherence Based on the Modified Morisky Scale by Cluster

	Cluster 1	Cluster 2	Cluster 3	P
Low adherence	43 (20)	26 (32)	21 (20)	.024
Medium adherence	88 (42)	77 (44)	60 (57) ^a	
High adherence	81 (38)	71 (63)	38 (23) ^b	

Data are presented as n (%) of patients.

^aSignificantly higher.

^bSignificantly lower.

we looked for explanations for these findings. We found that a younger age at the time of a stroke or acute coronary syndrome could possibly be associated with reduced medication adherence.⁵⁰ Although this was an inconclusive finding, it suggests that younger patients may be more likely to be nonadherent to preventive medications because of lower perceived risk of another CVD, misconceptions about the duration of treatment, or concerns about potential harm from statins.⁵¹ By analyzing the single variable age in relation to adherence in this population, there was no significant difference in adherence among the 3 age groups observed. Only when clustering the variables was there a significant difference between the groups on adherence. This also suggests that nonadherence manifests itself in interaction with underlying vulnerabilities.²⁷ Considering an unhealthy lifestyle as a marker for nonadherent behavior²⁷ seems to be confirmed in this study. Although clinical outcomes are well-known indicators for nonadherence,^{52,53} our cluster analyses did not show such association. Patients who did not reach target BP and LDL levels were not more likely to be nonadherent. There may be several explanations for this finding. In our population, LDL and BP were measured just at cardiovascular follow-up. Consequently, residual confounding may have limited our analyses. Another explanation could be the relatively young age of this group. With aging, the prevalence of metabolic syndrome (including hypertension and dyslipidemia) increases.⁵⁴ Thus, younger patients may already have a (sub)optimal level of LDL and BP before the cardiovascular event. Also, a suboptimal adherence level might still achieve clinical benefits with respect to BP and cholesterol levels.⁵⁵ Another remarkable finding was that, although a complex drug treatment plan is often associated with lower medication adherence,⁵⁶ only a small number of medications were used in the cluster that showed the poorest adherence. This could be explained by the clinical outcomes that already were at target. Indication for prescribing medication was simply less present. We expected there would be a difference between the clusters in the outcome of the BMQ. The clusters, however, showed no significant differences in the outcome categories of the BMQ. In our previous studies, the continuous outcome of the BMQ, that is, the necessity-concern

differential (NCD), was used.^{57,58} In these studies, the NCD corresponded with the outcome of the MMS; next to the high adherence rate, a high mean NCD score was present. In the present study, we applied the categorical outcomes of the BMQ, the 4 different belief groups, because categorical outcomes are the preferred measure for a cluster analysis. The difference between the continuous and categorical outcome may explain the absence of an association between the BMQ and the MMS.

This study had some limitations. First, we had to deal with nonresponders of the self-reported questionnaires BMQ and MMS. It is suggested that nonresponders have poorer adherence levels and beliefs about medication.⁵⁹ This may limit the extra polarity of the results obtained. Second, there are different methods available to measure adherence. Each method has advantages and disadvantages.⁶⁰ The MMS is a validated questionnaire that can be applied easily to large populations. However, as MMS is a subjective measure, adherence levels may be higher than what is expected in real life.⁶⁰ Other methods, such as the Medication Event Monitoring System or pill count, seem to influence patient's behavior through direct confrontation. Moreover, application of Medication Event Monitoring System is relatively expensive, especially when applied in standard care.⁶¹ Second, although comorbidities can play an important role in medication adherence, we did not have access to valid data for this study.⁸

Hence, determinants for nonadherent behavior are mostly complex and influence each other.⁹ Identifying nonadherent behavior in cardiovascular patients by clustering these determinants based on their structural cardiovascular screening outcomes can lead to a more effective CVRM. The group of patients that showed the poorest medication adherence was characterized by a relatively young age, using a limited number of medications. This might explain why interventions to improve medication adherence in cardiovascular patients were not very successful if they were targeting the elderly, polypharmaceutical patients. By developing a new intervention to improve medication adherence in cardiovascular patients, there should be a different approach, targeting a different patient group. Further research in interventions to improve medication adherence in this subgroup of cardiovascular patients is needed to confirm this presumption.

CONCLUSION

Cardiovascular patients who are relatively young and have an unhealthy lifestyle should be identified as patients who are at risk for nonadherent behavior. When identified, these patients should be offered more guidance on medication adherence. Specifically, adherence-

What's New and Important

- Identifying nonadherent behavior in cardiovascular patients by clustering determinants based on the structural cardiovascular screening outcomes can lead to a more effective approach to improve medication adherence.
- The group of patients that showed the poorest medication adherence was characterized by a relatively young age, using a limited number of medications. This is in contrast to the more traditionally known determinants of poor adherence (elderly age and polypharmaceutical use of medications).
- Further studies could lead to a different approach to improve medication adherence in patients with CVD, targeting a different patient group.

improving interventions targeting this population may be successful and should be subject for future research.

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