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Factors Associated With Nonadherence to Cardiovascular Medications
A Cross-sectional Study

Danielle M. van der Laan, MSc; Petra J. M. Elders, PhD, MD; Christel C. L. M. Boons, MSc;
Giel Nijpels, PhD, MD; Jacqueline G. Hugtenburg, PhD, Pharm

Background: Cardiovascular medications have well-established benefits in the primary and secondary prevention of cardiovascular diseases. Unfortunately, adherence to these medicines is often suboptimal. To develop interventions intended to enhance adherence to cardiovascular medications, more insight is needed into the complex character of medication nonadherence. **Objective:** The aim of the present study was to identify which factors are associated with nonadherence to cardiovascular medications in a sample of patients from Dutch community pharmacies. **Methods:** In this cross-sectional study, patients using cardiovascular medications from 23 community pharmacies were included. Patient demographics, medication and disease characteristics, knowledge, quality of life, attitude toward medicines, and satisfaction with information were assessed. Both an adherent sample (n = 146) and a sample of patients nonadherent to prescribed medications (n = 109) during the last 6 months as assessed with pharmacy refill data (proportion of days covered <80%) were selected. Associations with refill nonadherence were assessed using univariate and multivariate logistic regression analyses. **Results:** In total, 255 patients participated (53.3% men, 71.6 ± 10.9 years). Factors associated with cardiovascular medication nonadherence in multivariate analyses included experiencing difficulties with medication use due to forgetting, having insufficient knowledge on what to do when a dose is forgotten, and having an ambivalent attitude toward medicines (beliefs of high necessity and high concerns). **Conclusions:** Intervention strategies to enhance cardiovascular medication nonadherence should be targeted mainly to the unintentional dimension of nonadherence and include information and tools to prevent forgetting. Conversely, the influence of factors that underlie intentional nonadherence, particularly patients' beliefs about medicines, should also be addressed.

KEY WORDS: cardiovascular diseases, cross-sectional study, medication adherence, medication knowledge

Danielle M. van der Laan, MSc
Doctoral Student, Department of Clinical Pharmacology and Pharmacy and Amsterdam Public Health Research Institute, Amsterdam UMC, Vrije Universiteit Amsterdam, the Netherlands.

Petra J.M. Elders, PhD, MD
Postdoctoral Fellow, Department of General Practice & Elderly Care Medicine and Amsterdam Public Health Research Institute, Amsterdam UMC, Vrije Universiteit Amsterdam, the Netherlands.

Christel C.L.M. Boons, MSc
Doctoral Student, Department of Clinical Pharmacology and Pharmacy and Amsterdam Public Health Research Institute, Amsterdam UMC, Vrije Universiteit Amsterdam, the Netherlands.

Giel Nijpels, PhD, MD
Professor, Department of General Practice & Elderly Care Medicine and Amsterdam Public Health research institute, Amsterdam UMC, Vrije Universiteit Amsterdam, the Netherlands.

Jacqueline G. Hugtenburg, PhD, Pharm
Postdoctoral Fellow, Department of Clinical Pharmacology and Pharmacy and Amsterdam Public Health Research Institute, Amsterdam UMC, Vrije Universiteit Amsterdam, the Netherlands.

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Correspondence
Danielle M. van der Laan, MSc, Department of Clinical Pharmacology and Pharmacy and Amsterdam Public Health research institute, Amsterdam UMC, Vrije Universiteit Amsterdam, De Boelelaan 1117, Amsterdam, the Netherlands (d.vanderlaan1@vumc.nl).

Cardiovascular disease (CVD) is a major cause of disability and premature death, and its prevention and management have become a focus of healthcare providers (HCPs) worldwide.[1,2] After cancer, CVD is the most common cause of death in the Netherlands.[3] In 2017, almost 2 million people suffered from CVD, and the prevalence of CVD is higher in men.[3] Although mortality rates have declined in recent years, the disease and financial burden remain high due to hospitalizations and cardiac interventions.[4] Cardiovascular drugs have well-established benefits in the primary and secondary prevention of CVD.[5] Unfortunately, adherence to cardiovascular medications, defined as the extent to which patients take their medications as agreed upon with their HCP,[6] is suboptimal.[2,7] A meta-analysis in which adherence to 7 cardiovascular drug classes was measured using pharmacy refill data reported a nonadherence rate of 43%.[7] Depending on the drug class, nonadherence rates varied from 35% for angiotensin II receptor blockers to 72% for β-blockers.[7] It also matters whether medications are prescribed for primary or secondary prevention, with lower adherence rates being found for primary prevention.[7] The health consequences for patients with CVD or cardiovascular risk factors resulting from medication nonadherence are substantial, because nonadherence reduces the effectiveness of drug treatment and contributes to morbidity, mortality, and hospital admissions, as well as increased healthcare costs.[1,8–10]

The literature distinguishes between intentional and unintentional nonadherence.[11,12] Intentional nonadherence is considered an active and reasoned process in which patients decide to deviate from the treatment plan. Unintentional nonadherence is considered a passive process in which patients are careless, forgetful, or unable to adhere to the treatment plan for other reasons such as unable to collect their medications or not understanding the information on medications provided. However, notwithstanding this clear distinction, many factors underlying intentional nonadherence may also play a role in unintentional nonadherence.[2,13]

Medication (non-)adherence is influenced by multiple interrelating factors. The World Health Organization (WHO) therefore introduced the Multidimensional Adherence Model to classify factors that influence (non-)adherence according to 5 dimensions: social/economic, patient, condition, therapy, and healthcare team– and system-related factors.[14] Social/economic factors include poor health literacy, low level of education, unemployment, and limited social support. Patient-related factors include resources, knowledge, attitudes, and beliefs of patients. For example, when a patient has many concerns about the medicines or has weak beliefs about the necessity of using medicines, this is likely to have a negative effect on medication adherence. Condition- and therapy-related factors include factors related to the burden experienced by patients owing to the illness itself and the use of medicines. Similar to other chronic diseases, patients with CVD are confronted with a long-term disease course, an often relatively asymptomatic nature of the disease, comorbidities, the need for lifelong treatment, and multiple daily dosing. In addition, the occurrence of side effects can have a negative impact on medication adherence. Poor patient-HCP relationships and insufficient communication are considered healthcare team– and system-related factors. The comprehensive WHO model can be used to systematically study the various factors that influence medication adherence.

A better understanding of factors contributing to poor medication adherence is necessary to develop effective adherence-enhancing interventions. Therefore, the present study was performed with the aim to determine which factors are associated with nonadherence to cardiovascular medications in a sample of patients from Dutch community pharmacies. The results will be used for the development of an intervention program to enhance adherence to medications in the Netherlands.

Methods

Study Design

In an observational, cross-sectional study, patients using cardiovascular medications were recruited from 23 community pharmacies in the Netherlands (Figure). Pharmacists in training collected the study data as part of the community pharmacists' specialization program. Data were collected by means of a comprehensive patient questionnaire and patients' pharmacy medication records.

Study Population

Patients were eligible if they were 45 years or older and were prescribed at least 1 cardiovascular medication, which may have included antihypertensives (β-blockers, calcium antagonists, diuretics, angiotensin converting enzyme inhibitors, and angiotensin II receptor antagonists), antihyperlipidemics (statins), or anticoagulants (direct-acting oral anticoagulants). Patients who were unable to fill out a questionnaire or who had insufficient Dutch language skills were excluded. Also, patients who used repeat dispensing or pill packing, which are additionally offered, medication-intake-supporting services by the pharmacy, were excluded.

Selection Procedure

We intended to select workable and equally group-sized samples of patients who were adherent and nonadherent to their cardiovascular medications. According to what was achievable for the pharmacists in training in the time available, a feasible but rather large sample size was intended to be reached.
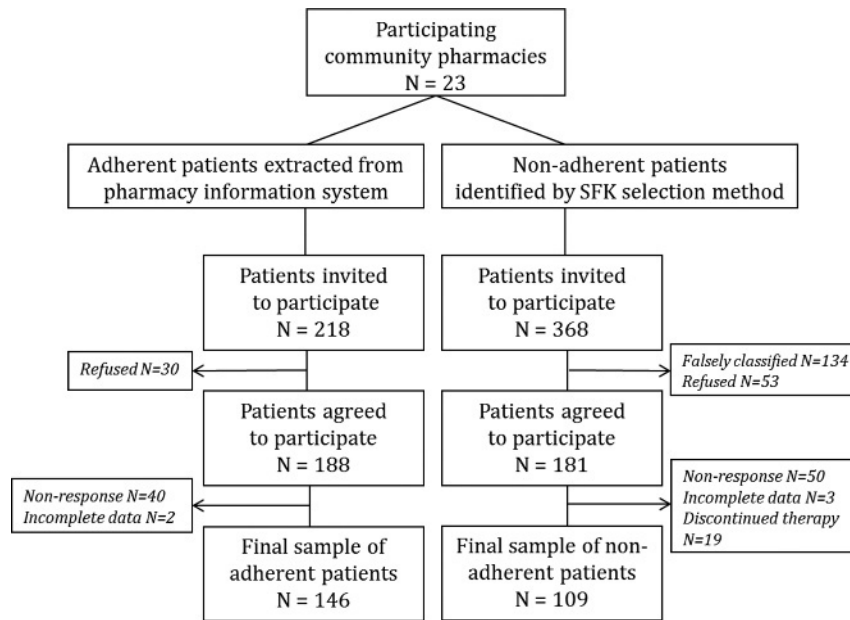
FIGURE. *Participants flow diagram. SFK indicates Foundation for Pharmaceutical Statistics.*

Nonadherent Sample

The selection method of the Foundation for Pharmaceutical Statistics (SFK) was used to select nonadherent patients.[15] The SFK was founded by the Royal Dutch Pharmacists Association and collects information on dispensed drugs. The SFK software automatically calculates the proportion of days covered (PDC) for the antihypertensive, antihyperlipidemic, and anticoagulant medication classes. For each pharmacy, a list of patients nonadherent (PDC <80%) to at least 1 of these 3 cardiovascular medication classes during the last 6 months was generated. Each pharmacy took a random sample from the list using a randomization table. A limitation of the SFK method is that data concerning medication refill or medication regimen changes may sometimes be missing. As a result, patients can be falsely classified as nonadherent. Therefore, each patient in the sample was contacted by the pharmacist in training to verify whether the low PDC could be explained by the following factors: (1) visits to another pharmacy, (2) hospital admissions, (3) an HCP-initiated discontinuation, or (4) changes to prescribed regimen. Patients able to explain their refill nonadherence with 1 of the above described aspects in the previous period were excluded from this study. Patients who denied these explanations were included in the final nonadherent sample and were asked for participation.

Adherent Sample

The pharmacy information and administration systems of the community pharmacies were used to identify patients adherent (PDC $\geq$ 80%) to their cardiovascular medications by making a list of all patients who met the inclusion criteria (ie, using antihypertensives, antihyperlipidemics, or anticoagulants) and being absent on the SFK list as described

above. Again, a sample of these patients was taken using a randomization table. Subsequently, they were contacted by the pharmacist in training and asked to participate.

Data Collection

Validated questionnaires and a small number of self-composed questions were administered to collect data on several factors covering all 5 dimensions of the WHO model. To provide a comprehensive but relevant overview, the research team made a selection of the multiple factors of the WHO model based upon their potential importance to the Dutch study population. Moreover, the factors' potential to be influenced and addressed in an intervention was also considered. For example, patient-related factors included gender, age, knowledge, attitudes and beliefs, and symptoms of depression/anxiety; condition- and therapy-related factors included the number of CVD diagnoses, the number of prescribed medications, the occurrence of and worries about side effects, and multiple daily dosing; health system/healthcare team–related factors included satisfaction with provided information about medicines; and social/economic factors included level of education, employment, and social support. Before administration, the self-composed questions were reviewed by experts and tested in a small sample of patients (n = 16). The questionnaire was slightly changed to optimize readability and comprehensibility but was not further adapted based upon the test results.

Patient Characteristics

Patient characteristics included gender, age, origin, education, employment status, living situation, and tobacco and alcohol use. Social activities including holidays and trips were also assessed because deviations from daily

routines might influence the regularity with which patients take their medications.[16]

Medication and Disease Characteristics

Medication- and disease-related questions included a self-reported overview of the number of CVD diagnoses, the number of prescribed medications, specialist visits in the past year, assistance with medication use from others, use of tools to prevent forgetting, occurrence of side effects, and worries about side effects.

In addition, patients were asked to indicate whether they experienced difficulties with the use of their medications due to the following reasons: too many pills, medicines not being effective, not knowing the purpose of use, side effects, being anxious about experiencing side effects, not motivated to take medications as prescribed, forgetting to take medications, not able to differentiate between different drugs, lack of symptoms, lack of health improvement, lack of necessity, lack of support from others, anxious about becoming dependent on medications, or social stigma.

Knowledge-Related Questions

To develop knowledge-related questions, the research team used the content of some items from the Specific Beliefs About Medicines Questionnaire (BMQ Specific)[17] and modified them to 6 knowledge-related questions. The items of the BMQ Specific were used as a source because these items describe important medication-taking aspects. The modified statements assessed the extent to which patients perceived having sufficient knowledge on different medication-related aspects, including "I know the purpose of my medicine use," "I know when to take my medicines," "I know how much medicines I must take," "I know the effects of my medicines," "I know the possible side effects of my medicines," and "I know what to do when a dose is forgotten." Responses were scored on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Subsequently, each item was dichotomized into sufficient (score 4–5) and insufficient (score 1–3) self-reported medication-related knowledge.

Quality of Life

Quality of life was assessed using the validated 12-item Short Form Health Survey.[18,19] The 12-item Short Form Health Survey consists of 12 questions covering 8 dimensions of health, that is, general health perception, physical functioning, limitations due to physical health problems, bodily pain, vitality, social functioning, emotional functioning, and general mental health. Two summary scores for physical health and mental health were calculated, both ranging from 0 to 100.

Attitude Toward Medicines

Patients' beliefs about medicines were assessed with the BMQ Specific.[17,20] The BMQ Specific can be divided into the Necessity and the Concern subscales, measuring patients' beliefs of the necessity of taking medicines and patients' concerns about taking medicines, respectively. Responses were scored on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Based on these 2 subscales, patients were categorized into 4 attitudinal groups: accepting (high necessity, low concerns), ambivalent (high necessity, high concerns), indifferent (low necessity, low concerns), and skeptical (low necessity, high concerns). The scale midpoint of 15 or above was used as a cutoff to define high beliefs.[21] Research shows evidence on good reproducibility and acceptable validity of the BMQ Specific.[17,20,22]

Satisfaction With Information About Medications

Patient satisfaction with received information about medications was assessed with the Satisfaction With Information About Medicines Scale.[23] The Satisfaction With Information About Medicines Scale consists of 17 items assessing the extent to which patients feel they received enough information on medication use–related topics using the following response options: too much, about right, too little, none received, and none needed. If a patient was satisfied (rated as about right or none needed) with the information, a score of 1 is given. If a patient was dissatisfied (rated as too much, too little, or none received), a score of 0 is given. An overall satisfaction rating is obtained by summing the score of all 17 items. The score ranges from 0 to 17, with a higher score indicating a higher degree of satisfaction with information. In addition, 2 subscales can be obtained, namely, patient satisfaction with information about the Action and Usage of Medications (items 1–9) and the Potential Problems of Medications (items 10–17).

Depression and Anxiety

The 4-item Patient Health Questionnaire (PHQ-4) was used to assess depression and anxiety symptom severity.[24] The PHQ-4 states the following questions: "Over the last 2 weeks, how often have you been bothered by the following problems: feeling nervous/anxious; not being able to stop worrying; feeling down/depressed; little interest or pleasure in doing things." Responses are scored as 0 (not at all), 1 (several days), 2 (more than half the days), or 3 (nearly every day). The total score ranges from 0 to 12. This total score was dichotomized into normal symptom severity (total score 0–2) and mild to severe symptom severity (total score 3–12) because the usual division in 4 quadrants (normal, mild, moderate, and severe) was not possible because of too small samples in the last 2 quadrants.

Data Analysis

Patient characteristics were provided by means and standard deviations for continuous variables and by frequencies and percentages for categorical variables. Univariate logistic regression analyses were used to examine the

association of each separate factor with nonadherence (PDC <80%) versus adherence (PDC ≥80%) as assessed by pharmacy refill data. Factors assessed included age, gender, origin, education, employment status, living situation, tobacco and alcohol use, social activities, assistance with medication use from others, number of CVD diagnoses, number of prescribed medicines, complexity of regimen, occurrence of side effects, worries about side effects, specialist visits in the past year, number of tools used to prevent forgetting, difficulties with medication use due to forgetting, side effects and too many pills, self-reported knowledge, quality of life, attitude toward medicines, satisfaction with information, and depression/anxiety symptom severity. All factors with a *P* value of ≤.10 in univariate analyses were subsequently tested in multivariate logistic regression analyses to adjust for the included factors. Variables were excluded until only factors with a *P* value of ≤.10 remained to also identify trends toward significance. *P* values of ≤.05 were considered statistically significant. Odds ratios (OR) with 95% confidence intervals (CI) are presented. Statistical analyses were performed using SPSS version 22.0 (IBM Corp, Armonk, New York).

Results

Selected Patients

A total of 586 patients from 23 community pharmacies were invited to participate (Figure), with 218 adherent patients and 368 nonadherent patients. In the preselected nonadherent sample, 134 patients were excluded because after verification, it seemed they were falsely classified as nonadherent by the selection method of SFK. The final sample consisted of 255 patients, including 146 patients in the adherent sample and 109 patients in the nonadherent sample.

Patient Characteristics

The characteristics of the patients are listed in Table 1. In the total study population (n = 255), the mean age was 71.6 years and 53.3% were male. Patients were predominantly of Dutch origin (86.7%) and retired (71.8%). About two-thirds of patients were diagnosed with fewer than 3 CVDs and used more than 3 medicines.

Univariate and Multivariate Analyses

The results of the univariate analyses are shown in Table 2. The following variables were significantly associated with nonadherence to cardiovascular medications: older age (OR, 1.03; CI, 1.01–1.05), using fewer tools to prevent forgetting (OR, 1.66; CI, 1.01–2.75), difficulties with medication use due to forgetting (OR, 3.72; CI, 1.39–9.94), difficulties with medication use due to too many pills (OR, 3.59; CI, 1.09–11.76), insufficient knowledge on what to do when a dose is

forgotten (OR, 3.32; CI, 1.81–6.08), and patients having an ambivalent attitude toward medicines (high necessity, high concerns) (OR, 2.30; CI, 1.23–4.32).

The results of the multivariate analysis are shown in Table 3. Difficulties with medication use due to forgetting (OR, 3.16; CI, 1.09–9.18), insufficient knowledge on what to do when a dose is forgotten (OR, 2.80; CI, 1.48–5.32), and having an ambivalent attitude toward medicines (OR, 2.26; CI, 1.16–4.37) remained significantly (*P* ≤ .05) associated with cardiovascular medication nonadherence in multivariate analyses.

Discussion

This study demonstrated that refill nonadherence to cardiovascular medications was mainly affected by factors related to forgetting to take medications and was also influenced by patients' attitude toward medicines. Although it seems that the problem of nonadherence is mainly affected by factors related to unintentional nonadherence, the influence of factors that underlie intentional nonadherence, such as beliefs about medicines, must also be recognized.

First, patients' self-reported insufficient knowledge of what to do when a dose is forgotten was associated with nonadherence in this study. This result shows the important role of providing adequate information to patients by HCPs, thereby increasing patients' knowledge to a sufficient level. Research and clinical guidelines make recommendations about how to involve patients in the decision to prescribe and how to support patients to enhance adherence to prescribed medications.[25–27] The provision of information should be individualized and should include information on the name of the medicine, how and when to take it, the benefits, and the possible adverse effects and contain instructions on what to do when a dose is missed.[27] A recent study in the Netherlands concluded that pharmacy staff members provided little medication-related information at the counter and rarely discussed possible adverse effects, the intended effect, barriers for taking medications, or consequences of nonadherence. Moreover, they did not encourage active patient participation. Further research is needed to clarify this finding.[28] Second, indicating difficulties with medication use due to forgetting was also associated with nonadherence. This finding highlights the complex issue of the unintentional dimension of nonadherence.[11,29] Finally, an ambivalent attitude toward medicines (ie, having certain doubts about using medicines) as compared with an accepting attitude was associated with nonadherence. Previous studies have also shown that patients' attitudes toward and beliefs about medicines are risk factors for medication nonadherence.[21,29–31] Patients often have to balance their feelings about the necessity of using their medications and dealing with the concerns that they experience. This cost-benefit

TABLE 1 Characteristics of the Study Population

	Total Study Population (n = 255)	Adherent Sample (n = 146)	Nonadherent Sample (n = 109)
Patient characteristics			
Age, y	71.6 ± 10.9 (46–103)	72.9 ± 11.2	69.8 ± 10.1
Gender			
Male	136 (53.3)	71 (48.6)	65 (59.6)
Origin			
Non-Dutch	34 (13.3)	20 (13.7)	14 (12.8)
Education			
Low to moderate	147 (57.6)	82 (56.2)	65 (59.6)
Employment status[a]			
Employed	45 (17.7)	22 (15.0)	23 (21.1)
Volunteer	23 (9.0)	15 (10.3)	8 (7.3)
Retired	183 (71.8)	109 (74.7)	74 (67.9)
Unemployed/disabled	17 (6.6)	9 (6.1)	8 (7.4)
Living situation			
Alone	75 (29.4)	46 (31.5)	29 (26.6)
Tobacco use			
Yes	35 (13.7)	18 (12.3)	17 (15.6)
Alcohol use			
Yes	45 (17.6)	30 (20.5)	15 (13.8)
Regular holidays or trips			
Yes	181 (71.0)	100 (68.5)	81 (74.3)
Medication/disease characteristics			
Assistance with medication use			
No	223 (87.5)	130 (89.0)	93 (85.3)
No. of CVD diagnoses			
>2	81 (31.8)	53 (36.3)	28 (25.7)
No. of prescribed medicines[b]			
>3	160 (65.0)	98 (68.5)	62 (60.2)
Complexity of regimen			
Multiple-daily dosing	155 (60.8)	91 (62.3)	64 (58.7)
Occurrence of side effects			
Yes	45 (17.6)	23 (15.8)	22 (20.2)
Worries about side effects			
Yes	60 (23.5)	28 (19.2)	32 (29.4)
Specialist visit in past year			
No	112 (43.9)	66 (45.2)	46 (42.2)
No. of tools to prevent forgetting			
≤1	115 (45.1)	58 (39.7)	57 (52.3)
Difficulties with medication use			
Yes	47 (18.4)	14 (9.6)	33 (30.3)
Knowledge			
Insufficient knowledge			
On purpose of medicines	13 (5.1)	8 (5.5)	5 (4.6)
On when to take medicines	6 (2.4)	4 (2.7)	2 (1.8)
On how much medicines to take	11 (4.3)	6 (4.1)	5 (4.6)
On medications effects	61 (23.9)	32 (21.9)	29 (26.6)
On side effects	117 (45.9)	67 (45.9)	50 (45.9)
On what to do when a dose is forgotten	60 (23.5)	21 (14.4)	39 (35.8)
Quality of life			
SF-12			
Physical health (0–100)	44.2 ± 10.5	43.3 ± 10.7	45.2 ± 10.2
Mental health (0–100)	53.4 ± 8.7	53.6 ± 9.2	53.1 ± 8.1
Attitudes and beliefs			
BMQ attitudinal quadrants			
Accepting	132 (51.8)	86 (58.9)	46 (42.2)
ambivalent	58 (22.7)	26 (17.8)	32 (29.4)
Indifferent	56 (22.0)	28 (19.2)	28 (25.7)
Skeptical	9 (3.5)	6 (4.1)	3 (2.8)

(continues)

TABLE 1 Characteristics of the Study Population, Continued	Total Study Population (n = 255)	Adherent Sample (n = 146)	Nonadherent Sample (n = 109)
Satisfaction with information			
SIMS			
Sum score (0–17)	10.7 ± 5.7	10.5 ± 5.9	11.0 ± 5.4
Subscale action and usage (0–9)	6.3 ± 2.8	6.2 ± 2.9	6.5 ± 2.8
Subscale potential problems (0–8)	4.4 ± 3.2	4.3 ± 3.3	4.5 ± 3.1
Depression and anxiety			
PHQ-4			
≥3 (mild to severe)	62 (24.3)	34 (23.3)	28 (25.7)

Data are presented as n (%) or mean ± SD (range).
Abbreviations: BMQ, Beliefs About Medicines Questionnaire; CVD, cardiovascular disease; PHQ-4, 4-item Patient Health Questionnaire; SF-12, 12-item Short Form; SIMS, Satisfaction With Information About Medicines Scale.
[a]Total exceeds 100%.
[b]Data from 9 participants are missing.

analysis appears to influence patients' drug-taking behavior. When comparing an ambivalent attitude with an accepting attitude, beliefs of the necessity of medication use are both high. The difference in attitudes may thus be found on the level of concerns. This finding is confirmed by multiple studies reporting on the negative impact that patients' concerns about medicines can have on medication adherence behavior.[20,29–31] It must be recognized that factors that were associated with nonadherence in this study might be interacting and related to both intentional and unintentional nonadherence, because some studies argue that factors that underlie intentional nonadherence can also predict unintentional nonadherence.[2,13,29] Moreover, unintentional nonadherence may be prognostic for future intentional nonadherent behavior.[13]

The factors male gender, using fewer tools to prevent forgetting, and patients' having an indifferent attitude toward medicines showed a trend toward significance in multivariate analysis. Using fewer tools to prevent forgetting underlines the findings in this study that forgetting is an complex issue. Having an indifferent attitude toward medicines underlines the findings in this study that exploring patients' beliefs about medicines is important. Patients with indifferent attitudes toward medicines experience low concerns about their medicines; however, they also experience low beliefs in the necessity of using their medications.[20] These patients are often nonadherent to their medications and their necessity beliefs must be explored by HCPs. For certain factors examined in this study, nonsignificant results were found, for instance, having multiple CVDs and complex medication regimens. It might be interesting to further explore their potential relationships with (non)adherence, given the increase of the overall population projected to be living with comorbid conditions requiring multiple medications.

The results of this study implicate that to enhance adherence to cardiovascular medications, HCPs must explore factors related to forgetting. It is important for HCPs to explore patients' experienced difficulties with using prescribed medications, with a special focus on forgetting. Patients must be provided with sufficient information on how to use medicines and what to do when doses are missed. Furthermore, HCPs should support patients when they experience conflicting beliefs and help patients to balance these feelings.

Strengths and Limitations

The strength of this study is that multiple factors were assessed covering all 5 adherence influencing dimensions as set by the WHO.[14] By assessing factors related to the patient, condition, therapy, health system/healthcare team, and social/economics, a complete overview of potential important factors was provided. This is needed since adherence to medications is a complex healthcare problem and influenced by multiple interrelating factors. Because it was not possible to assess all influencing factors of the WHO model, the research team made a selection to provide a number of workable and relevant factors. The selection was partly made based upon the applicability to our Dutch healthcare system. Therefore, for example, financial barriers to medications were not assessed. The Dutch healthcare system has been designed in such a manner—mandatory health insurance for all citizens—that an additional payment for medications is applicable for only a limited number of cases.

The selection method of SFK using pharmacy dispensing data is a simple and low-cost method to easily identify nonadherent patients. However, the accuracy of this selection method is limited. Sometimes, data in pharmacy records are missing whereupon it is possible to falsely classify patients as nonadherent. To minimize bias, the missing SFK data were verified with each selected patient and when needed a patient was excluded. In addition, it should be noted that dispensing data provides information about medication refill behavior and

TABLE 2 Results of Univariate Analysis of Variables Associated With Cardiovascular Medication Nonadherence			
Variables	OR	95% CI	P
Patient characteristics			
Older age	1.03	1.01–1.05	.027[a]
Male gender	1.56	0.95–2.58	.082[a]
Non-Dutch origin	0.93	0.45–1.93	.843
Low to moderate education	1.15	0.70–1.91	.579
Employed	1.59	0.83–3.06	.162
Retired	0.75	0.44–1.27	.285
Living alone	0.79	0.46–1.37	.396
Tobacco use	1.31	0.64–2.69	.454
Alcohol use	0.62	0.31–1.21	.162
Regular holidays or trips	1.33	0.77–2.31	.312
Medication/disease characteristics			
No assistance with medication use	0.72	0.34–1.50	.377
More CVD diagnoses (>2)	0.61	0.35–1.05	.073[a]
More prescribed medicines (>3)[b]	0.69	0.41–1.18	.177
Multiple-daily dosing	0.86	0.52–1.43	.559
Occurrence of side effects	1.35	0.71–2.58	.366
Worries about side effects	1.75	0.98–3.14	.059[a]
No specialist visit in past year	0.89	0.54–1.46	.633
Using less tools to prevent forgetting (≤1)	1.66	1.01–2.75	.047[a]
Difficulties with medication use			
Due to forgetting	3.72	1.39–9.94	.009[a]
Due to side effects	1.64	0.49–5.53	.423
Due to too many pills	3.59	1.09–11.76	.035[a]
Knowledge			
Insufficient knowledge			
On purpose of medicines	0.83	0.26–2.61	.749
On when to take medicines	0.66	0.12–3.69	.639
On how much medicines to take	1.12	0.33–3.78	.853
On medications effects	1.29	0.72–2.30	.386
On side effects	0.99	0.61–1.64	.998
On what to do when a dose is forgotten	3.32	1.81–6.08	≤.001[a]
Quality of life			
SF-12			
Physical health	1.02	0.99–1.04	.154
Mental health	0.99	0.97–1.02	.686
Attitudes and beliefs			
BMQ attitudinal quadrants			
Accepting		Reference	
Ambivalent	2.30	1.23–4.32	.009[a]
Indifferent	1.87	0.99–3.53	.053[a]
Skeptical	0.94	0.22–3.91	.926
Satisfaction with information			
SIMS			
Sum score	1.01	0.97–1.06	.542
Subscale action and usage	1.04	0.95–1.14	.366
Subscale potential problems	1.01	0.94–1.09	.778
Depression and anxiety			
PHQ-4			
≥3 (mild to severe)	1.14	0.64–2.03	.659

Abbreviations: BMQ, Beliefs About Medicines Questionnaire; CI, confidence interval; CVD, cardiovascular disease; OR, odds ratio; PHQ-4, 4-item Patient Health Questionnaire; SF-12, 12-item Short Form; SIMS, Satisfaction With Information About Medicines Scale.
[a]$P \leq .10$, included in multivariate logistic regression analysis.
[b]Data from 9 participants are missing.

does not reflect patients' actual intake of medications. Second, the adherence rate to cardiovascular medications in this sample could not be assessed because of the manner of patient inclusion. We have chosen for this manner to include equally group-sized samples of adherent and nonadherent patients to optimize the identification of associated factors. Third, a small number of questions in the patient questionnaire were designed by our research team and were modified based on other instruments. The validity and reproducibility of these self-composed questions remain unclear. Finally, scoring the measure of anxiety and depression (PHQ-4) together in this study might be seen as a limitation because both constructs may influence nonadherence in different ways. Therefore, the absence of a relationship of this measure with nonadherence might be a result of the confounded measure. However, the scores in severity of the constructs were relatively low and may also explain the absence of a relationship.

Conclusions

This study highlighted the potential influence of several factors on cardiovascular medication nonadherence according to pharmacy refill data. Particularly, factors related to forgetting to take medications and patients' beliefs about medicines should be addressed. To enhance cardiovascular medication nonadherence, intervention strategies should be developed mainly focusing on the unintentional dimension of nonadherence and should include information on what to do in case of a missed dose and tools for patients to prevent forgetting. However, the role of factors that underlie intentional nonadherence, in particular patients' beliefs about medicines, should also be addressed.

TABLE 3 Results of Multivariate Analysis of Variables Associated With Cardiovascular Medication Nonadherence			
Variables	OR[a]	95% CI	P
Male gender	1.58	0.93–2.70	.094
Using less tools to prevent forgetting (≤1)	1.62	0.95–2.77	.080
Difficulties with medication use			
Due to forgetting	3.16	1.09–9.18	.034[b]
Insufficient knowledge			
On what to do when a dose is forgotten	2.80	1.48–5.32	.002[b]
BMQ			
Accepting		Reference	
Ambivalent	2.26	1.16–4.37	.016[b]
Indifferent	1.80	0.92–3.52	.087
Skeptical	0.86	0.19–3.88	.841

Abbreviations: BMQ, Beliefs About Medicines Questionnaire; CI, confidence interval; OR, odds ratio.
[a]Adjusted for all other variables in the final multivariate analysis.
[b]$P \leq .05$ = statistically significant.

What's New and Important

- Several factors, especially related to forgetting and patient beliefs, influence adherence to cardiovascular medications.
- Healthcare providers must inform patients adequately about their medications and the issue of forgetting and should support patients when they experience conflicting medication-related beliefs or attitudes.
- To enhance adherence to cardiovascular medications, healthcare providers must explore the factors related to both the intentional and unintentional dimensions of nonadherence. It must also be recognized that these factors might be interacting.

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