Switching from vitamin K antagonists to direct oral anticoagulants: treatment satisfaction and patient concerns

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Received: 8 November 2019 | Accepted: 10 March 2020

DOI: 10.1111/jth.14793

ORIGINAL ARTICLE

jth

Switching from vitamin K antagonists to direct oral anticoagulants: Treatment satisfaction and patient concerns

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Abstract

Background: Since direct oral anticoagulants (DOACs) have been introduced for treatment and prevention of thromboembolic diseases, patients on vitamin K antagonists (VKA) have to decide whether to remain on VKA or switch to DOAC. The goal of this study was to evaluate treatment satisfaction, preferences, and concerns among those who already have switched from VKA to DOAC.

Methods: A questionnaire was sent to 2920 former patients of three anticoagulation clinics in the Netherlands, who switched from VKA to DOAC (2016-2017). Questions concerned demographics, treatment satisfaction, concerns, perspectives on antidotes, and monitoring. To identify predictors for being concerned about adverse events, logistic regression was used to estimate crude- and adjusted (age and sex) odds ratios (OR) and 95% confidence intervals (95% CI).

Results: One thousand, three hundred ninety-nine questionnaires (response rate 48%) were used for analysis. DOAC treatment satisfaction was high (mean 8.8 of a maximum 10-point score). A quarter of patients expressed concerns about adverse events. Predictors for being concerned were age < 60 years (vs age > 75 years, OR 4.1, 95% CI 2.6-6.4), female sex (OR 1.3, 95% CI 1.0-1.6), and high education (OR 1.6, 95% CI 1.2-2.2). Fifty-nine percent of all patients indicated antidote availability as important, 73% would be willing to participate in DOAC monitoring.

Conclusions: DOAC treatment satisfaction was high. A substantial number of patients expressed concerns about adverse events, especially women, patients aged < 60 years, or highly educated patients. Our findings among patients who already had switched to DOAC may assist in the process of shared decision-making when switching a patient from VKA to DOAC is considered.

KEYWORDS

anticoagulants, antithrombins, factor Xa inhibitors, patient satisfaction, patient preference

1 | INTRODUCTION

Direct oral anticoagulants (DOACs) are increasingly prescribed for thromboembolic prophylaxis in atrial fibrillation and for the treatment of venous thrombosis, at the expense of the more traditional vitamin K antagonists (VKA).[1] Having fewer interactions with co-medication and diet and a more stable pharmacokinetic profile than VKA, DOACs do not require routine laboratory monitoring. Recently, DOACs have replaced VKA in international guidelines as first choice of anticoagulant for treatment and prevention of thrombotic events.[2,3]

For patients who are already on treatment with VKA and are eligible for DOAC treatment, the decision whether to remain on VKA or switch to a DOAC can be individualized, depending on factors such as patient preference, time in therapeutic range, therapy adherence, and concerns about adverse outcomes.[2] Identifying patient preferences and concerns among patients who already have switched from VKA to DOAC may assist in this process of shared decision-making.

Traditionally, the need for routine plasma level monitoring for VKA treatment ensured structured follow-up of patients at anticoagulation clinics. For DOACs, which do not require routine monitoring, therapy evaluation at regular intervals with a health-care provider is recommended,[4] also due to the severity of potential complications with this treatment. Whether these recommendations are actually adopted in clinical practice, and how patients who have switched to a DOAC appreciate their new treatment is currently not well known.

In order to understand how former VKA patients evaluate their DOAC treatment and to identify patient preferences and concerns with DOACs, we sent a questionnaire to former VKA patients.

Essentials

- Treatment satisfaction and concerns about side effects with DOACs among previous VKA users are unknown.
- A questionnaire was sent to 2920 former VKA patients who switched to DOAC.
- Treatment satisfaction with DOACs was high; a quarter of patients expressed concerns about adverse events.
- These findings may assist in the process of shared decision-making when considering a switch from VKA to DOAC.

2 | METHODS

2.1 | Study population

Between May and July 2018, we sent a paper questionnaire to 2920 consecutive patients aged ≥ 18 years who were switched from a VKA to a DOAC by their treating physician (eg, cardiologist, internist, general practitioner). Patients were enlisted through three anticoagulation clinics (locations in Amsterdam, Leiden, and the Hague) in the Netherlands where they had used VKA (phenprocoumon or acenocoumarol) and were switched to a DOAC (rivaroxaban, apixaban, dabigatran, or edoxaban) between January 2016 and December 2017.

Relevant patient information (name, home address) was extracted from the computerized patient records of the anticoagulation clinics after which the paper questionnaire was mailed to the patient's home address. Patients were asked to return the questionnaire, which was anonymized, as no reference to home address or patient's name was included in the questionnaire. Of note, while this procedure guaranteed anonymity of the participants, it prevented sending reminders. This study was approved by the medical ethics committee of the Leiden University Medical Center (LUMC), the Netherlands.

2.2 | Study design

The questionnaire was developed in the LUMC by researchers and input was asked from medical specialists and the patient interest group "Harteraad" and a pilot study was conducted amongst a small group of eligible patients in which the goals were to assess if patients understood the questions, to test whether the questionnaire was not too long, and to get an idea about the response rate. Based on the pilot study, the length of the questionnaire seemed to be acceptable as the majority of the questionnaires were filled in properly. Based on patient feedback a number of questions were formulated differently. Several questions (eg, about concerns) were added after the pilot study (questions 17-22, Appendix S1 in supporting information). The adjusted questionnaire was then sent to all eligible patients. Patients who were willing to participate returned the survey in a pre-paid envelope to the LUMC. All collected data were self-reported. The acronym MONDOAC (MONitoring of Direct Oral Anticoagulants) was used for this study.

2.3 | Survey components and outcomes

The final survey (Appendix S1) required demographics, primary anticoagulation indication, information about previous VKA treatment, comorbidity, co-medication, DOAC type and dose, the date the DOAC was started, education level, treatment satisfaction, treatment concerns, bleeding complications, and patient perspectives on antidote availability and anticoagulant level monitoring. Primary outcomes of this study were treatment satisfaction and concerns about adverse events. Satisfaction with DOAC treatment was measured on a numeric scale (1-10), and patients were divided into the three following groups: unsatisfied (0-5), satisfied (6-7), very satisfied (8-10). Patients were considered satisfied with a DOAC when they filled in a 6 or higher of a maximum 10-point score. The cut-points were based on the assessment system that is most commonly used in Dutch education.[5] In this assessment system 5 or lower is considered unsatisfactory, 6 and 7 are considered as satisfactory, and 8-10 are considered as good–very good–outstanding. Treatment concerns were defined as feeling anxious about

potential DOAC-related complications, such as minor bleeding, major bleeding, thromboembolic events (eg, venous thrombosis or cerebral infarction), or death due to DOAC-related adverse events, and were measured on a 4-point scale (no concerns, or slightly, moderately, or extremely concerned). Patients were considered concerned when they had indicated to be slightly, moderately, or extremely concerned about the possible occurrence of bleeding, thromboembolic events, or death. To study which patients were most concerned about potential complications, exposures of interest were age, sex, education level, comorbidity, time on VKA before switching to a DOAC, frequency of previous international normalized ratio (INR) controls on VKA therapy, and time on DOAC. Also, to investigate which patients were more likely to consider antidote availability and DOAC monitoring as important, these same exposures were studied. High educational level was defined as having followed a higher professional education or a university education. Comorbidity was defined as suffering from any (chronic) illness that was different from the main anticoagulation indication, at the time of filling in the questionnaire. Time on VKA therapy before switching to a DOAC was considered long when it was more than 2 years. Patients were considered stable on VKA when the frequency of INR controls was less than once per month. Time on DOAC was defined as the time between switching to a DOAC and filling out the questionnaire, and was considered as long when it was more than 1 year. Patient perspectives on the importance of antidote availability and the preparedness of patients to monitor DOAC levels, as is common practice with VKA, were also asked. Antidote availability was considered as important when patient answered "(strongly) agreed" to the statement: "I think it is important that an antidote is available," and was considered as not important if patients answered "neutral" or "(strongly) disagreed." When patients were asked if they would consider anticoagulant level monitoring with DOACs, patients who answered "yes," regardless of the frequency they indicated (once per year/6 months/1 month or as often as may be needed), were considered patients who were willing to be monitored. For self-reported bleeding complications, minor bleeding was defined as any bleed (eg, superficial skin bleeding, nose bleed) that did not require hospital treatment. Major bleeding was defined as any bleed that required hospital treatment.

2.4 | Statistical analysis

Baseline characteristics are presented as numbers and percentages, or as overall means (±standard deviation [SD]), and stratified by DOAC type. The observation time was defined as the number of days between switch to a DOAC and the time that the questionnaire was completed or when DOAC therapy was ceased, whichever came first. Being concerned about adverse events was measured as a dichotomous variable for the total follow-up period and calculated as a proportion.

To identify potential predictors for being concerned on DOAC treatment, odds ratios (ORs) and their 95% confidence intervals (95% CIs) were estimated using univariable and multivariable logistic regression analysis, adjusting for age and sex where applicable. Potential predictors for the importance of a DOAC antidote and for willingness to monitor DOACs were also studied. In the case of a missing value, the variable was excluded from analysis.

All statistical analyses were performed with SPSS for Windows, release 25.0 (SPSS).

3 | RESULTS

3.1 | Study population MONDOAC

A total of 2920 eligible patients were identified through three Dutch anticoagulation clinics. Overall, 112 questionnaires were returned without being filled out (n = 91 due to a change in address that was not known from electronic patients records of the anticoagulation clinics; n = 29 patients died before receiving the questionnaire). A total of 1399 questionnaires were returned and were used for analysis, which led to a response rate of 48%.

The mean age of patients was 74 years (SD 10), 816 were male (60%), the mean time on DOAC therapy was 504 days (SD 260), and atrial fibrillation was the primary indication for anticoagulant therapy (in 1068 patients; 76%; see Table 1). The duration of VKA therapy before switching to a DOAC was longer than 2 years for 959 patients (70%). Comorbidity was present in 997 patients (75%), 465 patients (34%) reported a high education level, intervals of INR control during previous VKA treatment were weekly for 300 patients (23%) and monthly or less for 542 patients (41%). The location of INR control was at the anticoagulation clinic for 873 patients (64%), during a house visit for 114 patients (8%), and 370 patients (27%) used self-monitoring. Of the responders, 21% (n = 291) experienced a minor bleeding (one or more) during follow-up. The total number of reported events was 486, of which the majority were superficial skin bleeds (56%) and epistaxis (22%). Sixty patients (4%) experienced a major bleeding event (in total 63 events). Melena (21%), epistaxis (19%), haemoptysis (19%) were most often reported as events. Results were comparable for all DOAC types (Table S2).

3.2 | DOAC treatment satisfaction and concerns

The general therapy satisfaction for DOAC treated patients was high (mean 8.8 on a 10-point scale) (Figure S1); 1029 patients (88%) indicated they were "very satisfied," 120 patients (10%) indicated they were "satisfied," and only 23 patients (2%) indicated they were "unsatisfied" during the month before filling out the questionnaire (Table 2). After stratifying for anticoagulation indication (Table 2) and DOAC type (Table S1), results remained similar. Two hundred twenty-seven patients (16%) did not report satisfaction (did not fill in the question of interest); 322 patients (26%) indicated they were concerned (slightly to extremely concerned) about the occurrence of a major bleed (Table 3). The majority of patients indicated they were not concerned about the risk of major bleeding while on DOAC therapy (n = 959, 75%). These rates were similar for minor bleeding. Concerns for the occurrence of a thromboembolic event were

TABLE 1 Baseline characteristics of questionnaire responders (n = 1399)

	Total		Rivaroxaban		Apixaban		Dabigatran		Edoxaban	
Male sex	816	(60)	247	(58)	221	(61)	248	(63)	87	(53)
Age	74	(10)	72	(11)	74	(9)	75	(9)	75	(10)
Atrial fibrillation	1068	(76)	285	(66)	305	(81)	330	(82)	137	(84)
Venous thromboembolism	227	(16)	121	(28)	40	(11)	39	(10)	22	(13)
Other indications	129	(10)	29	(7)	27	(8)	33	(9)	15	(9)
Comorbidity	997	(75)	292	(69)	279	(76)	294	(76)	129	(80)
Diabetes	207	(15)	63	(15)	55	(15)	58	(15)	26	(16)
Hypertension	590	(42)	166	(39)	164	(44)	183	(47)	71	(44)
Days on DOAC therapy	504	(260)	530	(274)	499	(275)	531	(248)	382	(169)
Time on VKA therapy ≥ 2 years	959	(70)	296	(69)	256	(69)	274	(70)	123	(76)
High educational level	465	(34)	149	(35)	117	(32)	154	(39)	42	(26)
Interval INR control – weekly	300	(23)	101	(24)	79	(21)	84	(22)	30	(20)
Interval INR control – monthly or less	542	(41)	165	(40)	150	(40)	162	(42)	60	(39)
INR monitoring at anticoagulation clinic	873	(64)	275	(65)	250	(66)	249	(64)	90	(56)
INR monitoring at house visit	114	(8)	43	(10)	27	(7)	25	(7)	14	(9)
Self-monitoring INR	370	(27)	105	(25)	93	(25)	113	(29)	56	(35)

Note: Continuous variable denoted as mean (standard deviation), categorical variables as number (percentage).

Abbreviations: DOAC, direct oral anticoagulant; INR, international normalized ratio; MS, medical specialist; VKA, vitamin K antagonist.

TABLE 2 DOAC treatment satisfaction (scale 1-10) in the month before the questionnaire

	Total population (n = 1171)		AF (n = 1068)		VTE (n = 182)		Other (n = 100)	
Mean	8.8	(1)	8.8	(1)	8.7	(1)	8.9	(1)
Unsatisfied (0-5)	22	(2)	19	(2)	2	(1)	1	(1)
Satisfied (6-7)	120	(10)	82	(9)	20	(13)	11	(11)
Very satisfied (8-10)	1029	(88)	792	(89)	135	(86)	88	(88)

Note: Continuous variable denoted as mean (standard deviation), categorical variables as number (valid percentage)

"Other" indicates (self-reported) cardiac diseases (eg, heart failure, heart valve disease), vascular diseases, or other

Abbreviations: AF, atrial fibrillation; VTE, venous thromboembolism.

present in 286 patients (22%); 277 patients (22%) were concerned about death due to a bleeding or thromboembolic event while on DOAC therapy. One hundred thirty-two patients (9%) did not report their level of concern (did not fill in the question of interest).

3.3 | Antidote availability and anticoagulant level monitoring

When asked about the importance of the availability of an antidote for the anticoagulant of the patient, 103 patients (8%) (strongly) disagreed with the statement "The availability of an antidote is important."; 720 patients (59%) (strongly) agreed with the statement, and 406 patients (33%) had no opinion (neutral) about the statement (Table 4, Figure S2). The majority of patients (74%) indicated they were willing to engage in DOAC level monitoring (Table 5, Figure S3); 370 patients (29%) were prepared to undergo monitoring once per year, 337 patients (27%) once per 6 months, 100 patients (8%) once per month, and 123 patients (10%) as often as might be needed. Two hundred forty-one patients (27%) indicated they did not want DOAC monitoring.

3.4 | Predictors for being concerned about adverse events during DOAC therapy in MONDOAC

Predictors for being concerned about adverse events were age < 60 years (vs age > 75 years, adjusted OR 4.1, 95% CI 2.6-6.4), female sex (adjusted OR 1.3, 95% CI 1.0-1.6), and a high education level (adjusted OR 1.6, 95% CI 1.2-2.2) (Table 6, Figure S4). Patients who indicated that the availability of an antidote is important were 1.7-fold (95% CI 1.3-2.3) more likely to be concerned about the occurrence of adverse events than patients who did not consider the availability of an antidote as important. Patients who were willing to have their treatment monitored were 2.2-fold (95% CI 1.7-3.0)

TABLE 3 Direct oral anticoagulant treatment concerns

Concerns about major bleeding		
Not at all concerned	959	(75)
Slightly concerned	238	(19)
Moderately concerned	62	(5)
Extremely concerned	22	(2)
Concerns about minor bleeding		
Not at all concerned	977	(76)
Slightly concerned	243	(19)
Moderately concerned	50	(4)
Extremely concerned	14	(1)
Concerns about thromboembolic events		
Not at all concerned	985	(78)
Slightly concerned	208	(16)
Moderately concerned	60	(5)
Extremely concerned	18	(1)
Concerns about death due to bleeding or thromboembolic events		
Not at all concerned	1008	(78)
Slightly concerned	187	(15)
Moderately concerned	66	(5)
Extremely concerned	24	(2)

Note: Categorical variables as number (percentage).

more likely to be concerned. Other patient characteristics that were studied in relation to being concerned (duration of treatment with VKA before switch to DOAC, frequency of previous INR controls, the presence of comorbidity, and time between switch to DOAC and sending the questionnaire) could not be identified as predictors (Table 6).

4 | DISCUSSION

In this study of patients who recently switched from VKA to DOAC, treatment satisfaction with DOACs, as measured on a 10-point scale, was high (mean of 8.8 points). Concerns about adverse events were present in 22% to 26% of patients. Those who had concerns were more likely to be women, younger than 60 years, and highly educated compared with patients who had no concerns. About 720 (59%) of patients considered the availability of an antidote for their anticoagulant as important and 930 (74%) patients would consider participating in DOAC-level monitoring if that would improve outcome. These preferences were more likely to be present in patients who were concerned about adverse events.

Our results on treatment satisfaction are in line with earlier studies. In a recent systematic review that included 21 studies assessing patient-reported outcomes associated with DOAC use,[6] the majority of studies described high DOAC treatment satisfaction. Other characteristics have been less often studied, to our knowledge only in a survey from the United States in which 519 venous thrombosis patients who used VKA or DOAC for initial venous thrombosis

TABLE 4 Antidote availability and anticoagulant level monitoring

Availability of an antidote is important		
Strongly disagreed	37	(3)
Disagreed	66	(5)
Neutral	406	(33)
Agreed	500	(41)
Strongly agreed	220	(18)

Note: Categorical variables as number (percentage).

TABLE 5 Willingness to monitor direct oral anticoagulants

No, not at all	241	(27)
Yes, but not more often than once/year	370	(29)
Yes, but not more often than once/6 months	337	(27)
Yes, but not more often than once/month	100	(8)
Yes, as often as needed	123	(10)

Note: Categorical variables as number (percentage).

treatment were surveyed about their concerns and preferences regarding anticoagulant therapy.[7] They found that 16% to 33% patients were concerned about adverse events (venous thrombosis 33%, major bleeding 21%, minor bleeding 16%, death 29%), which was similar to our study results regarding concerns about bleeding, yet higher regarding concerns about thrombosis. This discrepancy could be explained by the difference in population (venous thromboembolism patients only), as the majority of our surveyed population consist of atrial fibrillation patients who received anticoagulants for thromboprophylaxis. Because their definition of being concerned (which included only the "extremely concerned" patients) is different from our definition, in which we also considered slightly and moderately concerned as noteworthy, results on this issue are difficult to compare. In the U.S. survey, older patients seemed to be more concerned about major bleeding (prevalence ratio 1.1, 95% CI 1.0-1.2 per 10-year increment), which is in contrast with our results showing people aged < 60 years have higher rates of concern when compared with patients > 75 years. As opposed to our results, they found no differences in likelihood of being concerned according to sex. Differences in studied outcomes (predictors for concerns about major bleeding and thromboembolic events studied separately versus predictors for concerns about all adverse events combined) and study population (DOAC and VKA users versus DOAC users only) and a smaller sample size of the U.S. study might explain these discrepancies.

Anticoagulant characteristics that patients considered important in the present study, such as the reversibility of an anticoagulant, were also studied by Lutsey et al[7] In their study, 53% of patients strongly agreed with the statement "I prefer a blood thinner that is reversible," which was higher than in our study in which only 18% strongly agreed with a similar statement (Table 4). This contrast may be explained by the fact that the U.S. study also included VKA

TABLE 6 Predictors for being concerned during DOAC therapy in MONDOAC

	Not concerned		Concerned		OR (95% CI)	OR[a] (95% CI)
>75 years	395	(69)	177	(31)	Reference	Reference
60-75 years	368	(64)	204	(36)	1.2 (1.0-1.6)	1.3 (1.0-1.6)
<60 years	37	(36)	66	(64)	4.0 (2.6-6.2)	4.1 (2.6-6.4)
Male	491	(66)	253	(34)	Reference	Reference
Female	301	(61)	190	(39)	1.2 (1.0-1.6)	1.3 (1.0-1.6)
Low education	342	(70)	146	(30)	Reference	Reference
High education	243	(58)	173	(42)	1.7 (1.3-2.2)	1.6 (1.2-2.2)
Time on VKA before switch ≥ 2 years	566	(66)	297	(34)	Reference	Reference
Time on VKA before switch < 2 years	234	(61)	147	(39)	1.2 (0.9-1.5)	1.2 (0.9-1.5)
INR control ≤ monthly	310	(66)	162	(34)	Reference	Reference
INR control ≥ weekly	171	(61)	109	(39)	1.2 (0.9-1.7)	1.2 (0.9-1.7)
No comorbidity	199	(65)	109	(35)	Reference	Reference
Comorbidity	591	(64)	333	(36)	1.0 (0.8-1.4)	1.1 (0.9-1.5)
Time on DOAC ≥ 1 year	401	(65)	220	(35)	Reference	Reference
Time on DOAC < 1 year	186	(61)	119	(39)	1.2 (0.9-1.6)	1.2 (0.9-1.6)
Antidote availability not important	367	(73)	135	(27)	Reference	Reference
Antidote availability important	410	(59)	290	(41)	1.9 (1.5-2.5)	1.7 (1.3-2.3)
Not willing to monitor DOAC	258	(78)	71	(22)	Reference	Reference
Willing to monitor DOAC	549	(60)	370	(40)	2.5 (1.8-3.3)	2.2 (1.7-3.0)

Abbreviations: DOAC, direct oral anticoagulant; INR, international normalized ratio; MONDOAC, Monitoring of DOAC Study; VKA, vitamin K antagonist.

[a]Adjusted for age and sex (where applicable).

patients (n = 218, 42% of the surveyed population), for which vitamin K is widely available as an antidote. Importantly, also in the study from Lutsey et al a substantial amount of patients did not consider the availability of an antidote for anticoagulant treatment as important, which is noteworthy because all anticoagulants carry the risk of bleeding when dosed too high.[8,9] The finding of Lutsey et al and our finding that some patients do not consider an antidote important when treated with a DOAC suggests that side effects from the treatment are not well transmitted to some patients who take a DOAC.

In previous studies in which patients were asked about regular anticoagulant level monitoring, results were similar to our study, in which 27% of patients were not willing to participate in anticoagulant-level monitoring. In the survey by Lutsey et al, 35% strongly agreed with the statement "regular blood tests to monitor a blood thinner's level would make me less likely to use that blood thinner." In another Dutch study,[10] 135 venous thromboembolism patients treated with VKA were asked whether they would switch to a DOAC if there was no need for laboratory monitoring, which 36% of patients indicated they would.

Despite the high treatment satisfaction, a substantial percentage of patients (~25%) was still concerned about the occurrence of bleeding or thromboembolic events. The patient groups we could identify as being the least concerned were those of older age and low education, which is a somewhat paradoxical finding as patients who share these characteristics are in general at a higher risk of adverse events like bleeding and thromboembolism.[11-14] The question then arises, whether these patients are aware of the potential severe complications of anticoagulant treatment. Interestingly, the statement included in our questionnaire about the importance of an available antidote was considered least important by the patients who were also least concerned. These results suggest that these patients are insufficiently aware of the potential complications of an anticoagulant. Regular follow-up by a physician may reinsure that patients are aware of treatment complications and may also provide an opportunity to discuss patient concerns. Although guidelines state that frequent follow-up with DOACs is necessary,[4] it is questionable whether this is also common practice, because we have shown in our accompanying article that only n = 547 (45%) patients on DOAC visited their treating physician or general practitioner once per year to discuss their use of anticoagulant treatment.[15] From our finding that the majority of patients (>70%) were prepared to monitor their DOAC albeit at least once per year follows that most patients would not have a problem with regular follow-up visits.

This study has strengths and limitations. A strength of the current study is the detailed questionnaire, which provides insights into the appreciation and possible pitfalls associated with DOAC use. Together with large clinical trials that studied DOAC safety and

efficacy, studies like these are crucial for post-marketing evaluation of how DOACs are adopted into daily practice and provide starting points for further improvement of DOAC use. Another strength is that we studied predictors for being concerned about adverse events that have not been studied before in the context of DOACs. As concerned patients were more likely to consider anticoagulant reversibility and level monitoring as important, anticoagulants with these characteristics might be a suitable choice for them.

Potential limitations of this study should be acknowledged. First, non-response bias cannot be excluded as the response rate of our questionnaire was 48%. This is an acceptable response rate of questionnaires in social sciences,[16] but may have affected our study results as non-response bias cannot be excluded. For example, the high number of responders with self-reported academic background (34% while in the Netherlands <20% of individuals have such an educational background) suggests that patients with low educational status were underrepresented. Also, patients who are not satisfied with DOAC treatment might have been unwilling to participate in the study. To establish the generalizability, we recommend confirmation of our study results, also because the topic is not well studied in general. The survey could provide a framework for others looking to do similar work in the future. Second, our questionnaire was sent to DOAC users who were former VKA users. Obviously, these patients were familiar with certain aspects of VKA (eg, level monitoring or wide availability of an antidote), which might have influenced their evaluation of DOACs. Therefore, repeating this study in patients who have not used VKA before they started with DOAC is interesting. Finally, we did not use standardized quality of life scores for measuring therapy satisfaction, as our study goal was to provide a general evaluation of DOAC treatment regarding several aspects of treatment rather than go into depth about quality of life. We collaborated however with a Dutch patient interest group while developing the questionnaire.

In conclusion, high treatment satisfaction was shown in patients who switched from VKA to DOAC. Still, a substantial number of patients expressed concerns about adverse events, with young age, female sex, high education, and appreciating antidote availability or level monitoring as important predictors. These factors could be used when switching from VKA to DOAC is considered. For future research, repeating this study in patients who did not use VKA before is recommended.

CONFLICTS OF INTEREST

MMA Toorop, N van Rein, FJM van der Meer, MC Nierman, HW Vermaas, SC Cannegieter and WM Lijfering have nothing to disclose. MV Huisman reports grants from ZonMW Dutch Healthcare Fund, grants and personal fees from Boehringer-Ingelheim, Pfizer-BMS, Bayer Health Care, Aspen, Daiichi-Sankyo, outside the submitted work.

AUTHOR CONTRIBUTIONS

Myrthe M. A. Toorop, Suzanne C. Cannegieter, and Willem M. Lijfering designed the research. Myrthe M. A. Toorop, Felix J. M. van der Meer, Melchior C. Nierman, Helga W. Vermaas, and Willem M. Lijfering collected the data. Myrthe M. A. Toorop, and Willem M. Lijfering analyzed the data. Myrthe M. A. Toorop and Willem M. Lijfering wrote the manuscript. Myrthe M. A. Toorop, Nienke van Rein, Felix J. M. van der Meer, Melchior C. Nierman, Helga W. Vermaas, Menno V. Huisman, Suzanne C. Cannegieter, and Willem M. Lijfering revised the paper for important intellectual content.

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REFERENCES

1. Gadsboll K, Staerk L, Fosbol EL, et al. Increased use of oral anticoagulants in patients with atrial fibrillation: temporal trends from 2005 to 2015 in Denmark. *Eur Heart J*. 2017;38:899-906.
2. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37:2893-2962.
3. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American college of cardiology/American heart association task force on clinical practice guidelines and the heart rhythm society. *J Am Coll Cardiol*. 2019;74:104-132.
4. Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. *Eur Heart J*. 2018;39:1330-1393.
5. Erasmus University Rotterdam E, Dutch grading system. https://www.eur.nl/en/education/practical-matters/studying-eur/educational-system/dutch-grading-system. Accessed February 2020.
6. Afzal SK, Hasan SS, Babar ZU. A systematic review of patient-reported outcomes associated with the use of direct-acting oral anticoagulants. *Br J Clin Pharmacol*. 2019;85(12):2652-2667.
7. Lutsey PL, Horvath KJ, Fullam L, et al. Anticoagulant preferences and concerns among venous thromboembolism patients. *Thromb Haemost*. 2018;118:553-561.
8. Reilly PA, Lehr T, Haertter S, et al. The effect of dabigatran plasma concentrations and patient characteristics on the frequency of ischemic stroke and major bleeding in atrial fibrillation patients: the RE-LY Trial (Randomized Evaluation of Long-Term Anticoagulation Therapy). *J Am Coll Cardiol*. 2014;63:321-328.
9. Astrup T. New aspects in blood coagulation and fibrinolysis and their relations to coronary thrombosis and coronary sclerosis. *Wiener Zeitschrift fur innere Medizin und ihre Grenzgebiete*. 1958;39:373-386.
10. Brekelmans MP, Kappelhof M, Nieuwkerk PT, Nierman M, Buller HR, Coppens M. Preference for direct oral anticoagulants in patients treated with vitamin K antagonists for venous thromboembolism. *Neth J Med*. 2017;75:50-55.
11. Cressman AM, Macdonald EM, Yao Z, et al. Socioeconomic status and risk of hemorrhage during warfarin therapy for atrial fibrillation: a population-based study. *Am Heart J*. 2015;170:133-140, 40 e1-3.
12. Cox AM, McKevitt C, Rudd AG, Wolfe CDA. Socioeconomic status and stroke. *Lancet Neurol*. 2006;5:181-188.
13. Goodman SG, Wojdyla DM, Piccini JP, et al. Factors associated with major bleeding events: insights from the ROCKET AF trial (rivaroxaban once-daily oral direct factor Xa inhibition compared with vitamin K antagonism for prevention of stroke and embolism trial in atrial fibrillation). *J Am Coll Cardiol*. 2014;63:891-900.
14. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. *JAMA*. 2001;285(18):2370.
15. Toorop MMA, van Rein N, Nierman M, et al. Self-reported therapy adherence and predictors for non-adherence in patients who

switched from vitamin K antagonists to direct oral anticoagulants. Accepted for publication by RPTH (10-01-2020). 2020.
16. Baruch Y, Holtom BC. Survey response rate levels and trends in organizational research. *Hum Relat*. 2008;61:1139-1160.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Toorop MMA, van Rein N, Nierman MC, et al. Switching from vitamin K antagonists to direct oral anticoagulants: Treatment satisfaction and patient concerns. *J Thromb Haemost*. 2020;18:1390–1397. https://doi.org/10.1111/jth.14793