A Survey on the Awareness and Attitude of Physicians on Direct Oral Anticoagulants in Qatar

Ahmed El-Bardissy, BSc, PharmD, BCPS[1], Hazem Elewa, RPh, PhD, BCPS[2], Shaban Mohammed, BSc, BCPS, AQ (Cardiology)[3], Ahmed Shible, RPh, BCPS, BCCCP[1], Rizwan Imanullah, BSc, MSc Clinical Pharmacy[4,5], and Abdul Moqeeth Mohammed, MBBS(Ind), P.G. Pathology(Ind), CCT(UK), MRCGP(UK), DRCOG(UK), DFSRH(UK), PG. Med. Edu(UK)[6]

Abstract

Direct oral anticoagulants (DOACs) are more commonly prescribed since their introduction. Reports on inappropriate prescribing have been observed which may indicate poor awareness on these agents. In this study, we aim to evaluate the extent of the physicians' knowledge on DOACs and its possible impact on physicians' confidence to prescribe these medications. A prospective cross-sectional survey was developed based on the literature review. Eligible participants were physicians and surgeons currently practicing at Hamad General Hospital in Qatar. The survey included questions on demographic and professional characteristics. It also evaluated the awareness and attitudes regarding safety, efficacy, and prescribing of DOACs. Over 6-month period, 175 practitioners responded to the survey. Overall awareness score was moderate (61% ± 18%). These scores were in alignment with participants' self-satisfaction with knowledge on DOACs (66% were not satisfied) and participants' confidence toward prescribing DOACs (48% were not confident). Age, degree of education, and years of experience had significant positive influence on awareness score. This survey indicates that practitioners have moderate awareness on DOACs. Future work should focus on reassessing practitioners' knowledge after providing well-designed education campaigns

Keywords

survey, direct oral anticoagulants, awareness

Introduction

For almost 80 years, warfarin has been the mainstay anticoagulant used in both treatment and prevention of various thromboembolic disorders such as atrial Fibrillation (AF), prosthetic heart valve, and venous thromboembolism (VTE).[1] Being the only oral anticoagulant for such duration created an in-depth knowledge, experience, and understanding of its clinical applications, management, and associated risks. However, its narrow therapeutic index, inter, and intrapatient variability led sometime to treatment failure or life-threatening adverse reactions that remain unexplained.[2,3]

Direct oral anticoagulants (DOACs) were introduced in 2010, with dabigatran—a direct thrombin inhibitor—followed by 4 factor Xa inhibitors (rivaroxaban, apixaban, edoxaban, and betrixaban).[1] Accumulated data from clinical trials and meta-analyses have shown that DOACs are noninferior to warfarin in stroke prevention for nonvalvular AF (NVAF), VTE, and recurrent VTE.[4] This has led to major changes in anticoagulation management.[5,6]

[1] Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar
[2] College of Pharmacy, Qatar University, Doha, Qatar
[3] Heart Hospital, Hamad Medical Corporation, Doha, Qatar
[4] Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar
[5] MSc Clinical Pharmacy Queen's University Belfast, Belfast, UK
[6] Consultant Ambulatory Internal Medicine Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar

Corresponding Author:
Hazem Elewa, Clinical Pharmacy and Practice Section, College of Pharmacy, Qatar University, Aljamaa Street, Doha 2713, Qatar.
Email: elewahazem@gmail.com

DOACs have practical advantages over warfarin including administration in fixed dosing, lack of frequent monitoring requirement, fewer drug, and food interactions, reduced risk of intracranial hemorrhage, and major bleeding.[1,4] Despite the advantages of DOACs over warfarin, those agents are not favorable in all patients, since they can increase the risk of gastrointestinal bleeding (especially rivaroxaban and dabigatran) and lack antidote (except for dabigatran).[6] Additionally, DOACs are not recommended or even contraindicated in certain situations. For example, DOACs are contraindicated in pregnant, lactating females, patients on renal dialysis, and those with advanced renal impairment. Limited data also support their use in morbidly obese patients.[7,8] Finally, cost-effectiveness of DOACs compared to warfarin remains an issue and totally depends on the health-care system strategy for each country.[9-11]

DOACs were introduced in Qatar in 2011, and currently, dabigatran and rivaroxaban are the only available agents on formulary at Hamad Medical Corporation (HMC), which is the main medical institution in the country. Our group has previously reported that over the 5-year period from 2011 till 2015, there has been a significant increase in the trend of usage of DOACs that reached 23% of all oral anticoagulants in 2015.[6] However, in a further analysis of this data, we have shown that DOACs were not always appropriately prescribed.[1]

To find out more about the reason for this inappropriate prescribing, we aim in this study to assess the knowledge and attitude of physicians from different specialties regarding DOACs and their reflection on their prescribing pattern.

Methods

Study Design and Population

A descriptive, cross-sectional survey using a self-administered questionnaire. The study took place over 6 months from December 2016 to June 2017. Eligible participants included all authorized physicians to prescribe anticoagulation at Hamad general hospital (HGH). Those who are not permitted to prescribe were excluded. The survey was hand-delivered by one of the investigators, and an introductory invitation cover page was attached explaining the purpose and objectives of the survey and assuring the anonymity of the participant's identity. The participants were approached based on sample of convenience.

Study Settings and Ethics Approval

The study was done at HGH which is a 603-bed tertiary teaching hospital in Qatar. The hospital covers all specialties except hematology–oncology and obstetrics. The study was approved by Hamad Medical Corporation's Institutional Review Board (HMC-IRB).

Sample Size Calculation

The sample size was calculated using Raosoft online calculator (www.roasoft.com)Given that the population size of medical practitioners in Qatar is 900, and to achieve a power of 80% with a margin of error of 5% and considering a 50% response distribution, a sample size of 140 participants was found to be adequate. Considering a 30% nonresponse rate, we aimed to recruit 175 participants.

Validation and Piloting

Structure and content of the survey were checked for validity (to ensure it produces true results) by 2 senior faculty members (one with expertise in surveys and pharmacy practice research and the other with clinical knowledge and teaching experience in clinical pharmacy), one clinical pharmacy specialist (with cardiovascular expertise), and internal medicine senior consultant. Modifications were made based on feedback provided. A pilot version was tested on randomly selected 10 participants with different specialties and years of experience. Respondents found the questionnaire clear and concise.

Survey Development

The survey was designed based on literature review on the effect of physician knowledge and attitude regarding DOACs and its impact on their prescribing pattern. The survey was composed of 4 domains (1) demographic and professional characteristics of the participants; (2) evaluating awareness regarding DOACs safety profile; (3) evaluating awareness regarding DOACs efficacy profile; and (4) evaluating the prescribing pattern of DOACs. Under the safety domain, 6 questions were designed to assess the general awareness on the safety of DOACs in comparison to warfarin. Under the efficacy domain, the attitude of participants regarding the efficacy of DOACs was assessed using 7 questions. The last domain had 7 questions to measure the physicians' prescribing pattern of DOACs and 1 question regarding the percentage of DOACs prescribed by participating physicians among patients requiring anticoagulation (Table 1).

Responses were on a 3-point Likert-type scale (disagree, don't know, and agree). The last question, however, was score ranging from (0% to 100%) with 20% intervals to rate the percentage of patients prescribed DOACs by the physicians.

Measured Outcome and Statistical Analysis

Descriptive and inferential statistical analyses were applied to the collected data using IBM Statistical Package for Social Sciences (IBM SPSS 24 software; IBM, New York). All variables were categorical including participants' demographics, professional information as well as their responses to questions assessing their knowledge and attitude toward the DOACs and were expressed as frequencies and percentages. Awareness score of 1 point was provided if the respondent agreed for true statements or disagreed for false statements and a score of zero point otherwise. This was done for all questions in the 3 domains except for the last question which was a score rating the percentage of patients prescribed DOACs by each

Table 1. Survey Awareness Domains, Questions, and Responses.

Agree—Respondents (%)	Don't know—Respondents (%)	Disagree—Respondents (%)
Attitude and awareness toward DOACs safety		
To what extent do you agree with the following statements?		
Can DOACs be used safely in patients with renal insufficiency?		
65 (37.1%)	26 (14.9%)	84 (48%)
Can DOACs be used safely in pregnant females?		
28 (16%)	66 (37.7%)	81 (46.3%)
Would DOACs interact with leafy green vegetables?		
19 (10.9%)	42 (24%)	114 (65.1%)
Do DOACs have an antidote?		
83 (47.4%)	20 (11.4%)	72 (41.1%)
Are DOACs associated with less major bleeding events compared to warfarin?		
95 (54.3%)	25 (14.3%)	55 (31.4%)
Would you suspect that DOACs have a lower risk for intracranial hemorrhage than warfarin?		
94 (53.7%)	32 (18.3%)	49 (28%)
Attitude and awareness toward DOACs efficacy		
To what extent do you agree with the following statements?		
Can DOACs anticoagulant effect be easily monitored?		
32 (18.3%)	11 (6.3%)	132 (75.3%)
Are DOACs given at fixed doses?		
136 (77.7%)	12 (6.9%)	27 (15.4%)
Are DOACs generally considered to be noninferior to warfarin in their efficacy?		
121 (69.1%)	18 (10.3%)	36 (20.6%)
Are majority of DOACs currently approved for VTE prevention in hip and knee replacement?		
95 (54.3%)	48 (27.4%)	32 (18.3%)
Are majority of DOACs currently approved for DVT and PE treatment?		
135 (77.1%)	23 (13.1%)	17 (9.7%)
Are majority of DOACs currently approved for stroke prevention in nonvalvular atrial fibrillation?		
127 (72.6%)	27 (15.4%)	21 (12%)
Would you prescribe DOACs to patients with mechanical valve replacement?		
31 (17.7%)	36 (20.6%)	108 (61.7%)
Attitude and awareness toward prescribing DOACs		
To what extent do you agree with the following statements?		
Would you prescribe DOACs to any new patient requiring anticoagulation therapy as long as they do not have contraindication?		
135 (77.1%)	12 (6.9%)	28 (16%)
Would you prescribe DOACs to any patient on warfarin requesting to switch to DOACs as long as they do not have contraindication?		
138 (78.9%)	18 (10.3%)	19 (10.9%)
Would you prescribe UFH or LMWH with the initiation of DOACs (especially dabigatran) for DVT and PE treatment?		
57 (32.6%)	43 (24.6%)	75 (42.9%)
Would you prescribe UFH or LMWH with the initiation of DOACs (especially rivaroxaban) for DVT and PE treatment?		
42 (24%)	43 (24.6%)	90 (51.4%)
Would you prescribe DOACs to any patient on warfarin who failed treatment due to lack of efficacy and/or increase incidence of bleeding as long as they do not have contraindication?		
104 (59.4%)	45 (25.7%)	26 (14.9%)
Are you satisfied with your knowledge on DOACs?		
61 (34.9%)	18 (10.3%)	96 (54.9%)
Do you feel confident upon prescribing DOACs?		
92 (52.6%)	15 (8.6%)	68 (38.9%)
What percentage of patients requiring anticoagulation do you prescribe DOACs for?		

Zero   20   40   60   80   100%

Abbreviations: DOACs, direct oral anticoagulants; LMWH, low molecular weight heparin; UFH, unfractionated heaprin; VTE, venous thromboembolism.

participant. The percentage awareness score (PAS) was calculated by dividing the participant score in each domain by the number of questions in that perspective domain (the maximum possible score) and multiplying the result by 100. Percentage awareness score was expressed as mean (standard deviation). Overall PAS was the sum of PAS in each domain. The *t* test

Table 2. Participants Baseline and Professional Characteristics.[a]

Demographics (n = 175)	
Age	
<36	101 (57.7%)
36-45	42 (24%)
>45	32 (18.3%)
Gender	
Female	29 (83.4%)
Male	146 (16.6%)
Specialty	
Internal medicine	120 (68.5%)
Cardiology	21 (12%)
Emergency	10 (5.7%)
Critical care	19 (10.9%)
Surgery	5 (2.9%)
Highest degree of education	
Consultants	55 (31.4%)
Fellows	40 (22.9%)
Residents	80 (45.7%)
Board certification	
Yes	80 (45.7%)
No	95 (54.3%)
Years of experience	
≤10	109 (62.3%)
11-20	48 (27.4%)
>20	18 (10.3%)

[a]Values are expressed as frequencies (%).

was used to test the effect of the profession as well as other demographic and professional parameters on the PAS. Analysis of variance test was used to test the effect of age on the PAS. A level of significance was set a priori at $P \leq .05$.

Results

Participants' Characteristics

Over 6-month period, 300 participants were approached among which 175 participated in the survey (response rate = 58.3%). Participants answered all survey questions. Majority (83.4%) of the participants were male, and about half (57.7%) of them were middle age (35 years of age or younger). One hundred fourteen (65%) physicians were internal medicine with the remaining from other specialties. Almost half of the respondents were residents (45.7%) while the remaining were consultants and fellows (31.4% and 22.9%, respectively). Almost half of the participants were board certified (45.7%; Table 2)

Evaluating Awareness Regarding DOACs

Awareness of physicians toward DOACs was assessed from different domains perspective (safety, efficacy, and prescribing). Participants' responses are reported in Table 1. Overall PAS was moderate (61% ± 18) and was lowest (52% ± 25) for awareness on safety and highest for awareness on prescribing (71% ± 24; Table 3). Interestingly, these scores were in alignment with participants' self-satisfaction with knowledge on DOACs (66% were not satisfied; Figure 1) and participants'

Table 3. Tested Domains and Scores.[a]

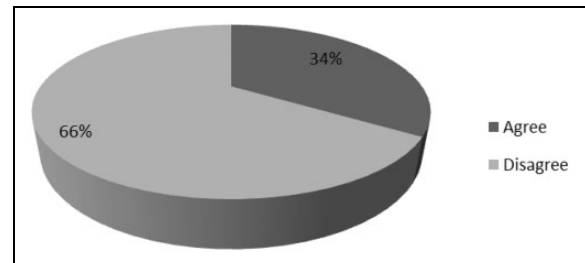| Domain	No of Items Tested	Score ± SD
Safety	6	52% ± 25
Efficacy	7	71% ± 24
Prescribing	7	60% ± 22
Overall	20	61% ± 18

[a]Values are expressed as mean (SD).

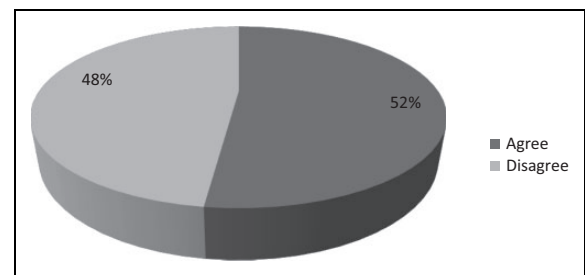**Figure 1.** Participants satisfaction with their knowledge regarding direct oral anticoagulants.

Figure 2. Participants confidence upon prescribing direct oral anticoagulants.

confidence toward prescribing DOACs (48% were not confident; Figure 2). As expected, age, degree of education, and years of experience had significant positive influence on PAS (Table 4). About two-third (59.3%) of the physicians were found to prescribe DOACs for 20% or less of their patients who require anticoagulation (Figure 3). When comparing the prescribing PAS score of the low DOAC prescribing physicians (20% or less) to the high DOAC prescribing physicians (40% or more), we did not find any significant difference (61.7 ± 22.5 vs 57.9 ± 21.9; $P = .29$).

Discussion

In this study, we attempted to assess the knowledge and attitude of physicians on DOACs, as well as their perceived satisfaction with self-knowledge and extent of DOACs they prescribe to patients in need for oral anticoagulation. The main finding of the study was that participants' DOACs awareness is moderate and matched their self-reported knowledge and confidence when prescribing DOACs. Although previous studies assessed physicians' attitude toward DOACs,[12-15] only few studies have tested the prescribers' knowledge and awareness. In 2016,

Table 4. Effect of Baseline and Professional Characteristics on Percentage Awareness Scores.[a]

Variable	PAS $\pm$ SD	P Value
Age		.027[b]
<36	58% $\pm$ 20	
36-45	64% $\pm$ 18	
>45	69 $\pm$ 11	
Gender		.4
Female	59% $\pm$ 20	
Male	62% $\pm$ 18	
Specialty		.4
Internal Medicine	62% $\pm$ 17	
Others	60% $\pm$ 21	
Highest degree of education		.023[b]
Consultants	68% $\pm$ 13	
Fellows	60% $\pm$ 18	
Residents	57% $\pm$ 20	
Board certification		.26
No	61% $\pm$ 19	
Yes	62% $\pm$ 18	
Years of experience		.021[b]
$\leq$10	57% $\pm$ 20	
11-20	62% $\pm$ 17	
>20	68% $\pm$ 15	

Abbreviations: PAS, percentage awareness score; SD, standard deviation.
[a]Statistical significance was tested using ANOVA for the following factors (age, highest degree of education and years of experience), while *t* test was used for (gender, board certification, and specially)
[b]P value <.05
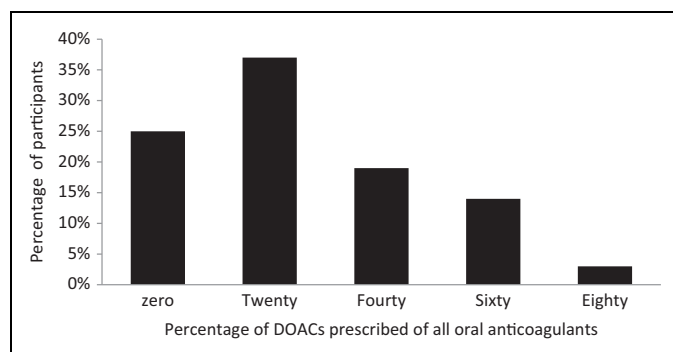
Figure 3. Extent of DOACs prescribed by participants for patients requiring oral anticoagulants. DOACs indicate direct oral anticoagulants.

Olaiya et al aimed to establish physicians' level of awareness of the different DOACs and to assess whether prescribers can recognize the level of anticoagulation in a hypothetical scenario.[16] Awareness on DOACs ranged from 50% to 88%. Additionally, recognizing the harm that could occur from performing an invasive procedure in a hypothetical clinical scenario was recognized by only 55% to 58%. These results seem to be in alignment with the current survey and yield the same conclusion. The declined level of awareness noted in this study also strongly explains our group's recent findings on the increased rate of inappropriate prescribing of DOACs in the

same study setting.[17] However, physicians are not expected to know all information on a drug in an individual therapeutic class; the situation is a bit different when it comes to a high alert medication class such as oral anticoagulants. Furthermore, inappropriate prescribing of DOACs (either through use of a wrong dose or for the wrong indication) can yield to major adverse events such as stroke, thrombosis, or bleeding. One thing to remember about DOACs compared to other anticoagulants is that they lack simple practical surrogate marker to use as a predictor for adverse reactions. Given the increasing number of patients using DOACs in clinical practice, prescribers' awareness is a very important aspect to ensure patient safety. Even if an individual clinician is unable to have perfect awareness on all agents in a certain class of medications, she or he should focus at least on the agents under formulary and those that are widely used at the institution.

In addition to our main finding above, we also observed that age, years of experience, and degree of education positively correlate with awareness on DOACs. Although one would think that recent graduates may have better awareness on these recently approved medications (DOACs), it seems that practical training and higher education degree was a more important factor in determining awareness of DOACs in our setting. Unexpectedly, we also found that the awareness of the frequent DOACs prescribers was not different compared to the unusual DOACs prescribers

Last but not least, our results have shown that for majority of the respondents, DOACs are not the first choice when prescribing oral anticoagulants. This finding is confirmed by our recent research work that explored the trend of use of oral anticoagulants in Qatar and found that in 2015, warfarin (77%) was still the main oral anticoagulant prescribed compared to DOACs (23%).[6] Similarly, a survey by Connell et al has found warfarin to be the most common choice of initial treatment of both deep venous thrombosis (DVT) (85.6%) and pulmonary embolism (PE) (89%) among attending physicians in the state of Rhode Island.[12]

A major limitation that we faced in this study is that our sample is not fully representative of all health-care providers in Qatar which limits its external validity. Survey fatigue and lack of time required to fill the survey is another challenge that could have affected our response quality. We attempted to resolve this issue by validating our survey instrument to ensure that it is not time-consuming yet clear, comprehensive, and easy to understand. Finally, survey instruments that use Likert scale are prone to central tendency bias (choosing "neutral/don't know" answers).[18] However, majority of our questions had low percentage of these type of answers which likely reduce the impact of this type of bias.

Despite the established advantage of DOACs over warfarin, their prescribing still requires good knowledge to make appropriate evidence-based recommendation. In conclusion, this survey indicates that practitioners have moderate awareness on DOACs. Age, years of experience, and level of education are factors associated with enhanced DOACs' awareness. Most practitioners don't widely prescribe DOACs for their patients

who require oral anticoagulation. Future work should focus on reassessing practitioners' knowledge after providing well-designed education campaigns. Education courses should be tailored more toward agents present on the formulary.

Authors' Note

Declaration of Conflicting Interests

Funding

References

1. Elewa H, El-Makaty H, Ali Z. Appropriateness of dabigatran and rivaroxaban prescribing in qatar: a 5-year experience. *J Cardiovasc Pharmacol Ther*. 2018;23(2):155-161. Epub 2017/10/06. doi:10.1177/1074248417731536.

2. David Livingston J, John M. Knowledge base and practice among clinicians regarding oral anticoagulant therapy: a questionnaire survey. *CHRISMED Journal of Health and Research*. 2017; 4(3):166-172. doi:10.4103/cjhr.cjhr_15_17.

3. Kimmel SE. Warfarin therapy: in need of improvement after all these years. *Expert Opin Pharmacother*. 2008;9(5):677-686. Epub 2008/03/19. doi:10.1517/14656566.9.5.677.

4. Finazzi G, Ageno W. Direct oral anticoagulants in rare venous thrombosis. *Intern Emerg Med*. 2016;11(2):167-170. Epub 2016/02/15. doi:10.1007/s11739-016-1398-6.

5. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease. *CHEST*. 2015;149(2):315-352. doi:10.1016/j.chest.2015.11.026.

6. Elewa H, Alhaddad A, Al-Rawi S, Nounou A, Mahmoud H, Singh R. Trends in oral anticoagulant use in Qatar: a 5-year experience. *J Thromb Thrombolysis*. 2017;43(3):411-416. Epub 2017/02/01. doi:10.1007/s11239-017-1474-4.

7. Mekaj YH, Mekaj AY, Duci SB, Miftari EI. New oral anticoagulants: their advantages and disadvantages compared with vitamin K antagonists in the prevention and treatment of patients with thromboembolic events. *Ther Clin Risk Manag*. 2015;11: 967-977. doi:10.2147/TCRM.S84210.

8. Lee LH. DOACs – advances and limitations in real world. *Thromb J*. 2016;14(suppl 1):17. doi:10.1186/s12959-016-0111-3.

9. Amin A, Bruno A, Trocio J, Lin J, Lingohr-Smith M. Real-world medical cost avoidance when new oral anticoagulants are used versus warfarin for venous thromboembolism in the United States. *Clin Appl Thromb Hemost*. 2016;22(1):5-11. Epub 2015/05/23. doi:10.1177/1076029615585991.

10. Amin A, Stokes M, Makenbaeva D, Wiederkehr D, Wu N, Lawrence JH. Estimated medical cost reductions associated with use of novel oral anticoagulants vs warfarin in a real-world non-valvular atrial fibrillation patient population. *J Med Econ*. 2014;17(11): 771-781. Epub 2014/08/19. doi:10.3111/13696998.2014.953682.

11. Wang Y, Xie F, Kong MC, Lee LH, Ng HJ, Ko Y. Cost-effectiveness of dabigatran and rivaroxaban compared with warfarin for stroke prevention in patients with atrial fibrillation. *Cardiovasc Drugs Ther*. 2014;28(6):575-585. Epub 2014/10/17. doi:10.1007/s10557-014-6558-1.

12. Connell NT, Butera JN. Attending physician attitudes toward choice of oral anticoagulant for the treatment of venous thromboembolism. *R I Med J*. 2015;98(7):32-36.

13. Flaker GC, Theriot P, Binder LG, Dobesh PP, Cuker A, Doherty JU. Management of periprocedural anticoagulation: a survey of contemporary practice. *J Am Coll Cardiol*. 2016;68(2):217-226. doi:10.1016/j.jacc.2016.04.042.

14. Leung LY, McAllister M, Selim M, Fisher M. Factors influencing oral anticoagulant prescribing practices for atrial fibrillation. *J Stroke*. 2017;19(2):232-235. doi:10.5853/jos.2016.01102.

15. Andrade JG, Krahn AD, Skanes AC, Purdham D, Ciaccia A, Connors S. Values and preferences of physicians and patients with nonvalvular atrial fibrillation who receive oral anticoagulation therapy for stroke prevention. *Can J Cardiol*. 2016;32(6): 747-753. doi:10.1016/j.cjca.2015.09.023.

16. Olaiya A, Lurie B, Watt B, McDonald L, Greaves M, Watson H. An observational study of direct oral anticoagulant awareness indicating inadequate recognition with potential for patient harm. *J Thromb Haemost*. 2016;14(5):987-990.

17. Elewa H, El-Makaty H, Ali Z. Appropriateness of dabigatran and rivaroxaban prescribing in qatar: a 5-Year experience. *J Cardiovasc Pharmacol Ther*. 2017. doi:10.1177/1074248417731536.

18. Foddy W. *Constructing Questions for Interviews and Questionnaires Theory and Practice in Social Research*. 1st ed. Cambridge, England: Cambridge University press; 1994.