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TITLE PAGE

Physicians' and pharmacists' views and experiences regarding use of direct oral anticoagulants in clinical practice

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What is already known about this subject:

- Direct oral anticoagulants (DOACs) are increasingly used compared to vitamin K antagonists (VKAs). Guidelines advocate a structured multidisciplinary approach in the management of patients using DOACs.
- Data on physicians' and pharmacists' views and experiences regarding DOACs are scarce.

What this study adds:

- Healthcare professionals expressed positive views towards DOACs and complementarity in physicians' and pharmacists' self-perceived knowledge levels may facilitate future multidisciplinary collaboration initiatives
- Opinions differed between healthcare professionals for statements relating to effectiveness, bleeding risks, adherence and drug-drug interactions with DOAC.
- Uncertainties remain on appropriate dosing in clinical practice.

ABSTRACT

Aim

Direct oral anticoagulants (DOACs) are increasingly used compared to vitamin K antagonists (VKAs). Guidelines advocate a structured multidisciplinary approach in the management of patients treated with DOACs. The aim of this study was to assess the views and experiences of physicians and pharmacists regarding DOAC use in clinical practice.

Methods

An online questionnaire was sent to both primary (general practitioners (GPs), community pharmacists) and secondary healthcare professionals (cardiologists, residents in internal medicine and hospital pharmacists) between March and July 2020. The questionnaire covered four topics: (i) current practice, (ii) prescribing behaviour (only for physicians), (iii) self-perceived knowledge about DOACs and (iv) views and opinions about DOACs versus VKAs.

Results

In total, 110 physicians and 111 pharmacists completed the survey. Healthcare professionals in secondary care had more experience with DOACs and felt more confident with higher self-perceived knowledge about DOACs compared to their colleagues in primary care. Healthcare professionals' self-perceived knowledge was more or less complementary, for example physicians felt less confident in managing drug-drug interactions (DDIs) where pharmacists reported being more confident in this

topic. Physicians reported uncertainties on the potential impact of risk factors – such as older age, lower body weight and DDIs – on appropriate DOAC dosing.

Conclusion

Complementarity in physicians' and pharmacists' self-perceived knowledge levels of DOACs may facilitate and necessitate future multidisciplinary collaboration initiatives for the management and follow-up of DOAC patients.

INTRODUCTION

Over the past decade, four direct oral anticoagulants (DOACs) – [dabigatran](#), [rivaroxaban](#), [apixaban](#) and [edoxaban](#) – have become available for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation (AF) and for the prevention and treatment of venous thromboembolism (VTE).¹⁻⁵ DOACs were developed to overcome the drawbacks of the vitamin K antagonists (VKAs), which had been the only available effective oral anticoagulants for over 50 years. Unlike VKAs, DOACs are designed to be administered in fixed doses without need for routine coagulation monitoring, have a lower propensity for food-drug and drug-drug interactions (DDIs) and have a rapid onset/offset of action. They also have shown non-inferiority^{2, 4} or even superiority^{1, 3} to VKAs, and are associated with less intracranial bleeding.¹⁻⁴ Consequently, international guidelines have expressed their preference for DOACs over VKAs.⁶⁻⁸ This caused a paradigm shift in anticoagulation therapy with DOACs being increasingly used compared to VKAs.⁹

However, studies have shown that DOACs are frequently prescribed inappropriately which can lead to an increased risk for adverse drug events.^{10, 11} In addition, patients with AF are often older with associated multimorbidity and polypharmacy.⁶ Consequently, multiple healthcare professionals are involved in the care and follow-up of most of these patients. Moreover, given the importance of stroke prevention in patients with AF¹², anticoagulation should not only be prescribed appropriately but should also be used adequately by the patient himself/herself (e.g. optimal medication adherence).¹³ Therefore, several healthcare professionals, such as physicians and pharmacists, have an important role in assessing and improving the proper use of anticoagulants to ensure optimal care of patients

with AF.^{14, 15} International guidelines advocate the integrated management of patients using anticoagulants including shared decision making with a structured multidisciplinary approach.⁶ It has been demonstrated that this integrated care approach in AF is associated with reduced cardiovascular hospitalisations and all-cause mortality.¹⁶

Despite the increased DOAC use worldwide, data on clinicians' views and experiences related to the use of DOACs are scarce as shown by a systematic review of Generalova et al.¹⁷ Yet, such data are essential, for example, for the development and design of future healthcare strategies that support the different healthcare professionals in taking up their role in optimising DOAC use.

Therefore, we conducted this study to assess the views and experiences of physicians who prescribe DOACs and of pharmacists who dispense DOAC therapy to patients in both primary and secondary care.^{18, 19}

METHODS

Study design and participants

A cross-sectional survey using an online questionnaire was conducted. A secure, web-based software platform, REDCap (Research Electronic Data Capture), was used for data collection.²⁰ The survey was sent to both primary (general practitioners (GPs), community pharmacists) and secondary healthcare professionals (cardiologists, residents in internal medicine and hospital pharmacists) between March and July 2020. In Belgium, all physicians (independent of their medical speciality) are allowed to prescribe DOACs. Hospital pharmacists and community pharmacists are responsible for the dispensation of DOACs to hospitalised and ambulatory patients, respectively, and are not allowed to prescribe DOACs. An invitation email to complete the online questionnaire was sent to the cardiology secretariats of all hospitals in the Dutch-speaking northern part of Belgium. They were asked to forward this email to the cardiologists of their department. Residents in internal medicine were recruited by an invitation email from the faculty's secretariat. Pharmacists and GPs were invited to participate via emails, websites' bulletins and social media platforms of the respective professional associations. One reminder email was sent after two weeks.

This study was approved by the Ethical Committee of Ghent University Hospital (B670202042721) and all participants provided their informed consent.

Survey questionnaire

A draft questionnaire was developed by the multidisciplinary research team (including a cardiologist, hospital pharmacist and community pharmacist) on the basis of a literature review. This draft questionnaire was reviewed by two physicians and five pharmacists for clarity and unambiguity. The final version of the questionnaire included four sections: (i) current practice, (ii) prescribing behaviour, (iii) self-perceived knowledge about DOACs and (iv) views and opinions about DOACs versus VKAs. The questionnaire for pharmacists did not include section (ii) as pharmacists in Belgium do not prescribe DOACs.

(i) Current practice

This section included questions on demographics, years of practical experience and experience with DOACs (type of DOAC frequently prescribed/dispensed, frequency of prescribing/dispensing reduced DOAC dose). In addition, we assessed what guidelines and resources physicians and pharmacists use when prescribing or dispensing DOACs.

(ii) Prescribing behaviour (only for physicians)

Physicians were asked to rate on a 5-point Likert scale (from strongly disagree to strongly agree) factors influencing their DOAC prescribing behaviour (such as the patient's characteristics, better experiences with a specific DOAC molecule, DOAC side effects profile...). There was an open textbox for optional comments. In addition, we presented three clinical cases of patients with AF, including different risk factors that can have an impact on bleeding and thromboembolic risk (i.e. older age, lower body weight and comedication with amiodarone). The European Heart Rhythm Association Practical Guide uses a colour code for translating additional risk factors into dosing recommendations,

for example by suggesting to consider dose reduction when two or more 'yellow' criteria are present.¹⁵

In each of the three clinical cases, two of such 'yellow' criteria were present. The first clinical case described a woman with older age (76 years) on [amiodarone](#). Physicians were asked what antithrombotic agent they would prescribe (DOAC, VKA or [acetylsalicylic acid](#)) and in what dose. They were asked to motivate/explain their choice. For the last two cases (a woman with low body weight (57kg) using amiodarone and an older man (81 years) with low body weight (57kg)) physicians were asked whether they would prescribe rivaroxaban in a standard (20 mg once daily) or a reduced dose (15 mg once daily).

(iii) Self-perceived knowledge of DOACs

Respondents were asked to rate on a 5-point Likert scale (from strongly disagree to strongly agree) their self-perceived knowledge on different topics concerning rational use of DOACs such as contraindications, DDIs, appropriate dosing, side effects and perioperative management of DOAC use.

(iv) Views and opinions about DOACs versus VKAs

Respondents were asked how often they prescribe/dispense a DOAC relative to a VKA. Furthermore, twelve statements regarding DOACs versus VKAs were formulated. These statements covered different views, perceptions and opinions such as differences in safety, effectiveness, prevalence of DDIs and medication non-adherence. Respondents were asked to evaluate each statement by answering 'yes', 'no' or 'no opinion'.

Data analysis

All statistical analyses were performed using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA). Continuous variables are described using the mean \pm standard deviation or median (interquartile range, IQR) depending on whether they followed a normal distribution.

Nomenclature of targets and ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in <http://www.guidetopharmacology.org>, and are permanently archived in the Concise Guide to PHARMACOLOGY 2019/20.

RESULTS

Demographics of respondents

In total, 221 healthcare professionals completed the survey: 110 physicians (54 cardiologists, 31 residents in internal medicine and 25 GPs) and 111 pharmacists (63 hospital pharmacists and 48 community pharmacists). All participants' characteristics can be found in Table 1.

(i) Current practice

Experience with DOACs

Characteristics related to the current use of DOACs (type of DOAC frequently prescribed/dispensed, frequency of prescribing/dispensing reduced DOAC dose) are listed in Table 1. There were differences in frequency of initiating DOACs between physicians with 90.7% of cardiologists, 32.3% of residents in internal medicine and none of GPs indicating to initiate DOACs at least weekly. The vast majority of pharmacists (95.5%) reported they dispense DOACs at least weekly. Apixaban and edoxaban were the two DOACs most frequently used in secondary care, while apixaban and rivaroxaban were the top two in primary care. A reduced DOAC dose was prescribed in one-fourth of patients according to cardiologists and in one-third of patients according to residents, GPs and community pharmacists. Hospital pharmacists stated that almost half of DOACs were dispensed in a reduced dose.

Use of guidelines and resources

Figure 1 displays the frequency of use of different guidelines/resources by respondents when prescribing or dispensing DOACs. The majority of cardiologists reported to consult the EHRA Practical Guide most frequently (67.9% (very) often). Residents in internal medicine and GPs used this guide less frequently; 34.4% and 4.5% of them, respectively, reported to consult this guide (very) often. The vast majority of residents in internal medicine (79.3%) and GPs (86.4%) (very) often consulted the drug register of the Belgian Center for Pharmacotherapeutic Information (BCFI)²¹, in which dose recommendations are based on DOACs' Summary of Product Characteristics (SmPCs). Remarkably, 36.0% of GPs were not aware of the existence of the EHRA Practical Guide, and an additional 24.0% of GPs did not know where to consult it. More than one-third (34.0%) of physicians (strongly) agreed with the statement that different guidelines differ in dosing criteria (20.0% (strongly) disagreed and 46.0% neither agreed nor disagreed). A similar proportion found it challenging to determine the appropriate DOAC dose (30.0% of physicians (strongly) agreed with this statement).

Community pharmacists mostly relied on supporting pharmacy software (72.4% (very) often) when dispensing DOACs, followed by the drug register of the BCFI (48.9% (very) often). More than 80% had never consulted the EHRA Practical Guide, mostly (67.4%) because they were not aware of the existence of this guideline. Hospital pharmacists (very) often consulted multiple guidelines and resources including the EHRA Practical Guide (54.2%), BCFI (49.2%) and the SmPCs of DOACs (60.9%).

(ii) Prescribing behaviour (only for physicians)

Factors influencing DOAC prescribing

Physicians' choice for a specific DOAC (Table 1) was mostly influenced by the patient's characteristics (e.g. age, body weight, renal function). Patient's personal preference for a specific DOAC or information from the companies' medical representatives seemed to have less influence on the selection process. Physicians' personal experiences with DOACs and the DOAC specific side effect profiles also played an important role for cardiologists but much less so for GPs. For example, 33.3% of all cardiologists reported they expect more gastrointestinal complications (such as haemorrhages) with rivaroxaban and dabigatran compared to apixaban and edoxaban.

Real-life clinical cases

For the first clinical case (older age (76 years) and concomitant use of amiodarone), the majority of physicians (93.9%) would prescribe a DOAC. None of them would initiate acetylsalicylic acid. The majority (48.0%) preferred apixaban, followed by edoxaban (25.5%), rivaroxaban (16.3%) and dabigatran (4.1%). The preference for apixaban was driven by the perception that its interaction with amiodarone was less clinically relevant compared to other DOACs. The preference for edoxaban and rivaroxaban was driven by the once-daily dosing regimen. Of those prescribing a DOAC, only 3.3% would prescribe the reduced dose. For the second (lower body weight (57kg) and concomitantly using amiodarone) and the third clinical case (older age (81 years) and lower body weight (57kg)) 6.5% and 26.9% of physicians, respectively, preferred the reduced dose of rivaroxaban.

(iii) Self-perceived knowledge

Respondents self-perceived knowledge about different topics concerning DOACs was assessed and results are displayed in Figure 2. Overall, cardiologists had more confidence in their knowledge

about the appropriate use of DOACs compared to residents and GPs. Physicians reported they know less about the identification and management of DDIs with DOACs compared to the other topics. Hospital pharmacists had higher self-perceived knowledge compared to community pharmacists, but were less confident in informing patients about side effects related to DOAC use.

(iv) Views and opinions towards DOACs and VKAs

All respondents reported they prescribe/dispense DOACs more frequently than VKAs (overall three times more frequently). This was most pronounced in cardiologists (DOACs prescribed seven times more frequently than VKAs), and least pronounced in community pharmacists (DOACs dispensed two times more frequently than VKAs) (Table 1).

Perceptions towards DOACs and VKAs were assessed by twelve statements (Figure 3). The majority of both physicians and pharmacists reported they have a personal preference for DOACs over VKAs. They also perceived the fact that DOACs do not require INR-monitoring as an advantage. Furthermore, the majority of healthcare professionals disagreed with the statements that they feel more confident in managing DDIs with VKAs and that VKAs should be preferred in frail or elderly patients or patients with high bleeding risk.

For all other statements, opinions differed between the healthcare professionals. The majority of hospital pharmacists disagreed with the statements that DOACs are associated with higher medication adherence and that DOACs have less DDIs compared to VKAs, while the majority of other healthcare professionals agreed with these two statements. The majority of cardiologists agreed that DOACs are more effective but cause more gastrointestinal bleeding compared to VKAs, while the

majority of other healthcare professionals disagreed. Lastly, the majority of GPs disagreed with the statement that DOACs cause less intracranial bleeding compared to VKAs, while the other healthcare professionals agreed.

DISCUSSION

We report the results of a survey regarding healthcare professionals' views and experiences of DOAC and VKA treatment about 10 years after the introduction of the first DOAC in Belgium. Meanwhile, current international treatment guidelines have expressed their preference for DOACs over VKAs.^{6,7} This was also broadly reflected in the daily practice of the healthcare professionals in our study. They reported prescribing/dispensing DOACs three times more frequently than VKAs. Our study also demonstrated that healthcare professionals in secondary care had more experience using DOACs compared to their colleagues in primary care. This was also reflected in the self-perceived knowledge about DOACs with cardiologists and hospital pharmacists feeling more confident and more knowledgeable about DOACs compared to GPs and community pharmacists.

This study demonstrated that on one hand healthcare professionals could benefit from more education on several aspects of DOAC therapy, as demonstrated by both the self-perceived knowledge and the views and opinions covering different topics regarding DOACs. On the other hand, our study showed that healthcare professionals' knowledge was more or less complementary, for example physicians felt less confident in managing DDIs where pharmacists reported they were more confident in this topic. This finding corroborates the suggestion that patient care in AF may benefit from a multidisciplinary approach, as was also advocated by the 2020 AF guideline of the European Society of Cardiology.⁶ Especially because these differences in self-perceived knowledge (with potential knowledge gaps) can be potentially dangerous if physicians and pharmacists do not work together.

Concerns have been raised about the effectiveness and safety of DOACs in the (very) elderly, as they were largely underrepresented in the RCTs.²² However, the majority of respondents in our study did not share these concerns and reported not to prefer the use of VKAs over DOACs in the elderly. Furthermore, this survey showed that the majority of healthcare professionals perceived DOAC users to have higher drug adherence compared to VKA users. They also believed DOACs have fewer interactions compared to VKAs. In contrast, the majority of hospital pharmacists did not share this opinion for both adherence and interactions with DOAC. Medication adherence to DOACs is indeed a matter of concern given the shorter half-life and the absence of routine monitoring with less clinical follow-up.¹³ Whether DOAC users have higher adherence compared to VKA users remains unclear.²³⁻²⁵ Also with DOACs, DDIs still need to be considered and data on clinical relevance of these DDIs are often lacking. Hospital pharmacists may possibly be more aware of these concerns since they are often involved in clinical pharmacy activities and antithrombotic stewardship programmes.^{26, 27} Such programmes are currently lacking in primary care in Belgium, which may explain the difference in perception between hospital and community pharmacists.

Our survey showed that the physicians' choice for a specific DOAC was mainly driven by patient's characteristics such as mentioned in the SmPC (dose reduction criteria). Especially for cardiologists, personal experience also played an important role. In addition, DOACs' specific side effects profile seemed to affect the decision making process of mainly cardiologists as they perceived the safety profile of apixaban and edoxaban as superior, with especially less gastrointestinal complications compared to rivaroxaban and dabigatran. However, it is important to note that this perception was probably based on indirect comparisons of multiple observational studies²⁸ in which

causality could not be established. Until now, no head-to-head randomised controlled trials of DOACs are available. Consequently, there is no hard evidence to recommend one agent over another.

Overall, respondents generally held very positive views towards DOACs with the majority having a personal preference for DOACs compared to VKAs. This was more pronounced for cardiologists than for GPs, and least pronounced for pharmacists. This preference may be driven by the perception of practical advantages of DOACs (e.g. absence of routine anticoagulation monitoring) and the perception of a more favourable safety profile with DOACs compared to VKAs.

Generalova et al. performed a systematic review of clinicians' views and experiences of DOACs in the management of AF.¹⁷ However, this systematic review identified only ten studies with important limitations in study design and reporting. Therefore, the research group of Generalova et al. performed a theory based cross-sectional study to determine prescribers' views and experiences on prescribing DOACs for the management of AF.²⁹ Similar to our study findings, respondents held positive views on DOACs and the lack of need for INR monitoring was considered as a positive aspect of DOAC use. Also in accordance with our study, Generalova et al. showed less agreement between prescribers on the simplicity to interpret DOAC guidelines and on the evidence base for DOAC effectiveness. In contrast with Generalova et al.²⁹, issues concerning the management of DOAC-related bleeding and identification of over- and under-anticoagulation did not arise from our study. Furthermore, our study did not only include DOAC prescribers, but also assessed views and experiences of pharmacists who dispense but do not prescribe DOACs in Belgium. Pharmacists' confidence in the area of anticoagulation was assessed in a cross-sectional international survey of Papastergiou et al.³⁰ They also

found that hospital pharmacists displayed higher confidence levels compared to community pharmacists. However, pharmacists' level of confidence was higher when advising patients on VKAs versus DOACs which was not confirmed in our study. For example, we found that the majority of pharmacists had a personal preference for DOACs and did not feel more confident in managing DDIs with VKAs compared to DOACs. This might be due to the increased experience with DOACs compared to 6 years ago when DOACs were rather new and accounted for an only modest proportion of the global anticoagulant market.

To inform physicians and pharmacists on the safe and effective use of DOACs in patients with AF, the EHRA developed a Practical Guide including dosing recommendations taking into account DDIs and other clinical factors with potential impact on thromboembolic and bleeding risk.¹⁵ Our study showed that this guide was well-known and widely used by cardiologists and hospital pharmacists. In contrast, the majority of GPs and community pharmacists were unaware of the existence of this guideline or were unfamiliar with it. The Practical Guide uses a colour code for translating DDIs and additional criteria into dosing recommendations, for example by suggesting to consider dose reduction or switching to a different DOAC. According to the EHRA Practical Guide, in all three clinical cases of the survey, a dose reduction of DOAC should be considered because of older age, lower body weight, and/or comedication with amiodarone. According to the SmPC, a standard dose should be prescribed in all these cases as these patients did not qualify for the SmPC's dose reduction criteria. Although the vast majority of cardiologists reported to preferably consult the EHRA Practical Guide for the selection of the appropriate DOAC dose, this was not reflected in their handling of the three clinical cases. Most cardiologists preferred to prescribe a DOAC in a standard dose. Also, it appeared that the clinical

relevance of the risk factors defined by the EHRA Practical Guide were estimated differently. Respondents considered the impact of the concomitant use of amiodarone to be less clinically relevant than older age or lower body weight. This can lead to inconsistencies and ambiguity in selecting the appropriate DOAC dose. These uncertainties were also identified in the survey as about one-third of physicians (strongly) agreed that the determination of the appropriate DOAC dose is challenging. In a previous study, we found that patients in which dosing recommendations differed between EHRA and SmPC had higher thromboembolic risk, were older, had more comorbidities and lower renal function and reported more adverse drug events.¹¹ Overall, more research is needed to understand the clinical impact of DDIs and risk factors on DOAC plasma levels and to ensure appropriate DOAC dosing in polymedicated and/or multimorbid patients.

Strengths and limitations

This cross-sectional online survey is, to our knowledge, the first in which perceptions, attitudes and knowledge concerning DOACs were evaluated in both physicians and pharmacists across primary and secondary care. Understanding their experiences and views is essential to enable a multifaceted and multidisciplinary approach for the integrated management of patients using DOACs across primary and secondary care. Our study had some limitations. First, we were not able to calculate a response rate as we do not know the exact numerator of healthcare professionals who received the invitation to participate in this survey. Second, as participation was voluntary, respondents may have been more interested in the topic of DOACs. This possible participation bias could have an impact on the generalisability of the study results. For example, one can assume that the level of self-perceived

knowledge may be overestimated. Third, the survey did not incorporate a validated DOAC knowledge questionnaire. Consequently, we cannot conclude that respondents with higher self-perceived knowledge were actually more knowledgeable. And fourth, although the survey was completed anonymously, desirability bias cannot be ruled out.

CONCLUSION

This study demonstrated that healthcare professionals in secondary care had more experience with DOACs and felt more confident with higher self-perceived knowledge about DOACs compared to their colleagues in primary care. Overall, both physicians and pharmacists held very positive views towards DOACs with the majority having a personal preference for DOACs compared to VKAs. However, uncertainties remained mainly on appropriate dosing in clinical practice. There was complementarity in physicians' and pharmacists' self-perceived knowledge levels of DOACs which may facilitate and necessitate future multidisciplinary collaboration initiatives for the management and follow-up of DOAC patients.

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Contributors All authors have made substantial contributions to the conception and design of the study. AC and ED were responsible for the acquisition, analysis and first interpretation of data. AC drafted the manuscript. EM, ED, TDB and KB revised the manuscript critically. All authors contributed to the article and approved the submitted version.

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Tables

Table 1 – Summary of demographics, current use of DOACs, factors influencing DOAC prescribing behaviour and use of DOAC relative to VKA for the different healthcare professionals

	CARDIO N = 54	RES N = 31	GPs N = 25	HPs N = 63	CPs N = 48
Demographics					
Age, years	44.2±10.7	28.9±3.2	40.0±16.5	32.8±7.7	36.9±10.2
Females	14 (25.9)	18 (58.1)	16 (64.0)	57 (90.5)	39 (81.3)
Years of practical experience					
≤ 5 years	7 (13.0)	28 (90.3)	12 (48.0)	25 (39.7)	14 (29.2)
6 – 15 years	20 (37.0)	3 (9.7)	7 (28.0)	28 (44.4)	18 (37.5)
16 – 30 years	16 (29.6)	0 (0.0)	1 (4.0)	8 (12.7)	12 (25.0)
> 30 years	11 (20.4)	0 (0.0)	5 (20.0)	2 (3.2)	4 (8.3)
Current use of DOACs					
Frequency of initiation/dispensing DOAC					
Never	0 (0.0)	1 (3.2)	1 (4.0)	0 (0.0)	1 (2.1)
Annually	1 (1.9)	4 (12.9)	13 (52.0)	0 (0.0)	0 (0.0)
Monthly	4 (7.4)	16 (51.6)	11 (44.0)	1 (1.6)	3 (6.3)
Weekly	40 (74.1)	9 (29.0)	0 (0.0)	9 (14.3)	25 (52.1)
Daily	9 (16.7)	1 (3.2)	0 (0.0)	53 (84.1)	19 (39.6)
Frequency of prescribing/dispensing ^a , %					
Apixaban	39.4±16.4	35.3±18.5	32.4±16.6	40.3±11.5	31.5±12.4
Edoxaban	32.0±17.3	39.4±18.9	22.0±13.9	24.7±8.5	21.1±10.7
Dabigatran	12.3±9.8	7.7±9.1	13.8±12.2	13.2±6.2	14.5±8.1
Rivaroxaban	16.3±14.9	17.8±14.0	31.7±20.3	21.5±7.9	32.9±12.6
Frequency of prescribing/dispensing DOAC in reduced dose ^b , %					

	24.0±14.3	31.8±13.0	36.0±23.7	48.3±13.6	28.4±15.5
Factors influencing DOAC prescribing behaviour					
Physicians (strongly) agreeing, %					
<i>The patient's characteristics (e.g. age, body weight, renal function)</i>	100.0	96.6	95.5	N.A.	N.A.
<i>Better experiences with a specific DOAC molecule</i>					
<i>DOAC specific side effects profile</i>	70.4	51.7	54.5	N.A.	N.A.
<i>Information from the company's medical representative</i>	59.3	44.8	27.3	N.A.	N.A.
<i>Patient's personal preference</i>	27.8	24.1	27.3	N.A.	N.A.
	29.7	20.7	18.1	N.A.	N.A.
DOAC versus VKA					
Frequency of prescribing/dispensing DOAC relative to VKA ^c , %	88.4±13.0	77.8±30.2	75.4±22.2	77.3±10.4	66.5±19.6

Data are presented as mean ± standard deviation or number (percentage); ^a'Please indicate (in percentage) how often you prescribe each of the four DOACs relative to each other?'; ^b'When prescribing/dispensing DOACs, how often (in percentage) do you prescribe/dispense a DOAC in the reduced dose compared to the standard dose (with 0% always the standard dose and 100% always the reduced dose)'; ^c'When prescribing/dispensing oral anticoagulants, how often (in percentage) do you prescribe/dispense a DOAC relative to a VKA?' (for example: 60% if you prescribe/dispense about 60% DOACs versus 40% VKAs); **CARDIO**: cardiologists; **RES**: residents in internal medicine; **GPs**: general practitioners; **HPs**: hospital pharmacists; **CPS**: community pharmacists; **DOAC**: direct oral anticoagulant; **VKA**: vitamin K antagonist

Figure Legends

Figure 1 Frequency of use of different guidelines/resources when prescribing or dispensing DOACs on 5-point Likert scale. *DOACs: direct oral anticoagulants; CDSS: Clinical Decision Support System; BCFI: Belgian Center for Pharmacotherapeutic Information; EHRA: European Heart Rhythm Association; SmPC: Summary of Product Characteristics*

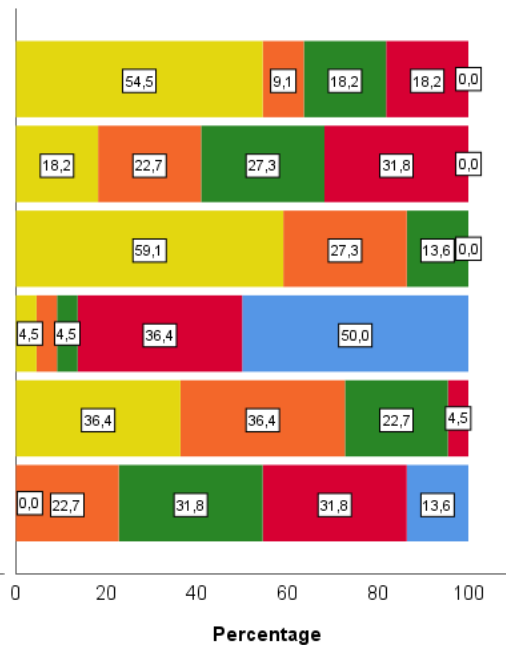
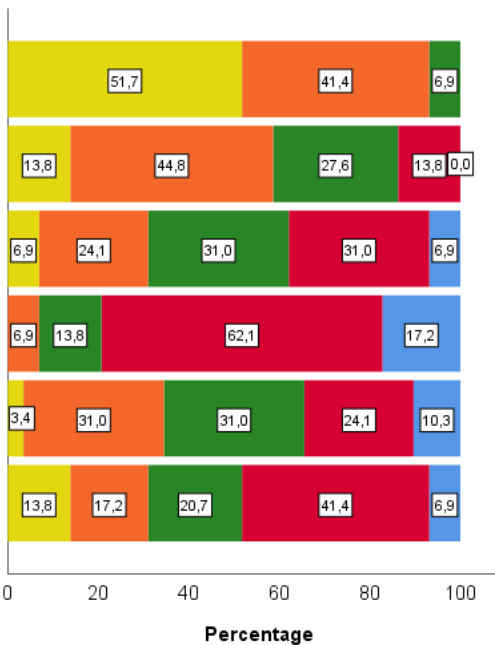
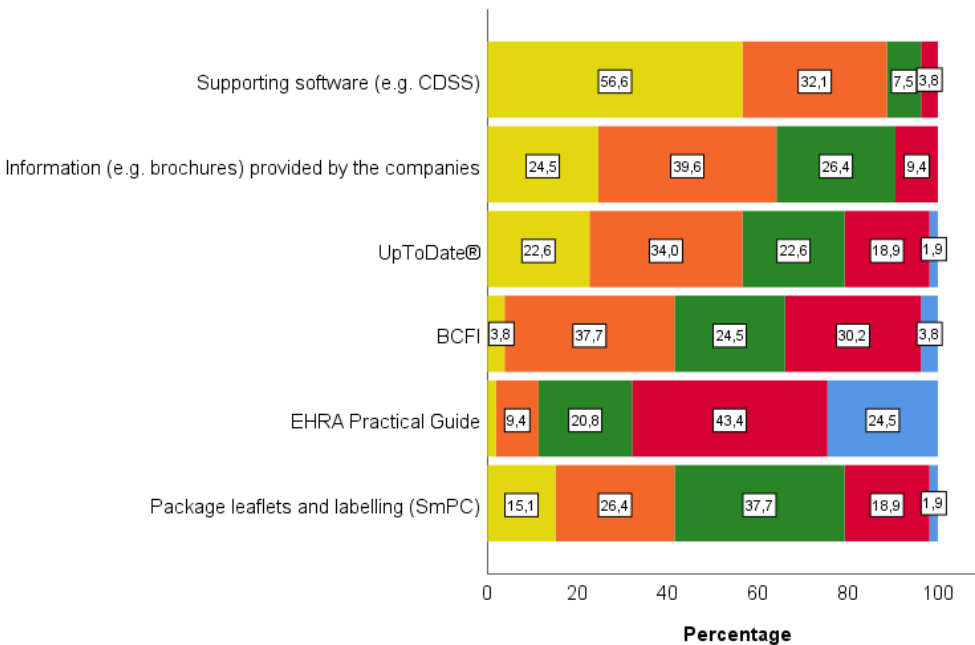
Figure 2 Self-perceived knowledge about different topics concerning DOACs on 5-point Likert scale. *DOACs: direct oral anticoagulants; DDIs: drug-drug interactions*

Figure 3 Perceptual statements about DOACs versus VKAs. *DOACs: direct oral anticoagulants; VKAs: vitamin K antagonists; DDIs: drug-drug interactions; INR: International Normalised Ratio*

CARDIOLOGISTS

RESIDENTS IN INTERNAL MEDICINE

GENERAL PRACTITIONERS

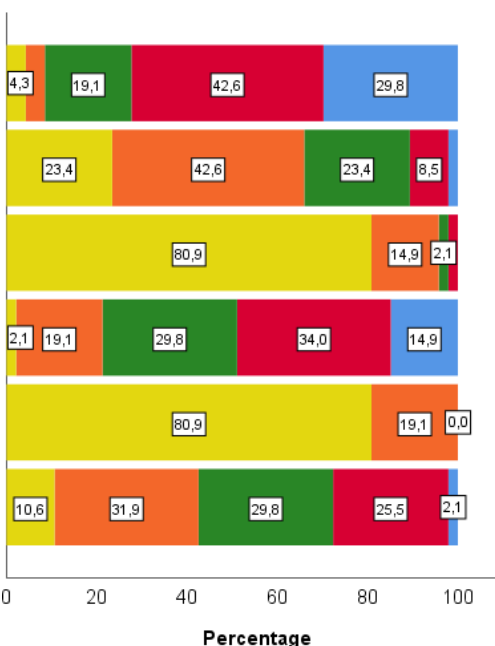
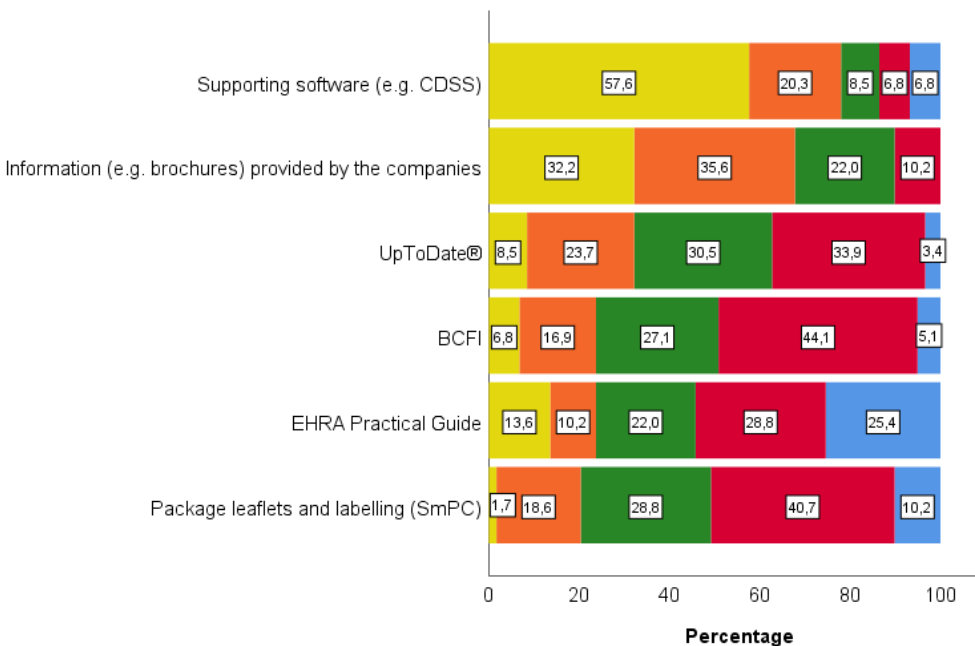


HOSPITAL PHARMACISTS

COMMUNITY PHARMACISTS

Legend

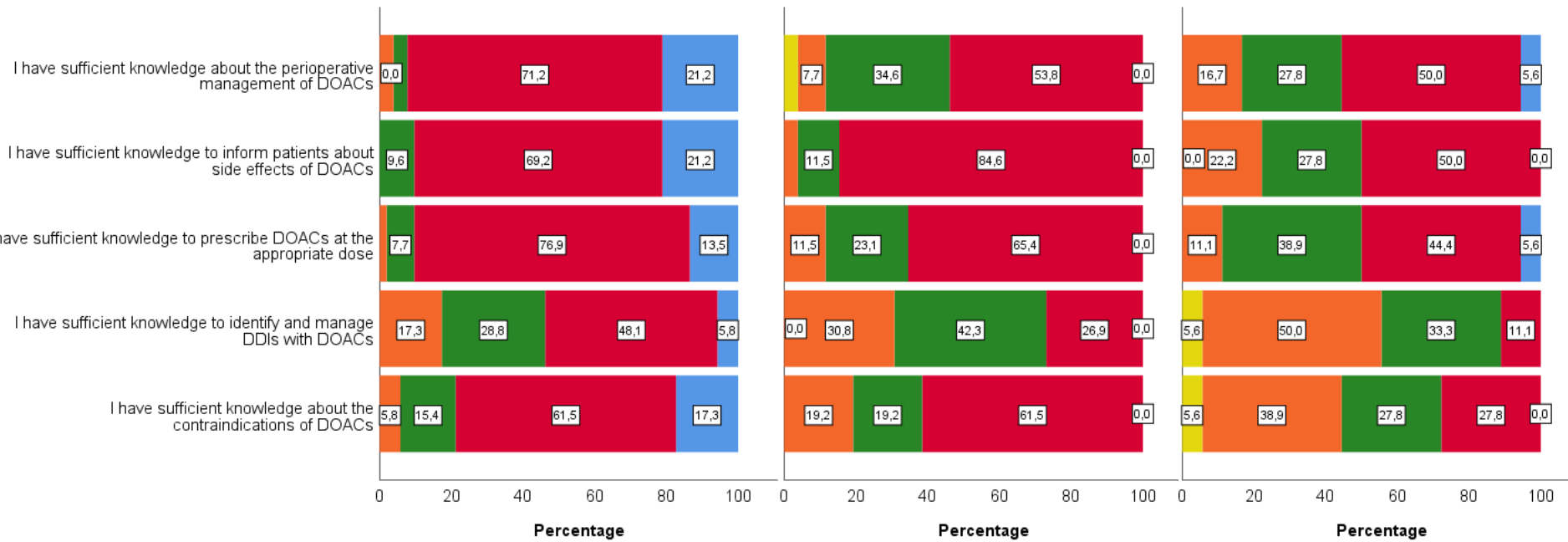
- Very often
- Often
- Sometimes
- Rarely
- Never



CARDIOLOGISTS

RESIDENTS IN INTERNAL MEDICINE

GENERAL PRACTITIONERS

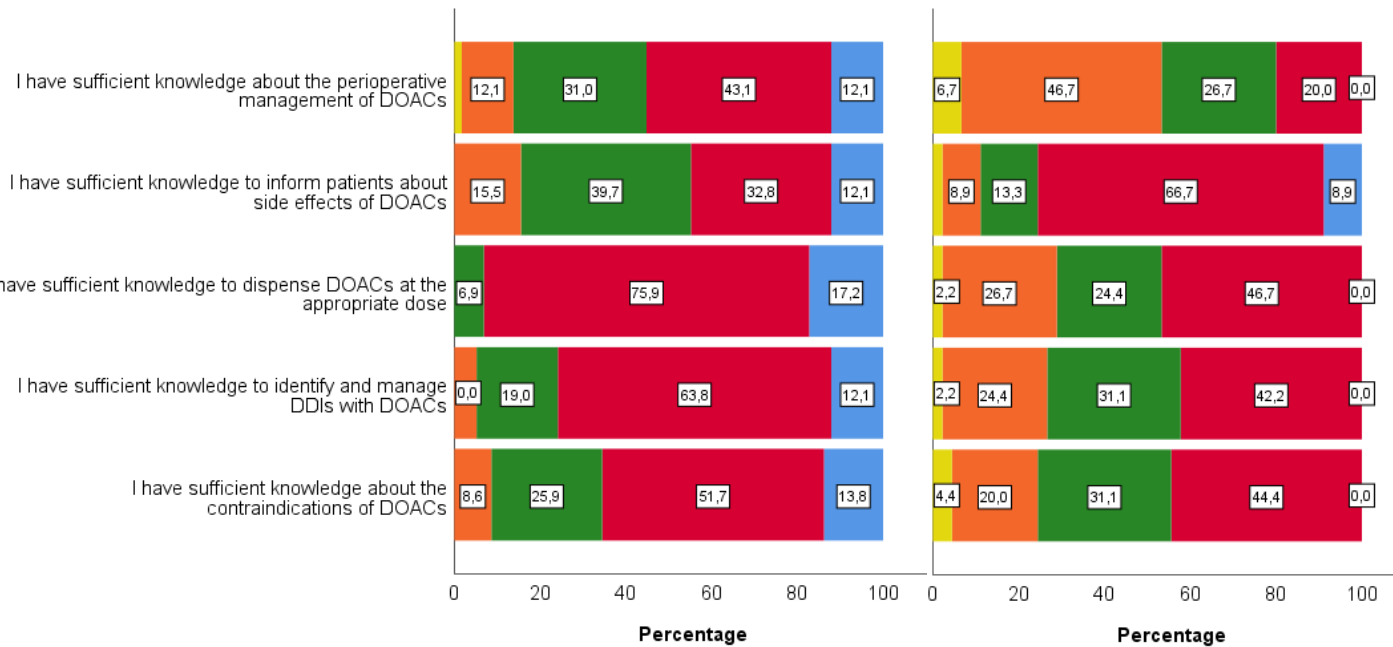


HOSPITAL PHARMACISTS

COMMUNITY PHARMACISTS

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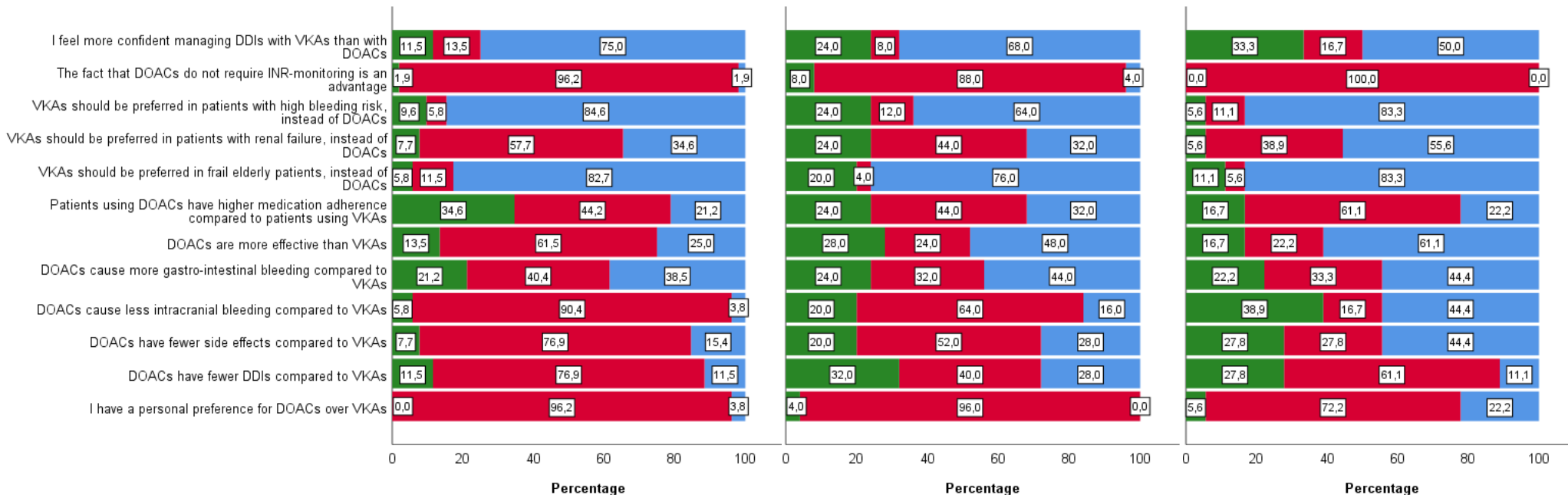
- Strongly agree
- Agree
- Unsure
- Disagree
- Strongly disagree



CARDIOLOGISTS

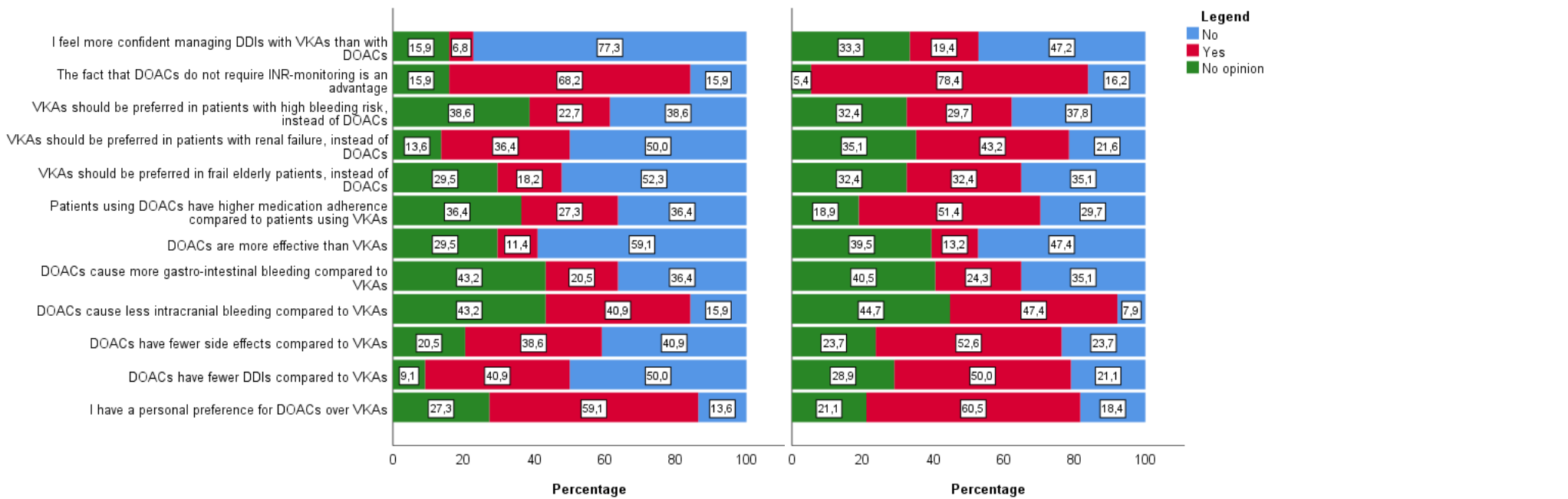
RESIDENTS IN INTERNAL MEDICINE

GENERAL PRACTITIONERS



HOSPITAL PHARMACISTS

COMMUNITY PHARMACISTS



Legend

- No
- Yes
- No opinion