Title Page

Report No.: PH-40370 **Date: 2018-06-06**

Version No.: 1.0

Author(s):

PPD

Department:

PPD

Title:
Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)

Test Compound Number(s):
BAY 597939

INN/Generic Name:
Rivaroxaban Factor Xa Inhibitor

Trade Name: Xarelto®

Study Number: 16167

Study Completion Date:
24-May-2018 as this is the interim report for the wave 2

Performing Laboratory:

France, Germany, Spain, and the United Kingdom.

PASS Information

Title	Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)
Version identifier of the final study report	Version 1.0 (Wave 2)
Date of last version of the final study report	24 May 2018 (Wave 2)
IMPACT study number	16167
EU PAS Register number	EUPAS3911
Active substance	INN: Rivaroxaban; ATC code: B01AF01
Medicinal product	Xarelto (rivaroxaban)
Product reference	EU/1/08/472/001-010 EU/1/08/472/022
Procedure number	EMEA/H/C/000944/X/00017
Marketing authorisation holder(s)	Bayer AG 51368 Leverkusen Germany
Joint PASS	No
Research question and objectives	The primary objective of this cross-sectional epidemiologic study is to measure physician and patient awareness and understanding of the key messages in the prescriber guide and patient alert card. Specifically, the following objectives will be addressed: ▪ Investigate whether physicians and their patients have received the educational materials. ▪ Assess knowledge and understanding among physicians regarding key safety information contained in the prescriber guide and assess how physicians use the materials in their daily practice. ▪ Assess knowledge and understanding of patients regarding the key safety information contained in the patient alert card and determine if the patients use and carry the patient alert card with them. Evaluations were planned for administration at approximately 18 months (wave 1), 3 years (wave 2), and 7 years (wave 3) post–drug launch. The wave 1 assessment was conducted among both patients and physicians. This report presents data from the wave 2 assessment which was conducted only among physicians.
Country(-ies) of study	France, Germany, Spain, and the United Kingdom
Author	PPD

Marketing authorisation holder(s)

Marketing authorisation holder(s)	Bayer AG 51368 Leverkusen Germany
MAH contact person	PPD

Table of Contents

List of Tables

List of Figures

1 Abstract

Title: Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)

24 May 2018

Keywords: Xarelto (rivaroxaban); post-authorisation safety study; evaluation of risk-minimisation measures; physician survey

Rationale and background: At the request of the European Medicines Agency (EMA), a prescriber guide and patient alert card were developed and distributed to increase awareness and understanding about risks associated with rivaroxaban. The current study was designed to evaluate physician and patient awareness and understanding of the key messages in these educational materials at 18 months (wave 1), 3 years (wave 2), and 7 years (wave 3) post–drug launch. The wave 1 assessment was conducted among both patients and physicians. Based on the results of wave 1 and in agreement with the EMA, the wave 2 and wave 3 assessments include physicians only. This report summarises results from the wave 2 assessment to evaluate physicians' knowledge of the key messages in the prescriber guide.

Research question and objectives: The primary objectives are to measure whether physicians and patients received and used the prescriber guide and patient alert card, respectively, and to evaluate their awareness and understanding of the key safety messages.

Study design: The study is an observational, cross-sectional study among physicians and patients with recent rivaroxaban experience. Eligible physicians and patients were invited to complete a brief questionnaire regarding their knowledge of key safety in the rivaroxaban educational materials.

Setting: France, Germany, Spain and the UK

Subjects and study size, including dropouts: Physicians were eligible to participate if they had prescribed rivaroxaban in the past 6 months for one of the indications of interest. A total of 19,310 physicians were invited to participate in wave 2; 1,950 responded. Of those who responded, 476 physicians opted not to participate, 3 did not provide informed consent, 106 did not meet eligibility criteria, 131 were excluded because the quota was already met for their physician speciality, and 8 started the questionnaire but did not answer enough of the questions to meet the definition for a completed survey. The remaining 1,226 physicians, between 304 to 310 per country, completed the questionnaire for an evaluable response rate of 6%.

Variables and data sources: Data were obtained through questionnaire responses.

Results: In general, physicians' knowledge of the key safety information in the Xarelto educational materials was high. Physicians' knowledge was particularly high for questions related to the risk of bleeding (94%), populations that are at increased risk of serious

side effects (69%-94%), and contraindications (73%-92%). Physician knowledge was also high for questions related to invasive procedures (80%) and medically important bleeding (59%-81%). Fewer physicians (62%) were aware that rivaroxaban (15 mg or 20 mg) should be taken with food for stroke prevention in atrial fibrillation (SPAF) and deep vein thrombosis (DVT) treatment and secondary prevention. Knowledge was lower for situations that require international normalised ratio monitoring (58%-76%), procedures for converting from vitamin K antagonist (VKA) to rivaroxaban (52%-66%) and from rivaroxaban to VKA (36%-62%), and for converting from parenteral anticoagulants to rivaroxaban (51%-54%). Physicians' knowledge of dosing recommendations varied by question. The proportion of correct responses was 75% for the standard recommended dose of rivaroxaban for SPAF, 58% for the recommended dose of rivaroxaban for SPAF in patients with renal impairment, and 62% for the recommended dose of rivaroxaban for DVT treatment and secondary prevention. More than half of physicians reported that they received the prescriber guide for rivaroxaban (57%), and of those physicians, 80% felt the guide was very helpful or extremely helpful. Most physicians (85%) reported that they would discuss information on the patient alert card with patients when first prescribing rivaroxaban.

Discussion: Physicians' knowledge was highest for the most important risks in the educational materials and lower for more complex aspects of safe use for which we would assume that physicians would consult the prescriber guide and/or label rather than relying on memory. Physicians' knowledge was consistent between waves 1 and 2.

Marketing Authorisation Holder(s): Bayer AG

Names and affiliations of principal investigators: PPD

2 List of Abbreviations

CI	confidence interval
DVT	deep vein thrombosis
EMA	European Medicines Agency
ENCePP	European Network of Centres of Pharmacoepidemiology and Pharmacovigilance
EU	European Union
EU PAS Register	European Union Electronic Register of Post-Authorisation Studies
INR	international normalised ratio
ISPE	International Society for Pharmacoepidemiology
PE	pulmonary embolism
PPD	PPD
SPAF	stroke prevention in atrial fibrillation (more completely, prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation)
UK	United Kingdom
VKA	vitamin K antagonist

3 Investigators

Table 1 provides information for the principal investigators of the study. Given the nature of the wave 2 data collection (i.e., online survey with physicians only), the study included only one country-level investigator in Spain to support the ethics committee process. Information for the investigator in Spain is also included in Table 1.

Table 1. Principal and Country-Level Investigators

Investigators	Country	Institutional Affiliation
Principal investigators		
PPD	United States	PPD
PPD	United States	PPD
Country-level investigator		
PPD PPD	Spain	PPD PPD

4 Other Responsible Parties

Bayer AG (Bayer) is the marketing authorisation holder of Xarelto (rivaroxaban) and the sponsor of the study. PPD an independent non-profit research

organisation, is responsible for the design, conduct, analysis, and reporting of the study. Bayer collaborated with PPD on the study design and is also responsible for fulfilling any obligations for reporting results to regulatory agencies. Kantar Health, a global research operations partner, was responsible for the ethics committee submission, physician recruitment, and data collection.

PPD USA
PPD Principal Investigator
PPD Principal Investigator PPD
PPD
PPD
PPD
PPD

Bayer AG Epidemiology Müllerstr. 178, S102, 01, 252 13353 Berlin, Germany
PPD

Kantar Health GmbH Landsberger Stra. 284, 80687 Munich, Germany
PPD

5 Milestones

Milestone	Actual Date
EMA endorsement of protocol version 1.0	09 December 2011
Registration in the EU PAS Register	06 December 2013
Wave 1 lead ethics committee approvals	05 November 2013 to 27 August 2014
Wave 1 data collection for physician assessment	15 September 2014 to 20 November 2014
Wave 1 data collection for patient assessment	11 November 2014 to 30 April 2015
Wave 1 summary report	16 October 2015
EMA endorsement of protocol version 4.0	21 July 2016
Wave 2 ethics committee approval (applicable to Spain only)	16 March 2017

Milestone	Actual Date
Wave 2 data collection for physician assessment	30 March 2017 to 12 June 2017
Wave 2 summary report	24 May 2018
Study progress reports	Every 12 months throughout the study, included in the Periodic Safety Update Reports

6 Rationale and Background

Rivaroxaban is approved in the European Union (EU) for the prevention of venous thromboembolism in adult patients undergoing elective hip or knee replacement surgery; prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, previous stroke or transient ischaemic attack, treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE); and prevention of recurrent DVT and PE in adults. In addition, rivaroxaban, coadministered with acetylsalicylic acid alone or with acetylsalicylic acid plus clopidogrel or ticlopidine, is indicated for the prevention of atherothrombotic events in adult patients after an acute coronary syndrome with elevated cardiac biomarkers.(1)

As a part of a safety risk-management plan revision for rivaroxaban, a physician-educational packet was developed that includes the prescriber guide and patient alert card, with the aim to increase awareness and understanding among physicians and patients about the potential bleeding risk during treatment with rivaroxaban. The patient alert card was initially provided to patients by their treating physicians. It is now included in the product packaging so patients receive the card every time they fill a prescription for rivaroxaban.

PPD is collaborating with Bayer to develop and implement this study to evaluate physician and patient awareness and understanding of the key messages in the prescriber guide and patient alert card. Evaluations of patient and physician use of these materials were planned for administration at 18 months (wave 1), 3 years (wave 2), and 7 years (wave 3) post–drug launch.

The wave 1 assessment was conducted among patients and physicians. Based on the results of wave 1 and in agreement with the European Medicines Agency (EMA), the wave 2 and wave 3 assessments include only physician assessments and no patient assessment. This report summarises results from the wave 2 assessment to evaluate physicians' knowledge of the key messages in the prescriber guide.

The five countries initially included in the study were the France, Germany, Italy, Spain, and the United Kingdom (UK). Because of drug approval delays in Italy, the wave 1 assessment was conducted only in four countries (France, Germany, Spain, and the UK). Italy was intended to be included in wave 2; however, it was again excluded based on the potential need to obtain individual ethics committee approval for 300 physicians in Italy, a process not considered feasible within the timeline agreed upon in the EU Risk-Management Plan.

7 Research Question and Objectives

The primary objective of this cross-sectional epidemiologic study is to measure physician and patient awareness and understanding of the key messages in the prescriber guide and patient alert card.

Specifically, the following objectives were to be addressed:

- To investigate whether physicians and their patients have received the educational materials.
- To assess knowledge and understanding among physicians regarding key safety information contained in the prescriber guide and to assess how physicians use the materials in their daily practice.
- To assess knowledge and understanding of patients regarding the key safety information contained in the patient alert card and to determine if the patients use and carry the patient alert card with them.

The wave 2 and wave 3 assessments include only physicians and no patients.

As part of good research practices, the protocol and European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) checklist were registered in the EU PAS Register(2) before the start of wave 1 data collection. The study was designed and implemented in line with the International Society for Pharmacoepidemiology (ISPE) *Guidelines for Good Pharmacoepidemiology Practices*(3); European Medicines Agency *Guidelines on Good Pharmacovigilance Practices, Module VIII – Postauthorization Safety Studies*(4) and ENCePP *Guide on Methodological Standards in Pharmacoepidemiology.*(5) The contract between PPD and Bayer includes independent publication rights.

The study received exemption from review by the PPD PPD for wave 2 data collection on 23 November 2016.

8 Amendments and Updates

None.

9 Research Methods

9.1 Study Design

The study is an observational, cross-sectional study of knowledge, understanding, and self-reported behaviour among a sample of physicians with recent rivaroxaban experience in a total of four European countries. A cross-sectional survey approach was selected for this study because the main information on knowledge and understanding of the educational material could be obtained only through direct interaction with physicians.

[1] PPD is a unit of the non-profit research organization PPD

Wave 2 of the study included a survey administered to general practitioners as well as physicians covering a variety of specialities (e.g., neurology, cardiology, haematology, oncology) to evaluate their knowledge of key safety messages outlined in the rivaroxaban educational materials.

The wave 2 survey aimed to evaluate the effectiveness of the risk-minimisation measures approximately 2 years after wave 2, during which time physicians would have gained additional experience prescribing rivaroxaban for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (SPAF) and DVT treatment and secondary prevention.

Physicians were recruited from an online physician panel.[1] A stratified random sample of physicians in the panel was selected to recruit such that the distribution of the physician specialities that were invited was proportional to the distribution of specialities seen in country-specific prescribing information supplied by Bayer. Soft recruitment quotas were set for each physician speciality to help ensure that the final distribution of respondents was consistent with the prescribing information and that all specialities were represented.

The survey was open to physicians who participated in the wave 1 assessment (i.e., repeat respondents), as well as physicians who did not participate in the wave 1 assessment (i.e., new respondents). The initial batch of invitations was sent to physicians who did not participate in wave 1 of the survey to maximise the number of new respondents with a goal of obtaining a minimum of 150 new respondents per country. Subsequent invitations included physicians who had participated in wave 1.

Invitations were extended via e-mail and phone to the selected sample of physicians, inviting them to participate and providing a link to a web-based questionnaire. Interested physicians logged in to the study website by entering a unique identification number and password. The physicians then completed an informed consent and a screening question to confirm that they had prescribed rivaroxaban to at least one patient within the past 6 months. Physicians who completed the consent and were deemed eligible could continue and complete the self-administered questionnaire.

The web-based format for completion of the consent form and self-administered questionnaire was chosen because of the efficiency and utility of the mode (e.g., question-branching logic and ability to stop respondents from going back to previous questions to change answers). Most physicians have convenient access to complete a web-based questionnaire, so the use of this technology is not believed to have introduced a respondent bias.

[1] The panel of physicians is maintained by a proprietary organisation. The panel comprises physicians derived from multiple sources (e.g., hospital books, medical directories, physician referrals). Each panel member is recruited by telephone and opts in to the panel twice. A stringent sampling procedure for panel member recruitment is in place to target a representative demographic cross section. A rigorous verification process is implemented to confirm potential panelists' practising status. The verification process includes checking physician background data against medical directories. Panel membership is only finalised once live contact and verification is made with the physician at an office location.

9.2 Setting

The wave 2 physician survey was conducted in four western European countries (France, Germany, Spain, and the UK). The four countries included were chosen to provide some diversity in physician specialities and practice patterns, and to observe differences in physician knowledge in these settings. In addition, prescribing levels in these countries were such that there was a sufficient number of eligible physicians with rivaroxaban experience to participate in the study.

Data collection ran from 30 March 2017 to 12 June 2017.

9.3 Subjects

The wave 2 survey was conducted with physicians who had prescribed rivaroxaban to at least one patient in the past 6 months for one of the following indications:

- Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation.
- Treatment of DVT and prevention of recurrent DVT and PE following an acute DVT in adults.

9.4 Variables

The wave 2 physician questionnaire contained closed-ended questions (e.g., multiple choice, true/false), with no free-text response fields and included items in the following content areas:

- Prescribing practices
- Knowledge of key safety messages outlined in the prescriber guide
  - Most important risk with taking rivaroxaban
  - Populations at higher risk of bleeding
  - Contraindications
  - Necessity of taking the 15-mg and 20-mg tablets with food
  - Use of coagulation tests and their interpretation
  - Converting from or to rivaroxaban treatment
  - Perioperative management
  - Actions related to medically important bleeding
  - Dosing recommendations
- Sources of information about rivaroxaban and ratings of their helpfulness
- Experience with information contained in the patient alert cards
- Physician and practice characteristics

Annex 2 contains the questionnaire.

9.5 Data Sources and Measurement

Self-reported data collected from physicians using a standard questionnaire with closed-ended response choices served as the source of information for wave 2.

The questionnaire was developed using best practices for instrument development. The questions were tailored to the study aims and the information provided in the prescriber guide for rivaroxaban. Additional questions were included to obtain the information needed to describe the study population and to assess potential differences across subgroups.

To thoroughly evaluate the questionnaire before fielding the study, the questionnaire was tested through cognitive interviews with physicians in France, Germany, Italy, Spain, and the UK before wave 1 data collection. The pretest interviews helped to identify problems with questionnaire items, wording, response choices, etc., and ensured that participants understood the questions. The cognitive testing helped to identify cultural or translational issues with the draft questionnaire so that it could be modified to meet the individual needs of each country while maintaining comparability across the study.

Nine interviews were first conducted with physicians in the UK to identify issues and optimise wording in English. After the UK interviews, the questionnaires were revised and translated into German, French, Italian, and Spanish. Four interviews (for a total of 16) were then conducted with physicians in each of the remaining countries to confirm wording and facilitate cultural adaptation to each country. Changes to the questionnaire were made based on the results of the cognitive testing and additional feedback from the sponsor before the start of wave 1 data collection. Subsequently, before wave 2 data collection, minor wording changes were made to the consent language and to a few questions for further clarification. In addition, two questions related to receipt and distribution of the patient alert card were removed because the card is now distributed in the product packaging and not by the physician.

9.6 Bias

In any observational study, researchers must address the potential for biases, particularly if there is a possibility that the respondents are not representative of the target population. Likewise, the potential for intervention effects and/or response error may present additional sources of bias. Efforts were made to both minimise and identify potential sources of bias in this study as described in the following sections.

9.6.1 Cognitive Pretesting

As noted above, the physician questionnaire was cognitively pretested prior to wave 1 data collection in order to identify any problems with the questionnaire items, wording, and response choices, and to ensure consistency across cultures and languages. The questionnaire was modified based on feedback from the cognitive interviews with physicians. This process helped to ensure that the questions measured the appropriate concepts consistently and accurately across all countries, and thus was intended to minimise bias in responses.

9.6.2 Sample Selection

To minimise sampling bias, physicians were randomly selected and invited to participate. Although a comparison of participating physician characteristics with nonparticipating physicians was not possible within the panel recruitment framework, the diversity of physician characteristics and experience with rivaroxaban in the final sample gave some assurance that the target population was well represented.

However, despite efforts to ensure a representative sample of physicians, participants may have differed from non-participants on key characteristics measured in the questionnaire (e.g., knowledge, reading the educational materials). The direction and magnitude of such potential bias is not known.

9.6.3 Data Collection Methods

The physician survey was administered as an online questionnaire. Physicians were not able to go back to previous questions. This kept them from changing their answers based on subsequent questions.

9.7 Study Size

The target sample size for the wave 2 physician survey was 300 physicians per country, for a total of 1,200. Ultimately, the number of completed physician surveys included 304 surveys each from France and Germany, 308 from Spain, and 310 from the UK for a total of 1,226. With a sample size of 300 physician responses for a given question, the maximum width of an exact 95% confidence interval (CI) around the percentage who responded correctly is 11.6%, and 1,200 responses gives a maximum width of 5.7%.

9.8 Data Transformation

Derived variables were created for each of the six knowledge questions that ask the respondent to select all that apply and that have more than one correct response option (questions 7, 10, 11, 12, 13, and 15); these variables indicate the number of correct responses selected.

9.9 Statistical Methods

All analyses were performed using SAS 9.4 statistical software (SAS Institute, Inc., Cary, North Carolina). No formal hypothesis testing was conducted.

9.9.1 Main Summary Measures

Data analyses were descriptive in nature and focused primarily on summarising the questionnaire responses. Summary tables consisting of frequencies with percentages were created for all questionnaire responses. Response distribution percentages for a question were based on the total number of respondents who had an opportunity to answer the question. This total excluded those who were asked to skip the question

because of an answer given in a previous question (skip pattern). The sum of respondents who were asked to skip the question was listed in a row labelled "Not applicable skip pattern" under the question with no percentage calculated for that row. The counts of respondents who had an opportunity but did not answer were included in the row labelled "No answer" with a calculated percentage.

Exact 95% CIs were generated around the percentage of participants who answered each knowledge question correctly. These CIs were calculated for the overall results and for each country but not for other stratified tables.

9.9.2 Main Statistical Methods

The analysis population consisted of respondents who were eligible for the study, provided informed consent, and completed at least one knowledge question in full (Question 5 – Question 18).

Questionnaire items were divided into the following categories: (1) physician and practice characteristics; (2) physician prescribing practices; (3) physician knowledge; (4) sources of information about rivaroxaban; (5) ratings of those sources; and (6) experiences with information contained in the patient alert cards. Separate analysis tables were generated to display the response distributions of the questions in each category. Table 2 presents the table numbers and question numbers that correspond to each table. The tables are provided in Annex 3 and include results overall and by country.

Table 2. Listing of Main Analysis Tables

Table Number	Table Title	Question Number(s)
Table A-1	Physician and Practice Characteristics	24-27
Table A-2	Physician Prescribing Practices	1-4
Table A-3	Knowledge Questions	5-18
Table A-4	Sources of Information About Xarelto	19
Table A-5	Ratings of Sources of Information About Xarelto	20
Table A-6	Physicians' Experiences With Information Contained in the patient alert cards	23

In addition, the knowledge questions were stratified to explore the association between each variable and physician knowledge levels. Note that some stratifications produced small sample sizes; thus, caution should be taken when interpreting the stratified data.

The stratification variables and associated sample sizes are as follows:

- Physician speciality (based on response to Question 24)
  - General/internal medicine: N = 693
  - Neurology: N = 112
  - Cardiology: N = 182
  - Haematology: N = 55
  - Oncology: N = 65

  - Other: N = 107
- Whether or not the physician is responsible for initiating Xarelto treatment or converting treatment from or to Xarelto (based on response to Question 4)
  - Is responsible for initiating or converting rivaroxaban treatment: N = 1,074
  - Is responsible for maintenance only: N = 152
- Whether or not the physician received the Xarelto prescriber guide (based on response to Question 19)
  - Received Xarelto prescriber guide: N = 701
  - Did not receive Xarelto prescriber guide: N = 513
- Indication(s) for which the physician prescribed rivaroxaban (based on response to screening Question 1)
  - SPAF only: N = 301
  - DVT only: N = 90
  - SPAF and DVT: N = 835

Table 3 presents the table numbers and the question numbers that correspond to each table. Annex 4 presents these stratified results tables.

Table 3. Listing of Other Stratification Analysis Tables

Table Number	Table Title	Question Number(s)
Table A-8	Physician Speciality	5-19
Table A-9	Whether or not Physician is Responsible for Initiating Xarelto Treatment or Converting Treatment From or to Xarelto	5-18
Table A-10	Whether or not Physicians Received Information From Xarelto Prescriber Guide	5-18
Table A-11	Indication(s) for Which Physicians Prescribed Xarelto	11-13

9.9.3 Missing Values

Missing values were treated as missing; no imputation was performed.

9.9.4 Sensitivity Analyses

None.

9.9.5 Amendments to the Statistical Analysis Plan

None.

9.10 Quality Control

This project was conducted in accordance with internal standard operating procedures of participating institutions. The PPD Office of Quality Assurance, an independent unit that reports to the Vice President of PPD oversaw quality assurance for this study.

Standard operating procedures were used to guide the conduct of the study. These procedures included rules for secure and confidential data storage, methods to maintain and archive project documents, quality-control procedures for programming, standards for writing analysis plans, and requirements for senior scientific review.

During data collection, the logic, range, and edit checks that were programmed in the electronic data capture system allowed for real-time resolution of data errors or data discrepancies.

In accordance with relevant standard operating procedures, the initial programmer reviewed all programme log files for errors and warning messages and retained electronic copies of all final log files in the project folder. The programmer accounted for the number of observations reported at each executed data step and noted in the programme code when the number of observations increased or decreased. Listings or output used to verify results were output and preserved in the quality-control folder or in the programme folder. A second programmer independently wrote programme code and confirmed the findings of the initial programmer. Quality-control checklists have been maintained for the project.

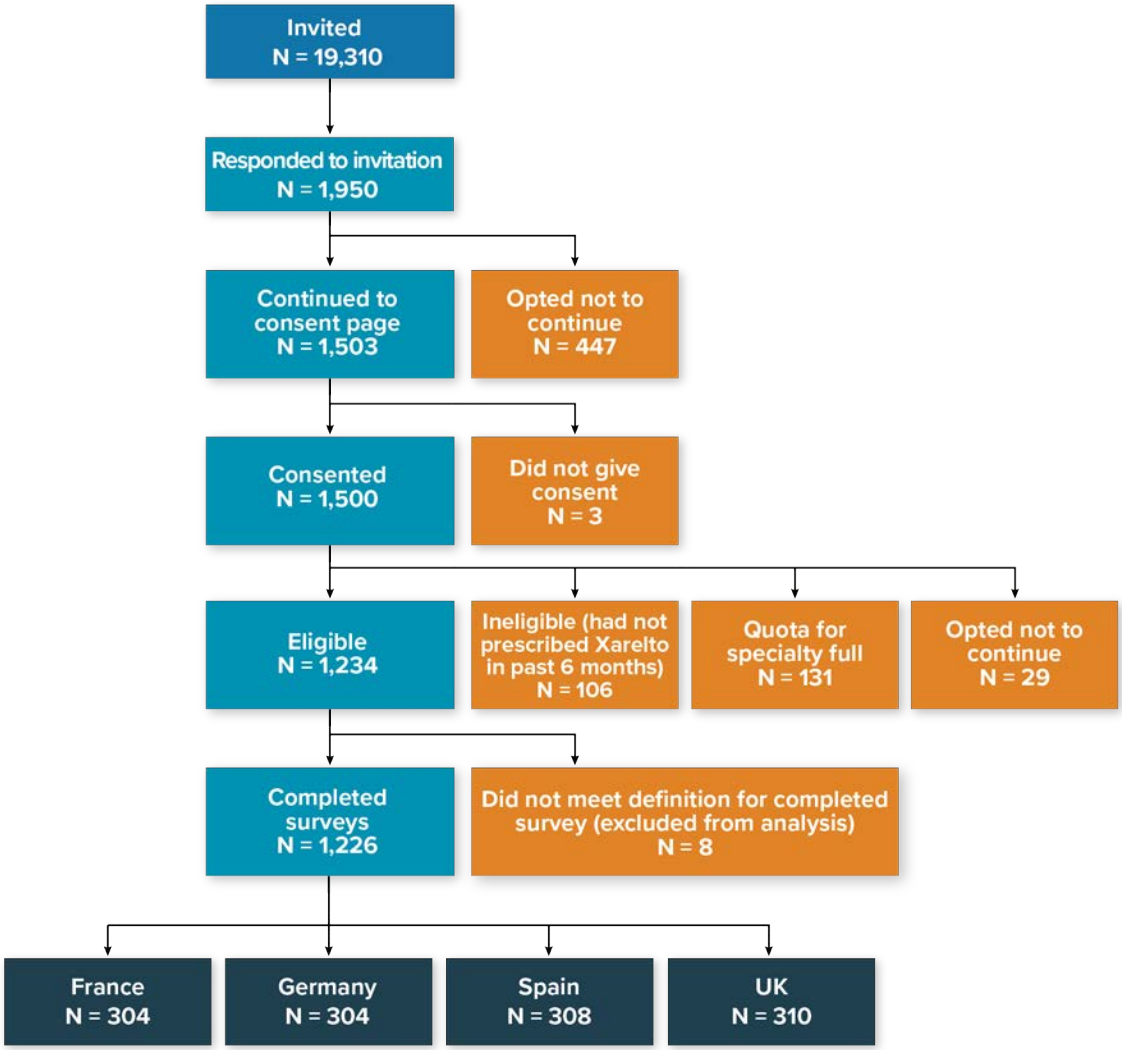
All key study documents, such as the analysis plan, data collection form, and study reports, underwent quality-control review, senior scientific review, and editorial review.

10 Results

10.1 Participants

A total of 19,310 physicians were invited to participate in the survey. Of those, 1,950 physicians responded to the invitation. Of the physicians who responded, 476 chose not to participate, 3 did not provide informed consent, 106 did not meet eligibility criteria, 131 were excluded because the quota was already met for their practice speciality, and 8 started the questionnaire but did not answer enough of the questions to meet the definition for a completed survey. The remaining 1,226 physicians (304 each in France and Germany, 308 in Spain, and 310 in the UK) completed the questionnaire. The overall evaluable response rate was 6%. Figure 1 presents the disposition of physicians invited to participate.

Figure 1. Disposition of Physicians



UK = United Kingdom.

Because of the limited number of eligible physicians on the panel, wave 2 included a mix of new participants and physicians who participated in wave 1. The numbers of new participants in wave 2 were as follows: 230 (76% of respondents) in France, 168 (55%) in Germany, 277 (90%) in Spain, and 298 (96%) in the UK.

10.2 Descriptive Data

Physicians were sampled using the speciality recorded for each physician in the online panel's database. However, physicians were also asked to specify their speciality as part of the questionnaire. The data on speciality provided in this report are based on the latter. Two response categories, "internal medicine" and "pulmonology", were added as new responses to the wave 2 questionnaire. The most frequent specialities represented in the survey population were general medicine (45%), cardiology (15%), internal medicine (11%), and neurology (9%) (Table 4).

A total of 63% of physicians reported that they practised in a general setting, and 41% of physicians reported that they practised at a hospital-based clinic.[1] Physicians' experience (as measured by years in practice) was categorised into 5-year increments up to 25 years. Most physicians (91%) reported practising medicine for more than 10 years, and 27% reported practising medicine more than 25 years. Most participants (74%) were male.

[1] This was a "select all that apply" question; thus, the sum of responses can be greater than 100%.

Table 4. Physician and Practice Characteristics

Characteristic	France N = 304 n (%)	Germany N = 304 n (%)	Spain N = 308 n (%)	UK N = 310 n (%)	Overall N = 1,226 n (%)
Physician speciality					
General medicine (including GPs)	135 (44)	120 (39)	112 (36)	186 (60)	553 (45)
Neurology	35 (12)	35 (12)	32 (10)	10 (3)	112 (9)
Cardiology	57 (19)	44 (14)	52 (17)	29 (9)	182 (15)
Haematology	6 (2)	4 (1)	29 (9)	16 (5)	55 (4)
Accident & emergency medicine	16 (5)	11 (4)	6 (2)	6 (2)	39 (3)
Oncology	7 (2)	4 (1)	23 (7)	31 (10)	65 (5)
Other	15 (5)	6 (2)	3 (1)	13 (4)	37 (3)
Internal medicine	19 (6)	75 (25)	32 (10)	14 (5)	140 (11)
Pulmonology	10 (3)	3 (1)	16 (5)	2 (1)	31 (3)
No answer	4 (1)	2 (1)	3 (1)	3 (1)	12 (1)
Years practising medicine					
5 years or less	2 (1)	1 (<.5)	1 (<.5)	1 (<.5)	5 (<.5)
6 to 10 years	18 (6)	13 (4)	33 (11)	24 (8)	88 (7)
11 to 15 years	50 (16)	51 (17)	67 (22)	59 (19)	227 (19)
16 to 20 years	63 (21)	74 (24)	70 (23)	96 (31)	303 (25)
21 to 25 years	65 (21)	74 (24)	59 (19)	65 (21)	263 (21)
More than 25 years	102 (34)	89 (29)	75 (24)	62 (20)	328 (27)
No answer	4 (1)	2 (1)	3 (1)	3 (1)	12 (1)
Are you...?					
Male	240 (79)	246 (81)	206 (67)	214 (69)	906 (74)
Female	60 (20)	56 (18)	99 (32)	93 (30)	308 (25)
No answer	4 (1)	2 (1)	3 (1)	3 (1)	12 (1)
Practice type[a]					
General practice	164 (54)	230 (76)	191 (62)	191 (62)	776 (63)
Hospital-based clinic	133 (44)	81 (27)	175 (57)	117 (38)	506 (41)
Nursing home	15 (5)	5 (2)	8 (3)	0	28 (2)
Other	4 (1)	3 (1)	4 (1)	3 (1)	14 (1)
No answer	4 (1)	2 (1)	3 (1)	3 (1)	12 (1)

UK = United Kingdom; GP = general practitioner.

[a] This was a "tick all that apply" question; thus, the sum of responses can be greater than 100.

10.3 Outcome Data

Not applicable.

10.4 Main Results

In the following sections, we present key results from physicians who completed the questionnaire. The results are organised in the following categories: (1) physician prescribing practices; (2) knowledge of key safety information; (3) sources of information about rivaroxaban and ratings of those sources; and (4) physicians' experiences with information contained in the patient alert cards.

Knowledge of key safety information is described for the overall sample, then stratified by country, physician speciality, physician prescribing responsibility (initiating or converting vs. maintenance only), whether the physician reported receiving the prescriber guide for rivaroxaban, and the indication for which the physician prescribes rivaroxaban.

Graphs highlight the stratification results in which the largest differences were seen or where the stratifications seem of most interest. In general, on most of the knowledge questions, physicians who reported specialities in neurology, cardiology, haematology, and general/internal medicine had a somewhat higher proportion of correct responses than physicians in oncology or other speciality categories. Likewise, physicians responsible for initiating rivaroxaban treatment or for converting treatment from or to rivaroxaban had a higher proportion of correct responses than those who were only prescribing maintenance treatment. Physicians who reported receiving the prescriber guide for rivaroxaban also consistently provided more correct responses than those who did not report receiving the guide.

Annex 3 includes tables presenting the complete set of knowledge question results for physicians overall and by country. Annex 4 includes tables presenting results by other stratification variables.

10.4.1 Physician Prescribing Practices

Most physicians (79%) had written a prescription for rivaroxaban less than 1 month before completing the survey. Almost all physicians (98%) had prescribed rivaroxaban for SPAF in the past 6 months, and most physicians (85%) had prescribed rivaroxaban for DVT treatment and secondary prevention in the past 6 months. In Spain, where rivaroxaban is not approved for reimbursement for DVT, one-quarter of physicians reported that they had not prescribed rivaroxaban for DVT in the past 6 months. Most physicians (88%) reported that they were responsible for initiating rivaroxaban treatment or converting from or to rivaroxaban, and the majority (70%) reported that they wrote follow-up (maintenance) prescriptions (see Annex 3, Table A-2; Questions 1, 2, 3, and 4).[1]

[1] This was a "tick all that apply" question; thus, the sum of responses can be greater than 100.

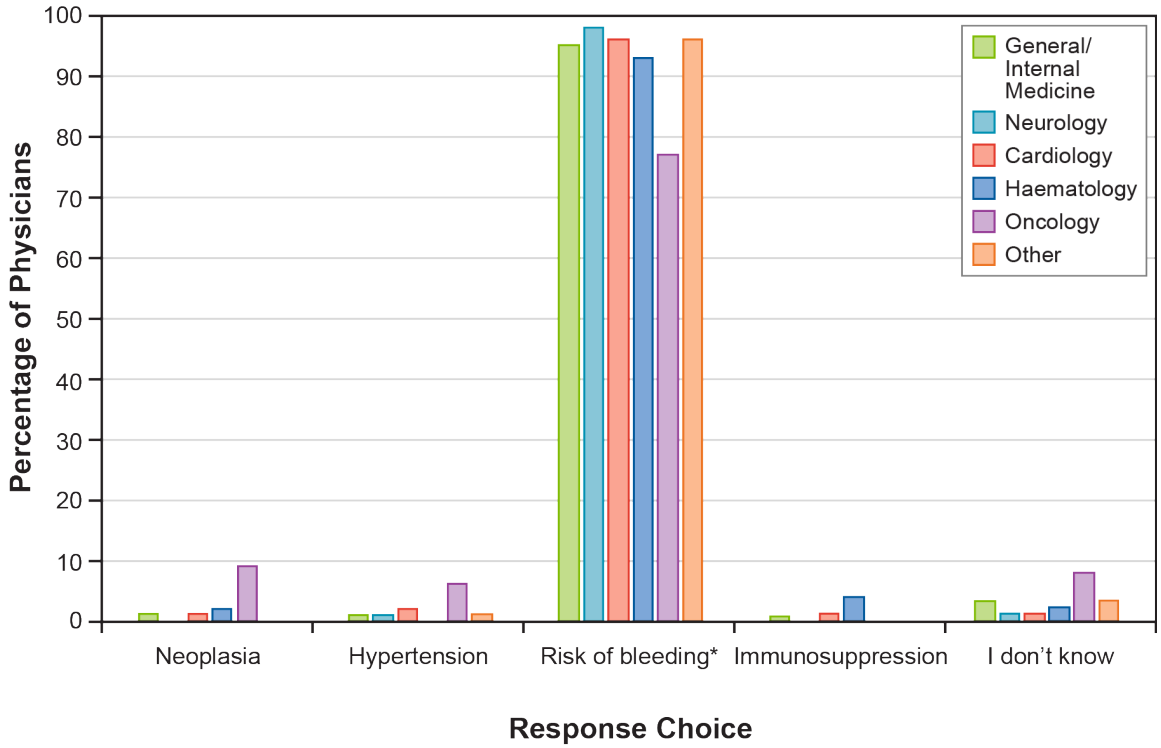
10.4.2 Knowledge of Key Safety Information

Risks of Side Effects and Safe Use

Almost all physicians (94%) correctly reported that the most important risk associated with taking rivaroxaban is the risk of bleeding. Results were consistent across the countries, ranging from 91% correct in Spain to 98% in the UK (Annex 3, Table A-3; Question 5). Overall, knowledge of this risk was 93% or higher among each category of specialist except for oncologists (77%) (Figure 2).

Physicians responsible for initiating rivaroxaban treatment or converting treatment to or from rivaroxaban performed similarly to those responsible for writing maintenance prescriptions only (95% vs. 91% correct), as did physicians who said they received the prescriber guide for rivaroxaban compared with those who did not (94% vs. 95%) (Annex 4, Tables A-9 and A-10; Question 5).

Figure 2. Responses to Question 5: What Is the Most Important Risk Associated With Taking Xarelto? (N = 1,214)

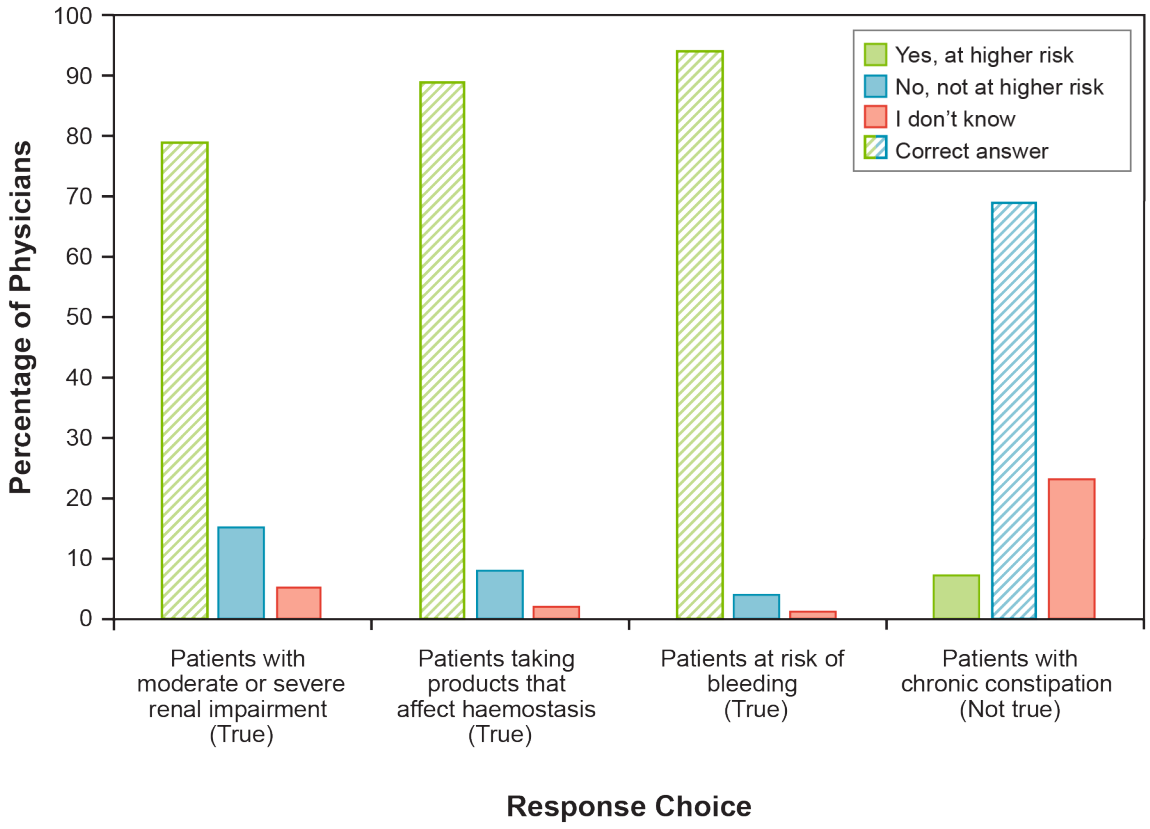


*Correct response is marked with an asterisk.

Physicians' knowledge of patient populations at risk of experiencing serious side effects with rivaroxaban was also high, ranging from 69% to 94% correct for the individual response options, with the lowest percentage (69%) for those who correctly identified "chronic constipation" as a false response (Figure 3). The item regarding chronic constipation also had the most variation in correct responses across countries, with 79% of the physicians in Germany answering correctly versus 72% in France, 67% in Spain, and 56% in the UK. Correct responses to other side effect items were much more consistent across countries (Annex 3, Table A-3; Question 6).

For most of the side effect questions, the correct response proportions were similar across specialities except for oncology, which tended to be slightly lower (Annex 4, Table A-8; Question 6). The proportions of correct responses were approximately 3% to 6% higher for each of these questions for physicians responsible for initiating rivaroxaban treatment or converting treatment to or from rivaroxaban compared with those responsible only for maintenance treatment (Annex 4, Table A-9; Question 6). There was no notable difference in the proportions of correct responses between physicians who reported receiving the prescriber guide for rivaroxaban and those who did not (Annex 4, Table A-10; Question 6).

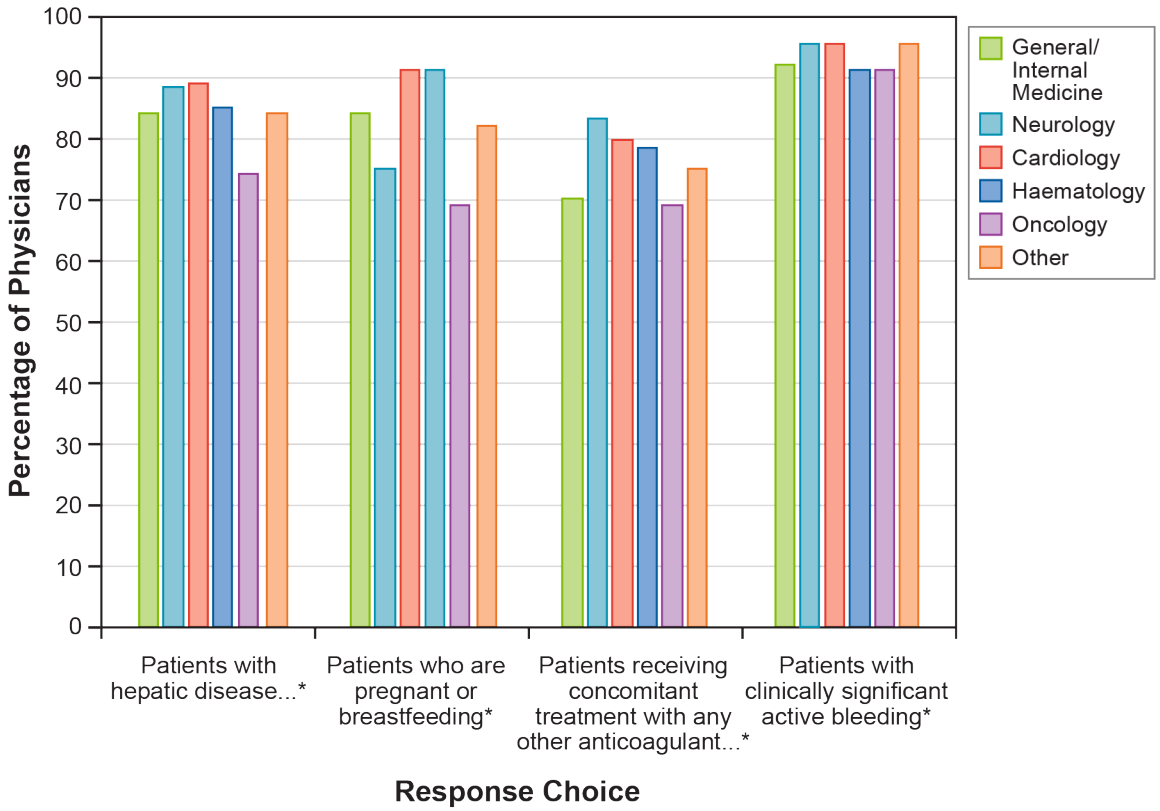
Figure 3. Responses to Question 6: Which of the Following Populations Are at an Increased Risk of Experiencing Serious Side Effect(s) Associated With Xarelto?



Most physicians (60%) correctly identified all four patient groups for which rivaroxaban is contraindicated; 83% correctly identified at least three of the four, with the correct response proportions being relatively consistent across countries (Annex 3, Table A-3; Question 7). The proportions of correct responses were similar across specialities, except for oncologists, whose correct responses were on average about 10% lower than other physicians (Figure 4).

Physicians responsible for initiating and/or converting rivaroxaban treatment responded very similarly on all four responses compared with those responsible for writing maintenance prescriptions only (Annex 4, Table A-9; Question 7). Physicians who reported receiving the prescriber guide for rivaroxaban had a higher proportion of correct responses compared with those who did not report receiving the rivaroxaban prescriber guide, with 64% selecting all four correct responses compared with 55%, respectively (Annex 4, Table A-10; Question 7).

Figure 4. Responses to Question 7: To Which Patient Groups Is Xarelto Contraindicated? (Tick all that apply.) (N = 1,214)

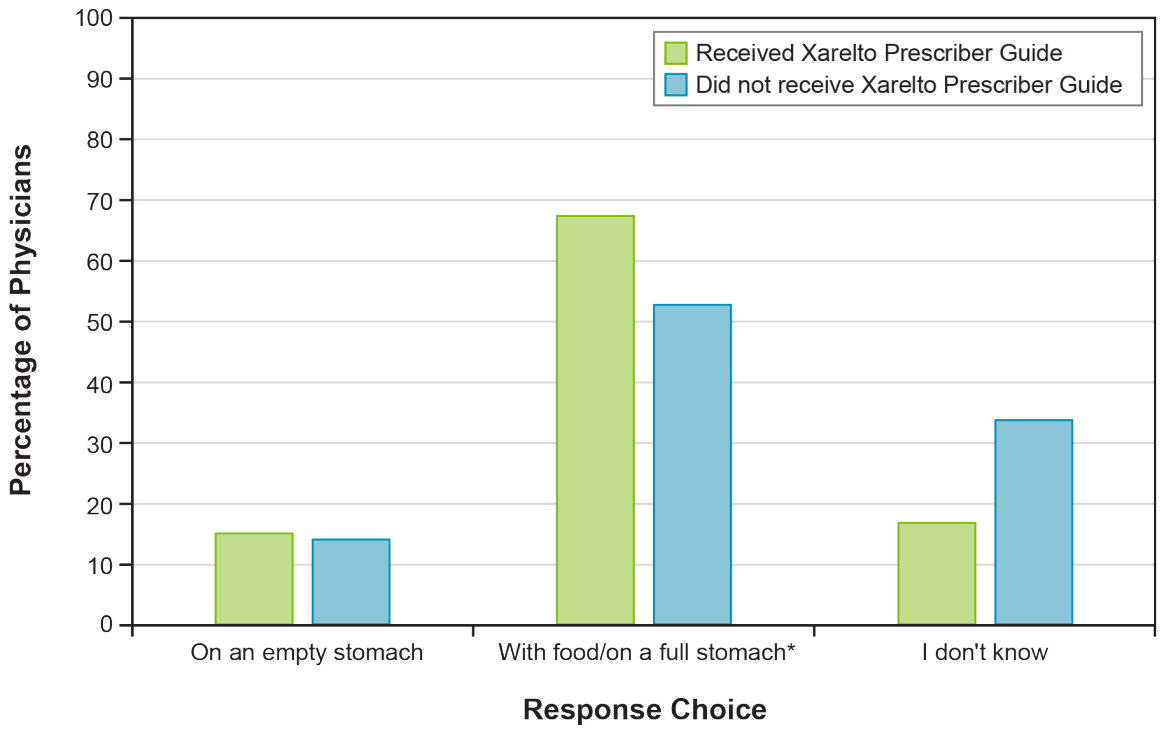


*Correct response is marked with an asterisk.

Physicians were asked whether rivaroxaban could be taken on an empty stomach or whether it must it be taken with food. Sixty-two percent correctly answered that rivaroxaban should be taken "with food/on a full stomach." Physicians in Germany and France had the highest proportion of correct responses to this question (69% and 68%, respectively) and physicians from the UK had the lowest proportion of correct responses to this question (48% correct) (Annex 3, Table A-3; Question 8). Across prescriber specialities, physicians in oncology and general/internal medicine had noticeably lower correct responses (52% and 57%, respectively) than the other physician specialities (66%-74% correct) (Annex 4, Table A-8; Question 8).

There was a particularly large difference in the proportion of correct responses between physicians responsible for initiating and converting rivaroxaban treatment (64% correct) and those responsible for writing maintenance prescriptions only (47% correct) (Annex 4, Table A-9; Question 8). Physicians who reported that they had received the prescriber guide for rivaroxaban were more likely to respond correctly than those who did not report receiving the prescriber guide (68% vs. 53%) (Figure 5).

Figure 5. Responses to Question 8: Xarelto (15 or 20 mg) Must Be Taken….? (N = 1,214)



*Correct response is marked with an asterisk.

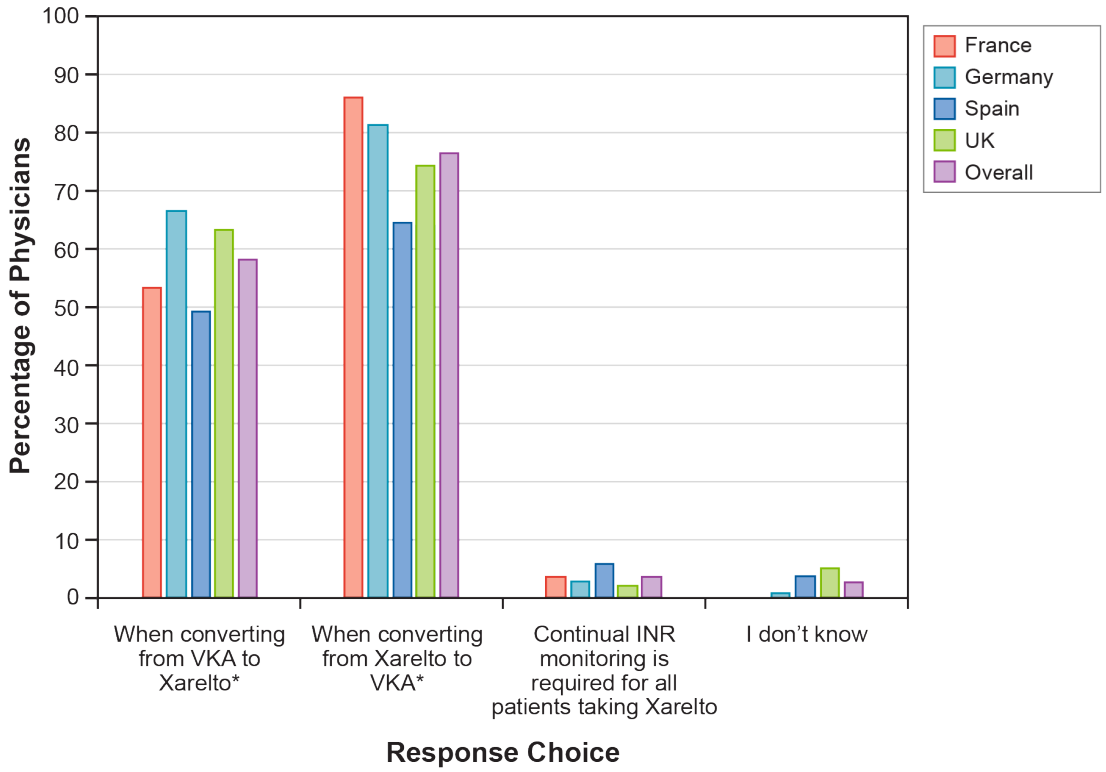
Monitoring and Converting

Almost all physicians (95%) knew that routine coagulation monitoring is not required for patients taking rivaroxaban, and there was little variability across the subgroups, except among oncologists, 80% of whom answered this question correctly. All other specialist categories had at least 90% correct response proportions, and most had 95% or higher correct response proportions (Annex 3, Table A-3; Question 9 and Annex 4, Tables A-8, A-9, and A-10; Question 9).

Knowledge was lower when physicians were asked about what situations require international normalised ratio (INR) monitoring: 58% correctly indicated there was a need when converting from vitamin K antagonist (VKA) to rivaroxaban, and 76% correctly indicated there was a need when converting from rivaroxaban to VKA. There was some difference in correct response proportions by country; physicians from Spain had the lowest proportion of correct responses on both responses (49% and 64%, respectively) (Figure 6). There was consistency across physician specialities except for oncologists, who had slightly lower proportions of correct responses on both responses (52% and 65%, respectively) (Annex 4, Table A-8; Question 10).

Physicians responsible for initiating rivaroxaban treatment had somewhat higher proportions of correct responses than those responsible for maintenance only (Annex 4, Table A-9; Question 10), and physicians who reported receiving the prescriber guide for rivaroxaban had higher proportions of correct responses than those who did not report receiving the prescriber guide (Annex 4, Table A-10; Question 10).

Figure 6. Responses to Question 10: In Which of the Following Situations Is INR Monitoring Needed? (Tick All That Apply.) (N = 1,226)



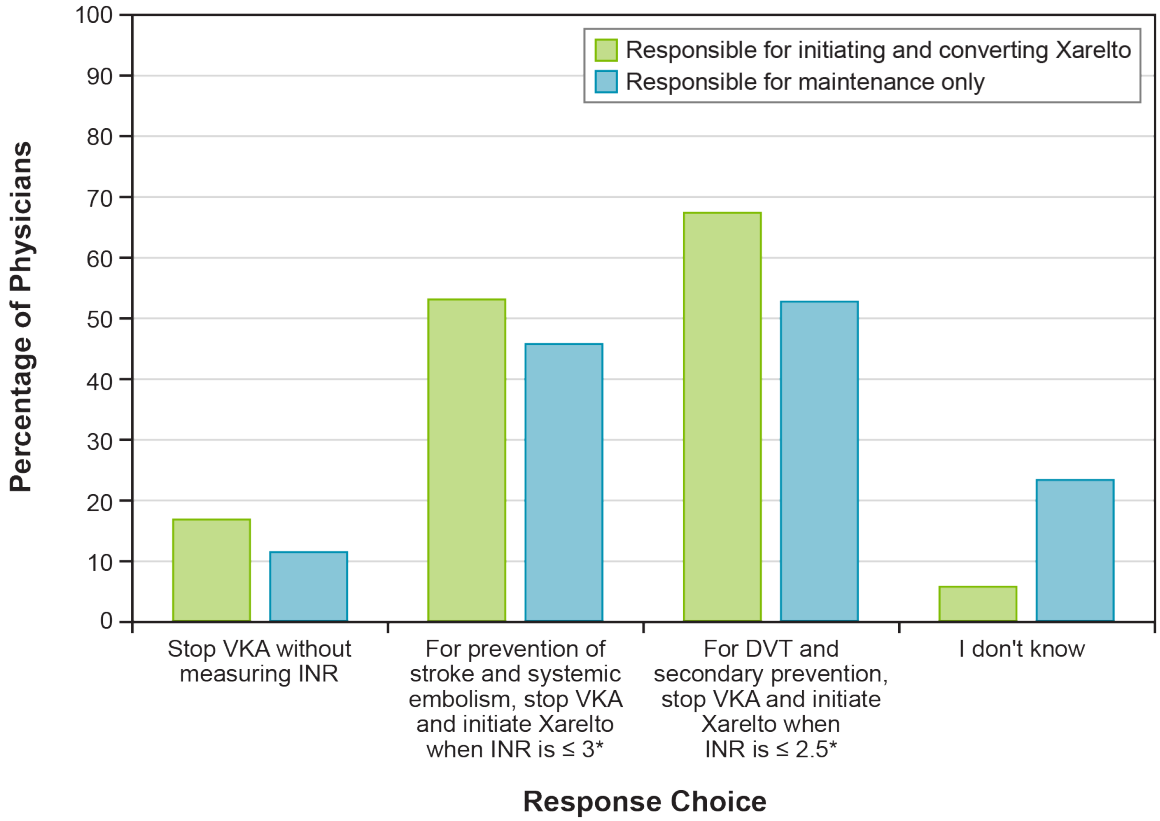
INR = international normalised ratio; VKA = vitamin K antagonist.

* Correct response is marked with an asterisk.

In two separate "tick all that apply" questions, physicians were asked about procedures for converting patients from VKA to rivaroxaban and from rivaroxaban to VKA. There were two correct responses for each question. For both questions, few physicians selected both correct responses, and 80% and 85%, respectively, selected at least one correct response. There was no pattern across countries (Annex 3, Table A-3; Questions 11 and 12). Oncologists had slightly lower proportions of correct responses than the other specialities (Annex 4, Table A-8; Questions 11 and 12).

Physicians responsible for initiating or converting rivaroxaban treatment had a higher proportion of correct responses than those responsible for writing maintenance prescriptions only (Figure 7 and Figure 8). Likewise, physicians who reported receiving the prescriber guide for rivaroxaban had higher proportions of correct responses than those who did not report receiving the prescriber guide (Annex 4, Table A-10; Questions 11 and 12).

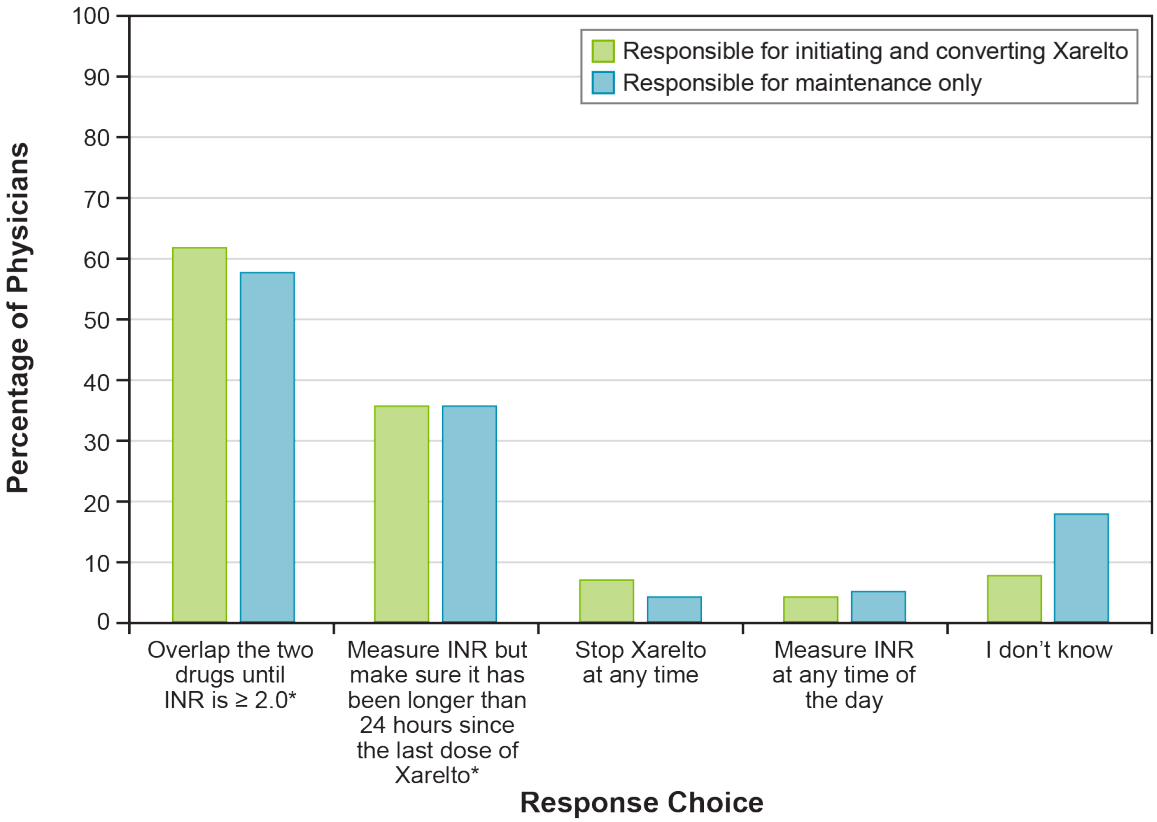
Figure 7. Responses to Question 11: Which of the Following Steps Should Be Taken When Converting Patients From VKA (e.g., Warfarin) to Xarelto? (Tick All That Apply.) (N = 1,226)



DVT = deep vein thrombosis; INR = international normalised ratio; VKA = vitamin K antagonist.

*Correct response is marked with an asterisk.

Figure 8. Responses to Question 12: Which of the Following Steps Should Be Taken When Converting Patients From Xarelto to VKA (e.g., Warfarin)? (Tick All That Apply.) (N = 1,226)



INR = international normalised ratio; VKA = vitamin K antagonist.

*Correct response is marked with an asterisk.

Physicians were also asked about procedures for converting patients from parenteral anticoagulants to rivaroxaban. There were two correct response items for the question. The correct responses were selected by 51% and 54% of all physicians, respectively, and 81% selected at least one of the correct responses. Physicians in the UK had lower proportions of correct responses than physicians from the other countries (Annex 3, Table A-3; Question 13). In general, neurologists, cardiologists, and haematologists had higher proportions of correct responses than other physician specialities (Annex 4, Table A-8; Question 13).

Physicians responsible for initiating or converting rivaroxaban treatment had higher proportions of correct responses than those who did maintenance prescriptions only, and physicians who reported receiving the prescriber guide for rivaroxaban had higher proportions of correct responses than those who did not report receiving the prescriber guide. In both cases, the differences were approximately 20% for each correct response (Annex 4, Tables A-9 and A-10; Question 13).

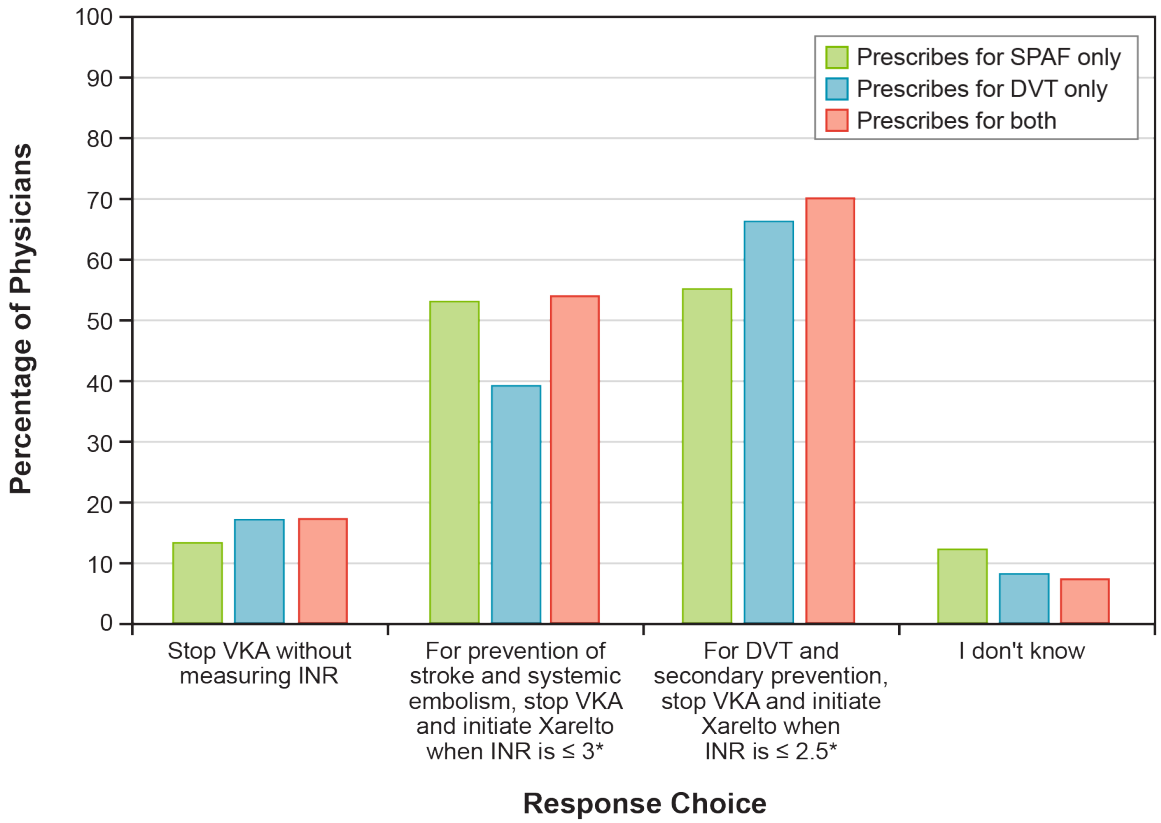
Monitoring and Converting Stratified by Indication

Questions about converting patients to or from rivaroxaban (Questions 11, 12, and 13) were also stratified by the indication(s) for which physicians reported that they prescribed rivaroxaban (in screening Question 1). The stratification consisted of physicians who prescribe rivaroxaban for the following:

- SPAF only
- DVT and secondary prevention only
- Both SPAF and DVT

In response to Question 11, physicians who prescribed for SPAF only had a higher proportion of correct responses than physicians who prescribed for DVT only for the response category that was specific to SPAF (53% vs. 39%), and the proportion of correct responses for those who prescribed for both indications was similar to those who only prescribed for DVT (54%) (Figure 9). Physicians who prescribed for DVT only had a higher proportion of correct responses than physicians who prescribed for SPAF only for the response category specific to DVT (66% vs. 55%), and physicians who prescribed for both indications had the highest proportion of correct responses (70%).

Figure 9. Responses to Question 11: Which of the Following Steps Should Be Taken When Converting Patients From VKA (e.g., Warfarin) to Xarelto? (Tick All That Apply.) (N = 1,226)

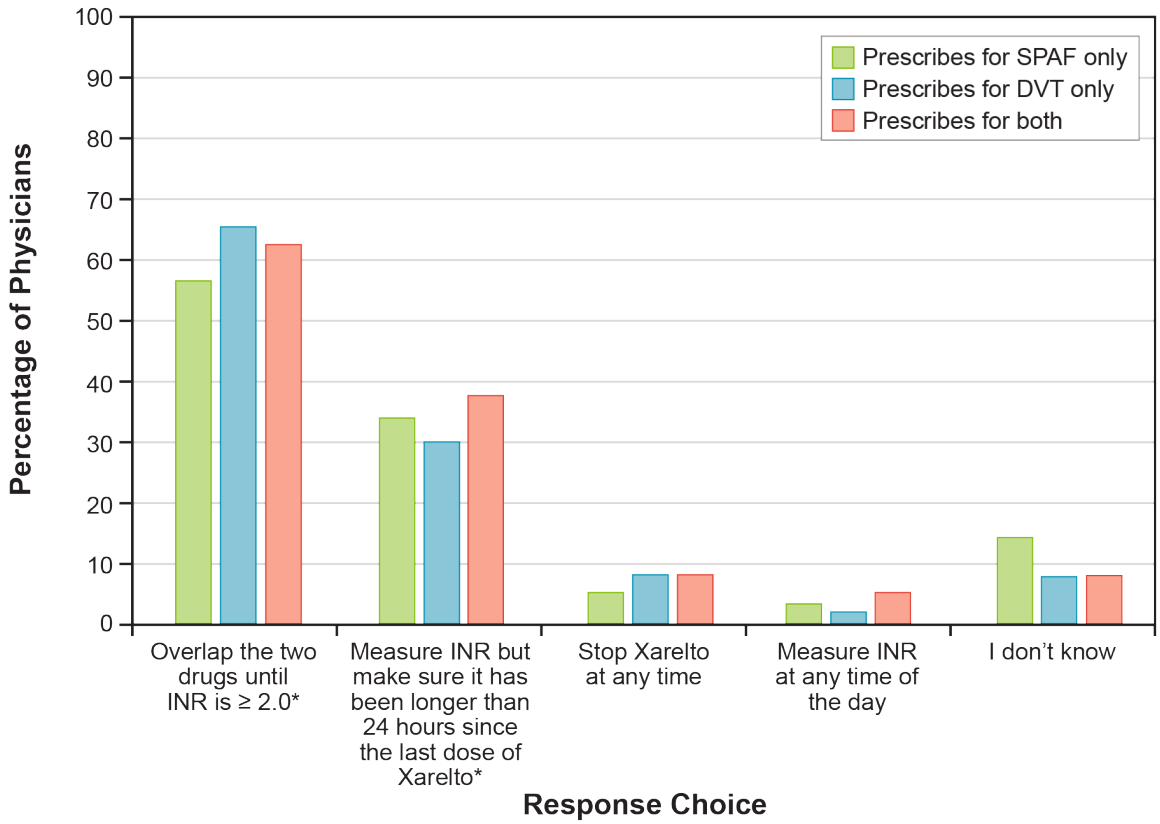


DVT = deep vein thrombosis; INR = international normalised ratio; SPAF = stroke prevention in atrial fibrillation; VKA = vitamin K antagonist.

*Correct response is marked with an asterisk.

In response to Question 12, the correct response proportion for physicians who prescribed for DVT only was higher compared with physicians who prescribed for SPAF only for the response category "Overlap the two drugs until INR is ≥ 2.0" (66% vs. 57%) but slightly lower for "Measure INR but make sure it has been longer than 24 hours since the last dose of Xarelto" (30% vs. 34%). Those who prescribed for both SPAF and DVT were similar for both response categories (63% and 38%, respectively) (Figure 10).

Figure 10. Responses to Question 12: Which of the Following Steps Should Be Taken When Converting Patients From Xarelto to VKA (e.g., Warfarin)? (Tick All That Apply.) (N = 1,226)



DVT = deep vein thrombosis; INR = international normalised ratio; SPAF = stroke prevention in atrial fibrillation; VKA = vitamin K antagonist.

*Correct response is marked with an asterisk.

In addition, correct response proportions for Question 13 were slightly higher among physicians who treated DVT only than for those who treated SPAF only (48% vs. 46% for one response option and 54% vs. 47% for the other), and physicians who treated both SPAF and DVT had the same or slightly higher proportions of correct responses on both items (53% and 56%, respectively) (Annex 4, Table A-11; Question 13).

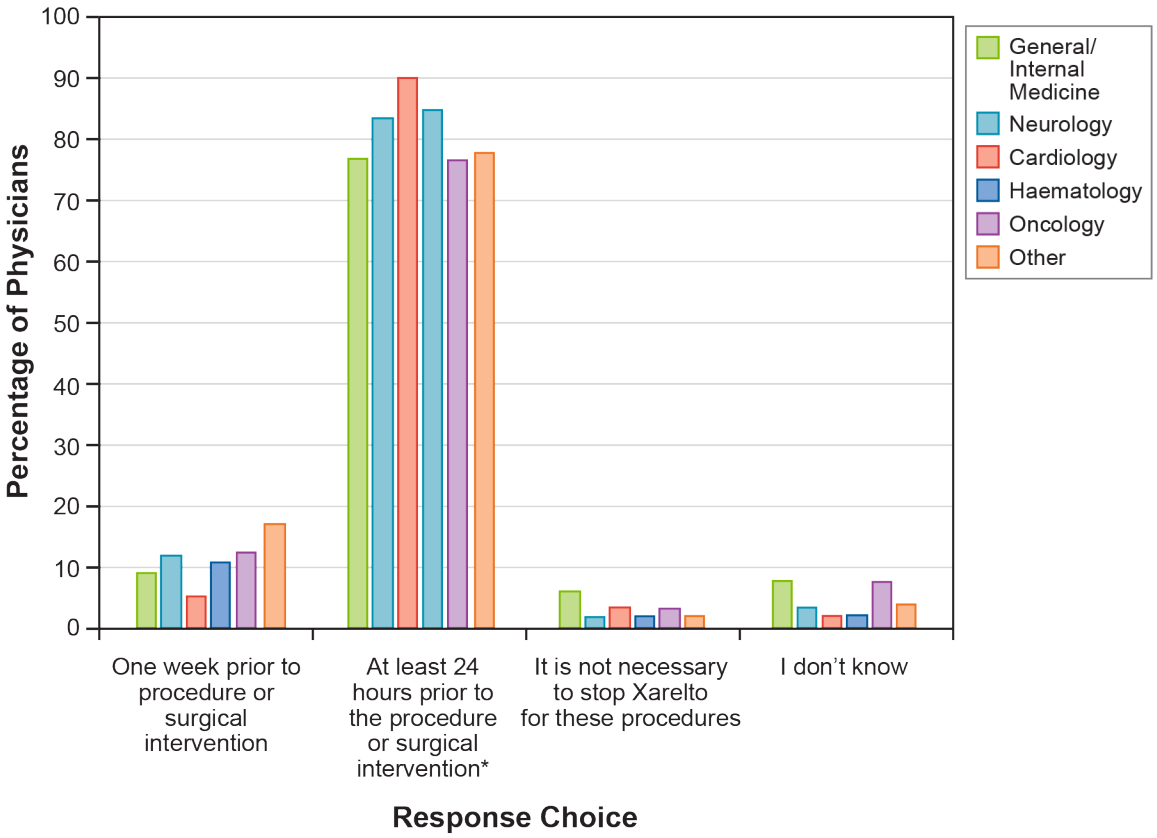
Invasive Procedure and Medically Important Bleeding

Overall, 80% of physicians correctly responded that rivaroxaban treatment should be suspended at least 24 hours prior to an invasive procedure or surgical intervention. The correct response proportions varied considerably across countries, from 90% in Germany to 69% in France (Annex 3, Table A-3; Question 14). Haematologists (85%),

cardiologists (90%), and neurologists (84%) had the highest correct response proportions among physician specialities (Figure 11).

Physicians responsible for initiating rivaroxaban treatment or converting treatment to or from rivaroxaban had a much higher correct response proportion (82%) than physicians responsible for writing maintenance prescriptions only (65%). Physicians who reported receiving the prescriber guide for rivaroxaban had a slightly higher proportion of correct responses than those who did not (83% vs. 76%) (Annex 4, Tables A-9 and A-10; Question 14).

Figure 11. Responses to Question 14: If an Invasive Procedure or Surgical Intervention Is Required, When Should Treatment With Xarelto (15 to 20 mg) Be Suspended (If Possible, Based Upon Clinical Judgement of Physician)? (N = 1,214)

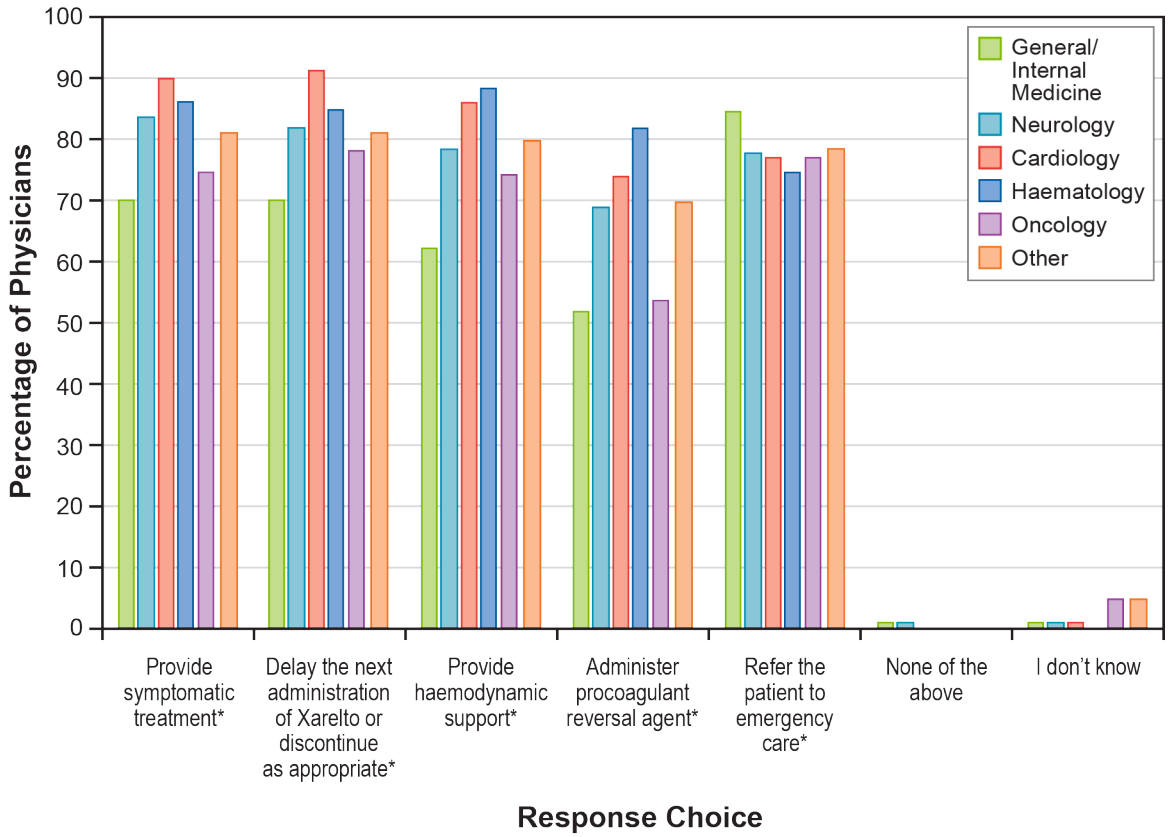


*Correct response is marked with an asterisk.

Physicians were asked to select the most appropriate actions if a patient taking rivaroxaban presents with a medically important bleeding complication; there were five correct responses for this question. The proportions of correct responses for the five options ranged from 59% for the option "administer procoagulant reversal agent (for life-threatening bleeding)" to 81% for the option "refer the patient to emergency care." Forty-two percent of physicians selected all five correct responses. Physicians in Germany had slightly higher proportions of correct responses among the countries on this question (Annex 3, Table A-3; Question 15). Cardiologists and haematologists more often selected the correct response options (59% and 60% selected all five correct answers compared with 35% to 51% for other specialists) (Figure 12).

Physicians responsible for initiating or converting rivaroxaban treatment had a higher proportion of correct responses than did physicians who wrote only maintenance prescriptions (44% vs. 30% selected all 5 correct answers). In addition, physicians who reported receiving the prescriber guide for rivaroxaban had a higher proportion of correct responses than those who did not receive the prescriber guide (50% vs. 33% selected all 5 correct answers) (Annex 4, Tables A-9 and A-10; Question 15).

Figure 12. Responses to Question 15: What Are the Most Appropriate Actions You Should Take if a Patient Taking Xarelto Presents With a Medically Important Bleeding Complication? (Tick All That Apply.) (N = 1,214)



*Correct response is marked with an asterisk.

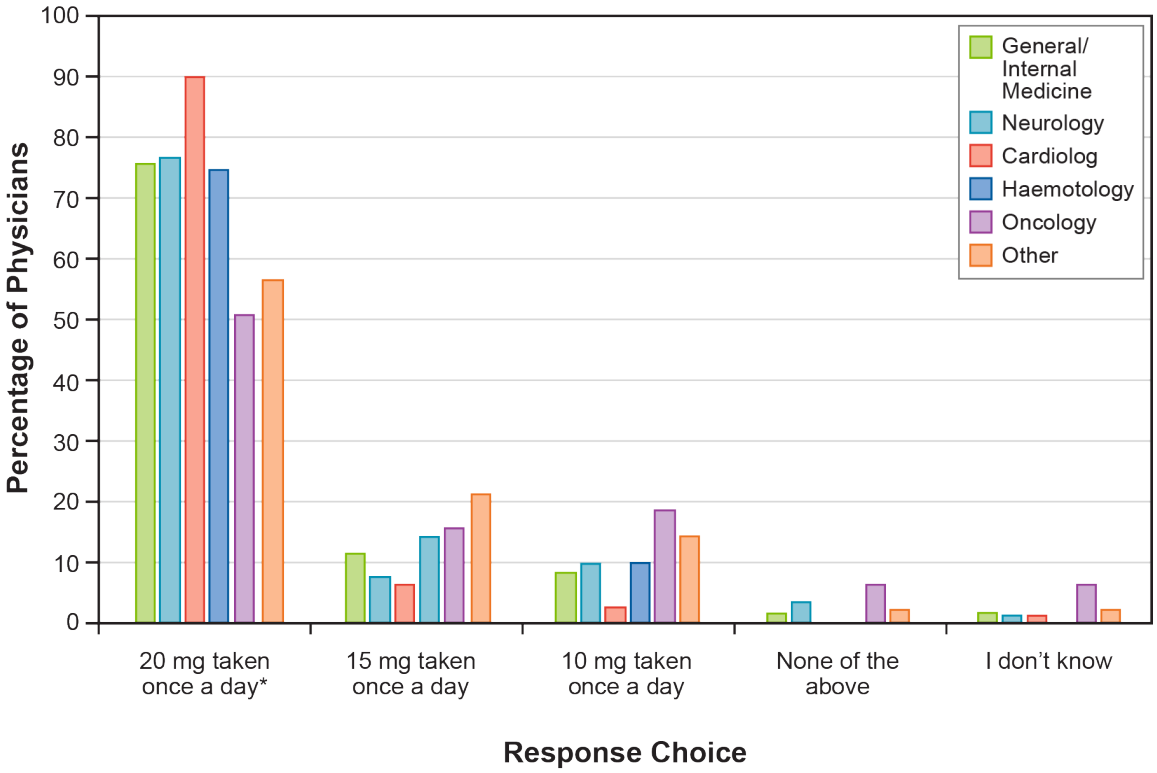
Dosing

Prevention of Stroke and Systemic Embolism in Patients With Non-valvular Atrial Fibrillation[1]

Of the physicians who reported that they prescribed for SPAF, 75% correctly reported 20 mg taken once daily was the standard recommended dose of rivaroxaban for this indication, while 58% of physicians were aware that 15 mg taken once daily was the recommended dose of rivaroxaban for SPAF patients with moderate or severe renal impairment. For both questions, physicians in Germany had noticeably higher proportions of correct responses (82% and 70%) than did physicians from the other countries (Annex 3, Table A-3; Questions 16 and 17). Cardiologists had the highest correct response proportions for these two questions, with 90% and 81% correct, respectively (Figure 13).

Physicians responsible for initiating or converting rivaroxaban treatment had a much higher correct response proportion than did those responsible for maintenance prescriptions only (76% vs. 62% on the first question; 62% vs. 35% on the second question). In addition, physicians who reported receiving the prescriber guide for rivaroxaban had a higher correct response proportion than those who did not report receiving the prescriber guide (78% vs. 71% on the first question; 66% vs. 49% on the second question) (Annex 4, Tables A-9 and A-10; Questions 16 and 17).

Figure 13. Responses to Question 16: What is the Standard Recommended Dose of Xarelto for the Prevention of Stroke and Systemic Embolism in Patients With Non-valvular Atrial Fibrillation? (N = 1,187)



*Correct response is marked with an asterisk.

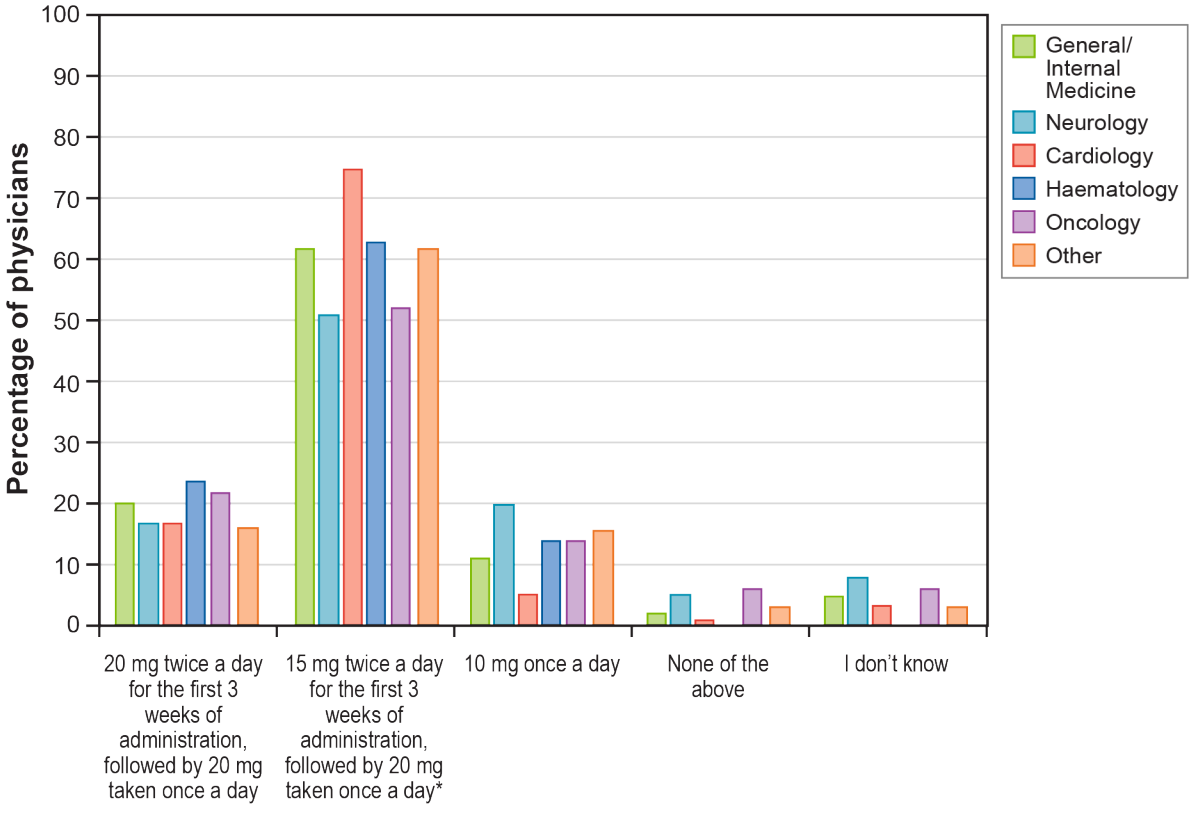
[1] Only a subset of physicians who reported that they prescribed for SPAF were presented with the questions in this section.

Deep Vein Thrombosis Treatment and Secondary Prevention[1]

Of the physicians who reported that they prescribed rivaroxaban for DVT and secondary prevention, 62% correctly selected the response option for the standard recommended dose for this indication. Physicians from Spain, where rivaroxaban is not reimbursed for the treatment of DVT, were less likely than physicians from the other three countries to select the correct response option (53% vs. 62%, 64%, and 67% in France, Germany and the UK, respectively) (Annex 3, Table A-3; Question 18). Again, cardiologists got a particularly high proportion correct (75%) on this question, while no other speciality category was above 63% (Figure 14).

Physicians responsible for initiating rivaroxaban treatment had a slightly higher proportion of correct responses than did those responsible for maintenance prescriptions only (62% vs. 56%). A somewhat larger difference was seen between physicians who reported receiving the prescriber guide for rivaroxaban and those who did not (67% vs. 56%) (Annex 4, Tables A-9 and A-10; Question 18).

Figure 14. Response to Question 18: What Is The Standard Recommended Dose for Patients Receiving Xarelto for Deep Vein Thrombosis Treatment and Secondary Prevention? (N = 1,031)



*Correct response is marked with an asterisk.

[1] Only a subset of physicians who reported that they prescribed for DVT were presented with the questions in this section.

10.4.3 Sources of Information About Rivaroxaban and Their Ratings

Overall, as well as within each of the four countries, the three most frequently reported sources of information received about rivaroxaban were the following:

- Briefing from a company representative (59%)
- The summary of product characteristics (58%)
- The prescriber guide (57%).

Physicians in Germany reported the highest rates of receipt of each of these sources of information (73%, 85%, and 73%, respectively), whereas physicians in the UK reported the lowest rates of receipt for each (40%, 39%, and 32%, respectively) (Annex 3, Table A-4; Question 19). Reported receipt of the prescriber guide ranged from 51% among general/internal medicine physicians to 78% among haematologists (Annex 4, Table A-8; Question 19). Other response options included "Clinical trials published in the medical literature" (selected by 38% of all physicians), "Discussion with a clinical expert" (24%), and "Other" (7%) (Annex 3, Table A-4; Question 19).

Of the physicians who reported receiving the prescriber guide for rivaroxaban, 80% rated it as either very helpful or extremely helpful. Of those who listed "briefing from a company representative," 70% rated that source as very helpful or extremely helpful. Of those who selected "discussion with a clinical expert," 79% rated these discussions very helpful or extremely helpful. Of those who selected "summary of product characteristics," 75% rated the summary as very helpful or extremely helpful; and of those who selected "medical publications," 82% rated these publications as very helpful or extremely helpful (Annex 3, Table A-5; Question 20).

10.4.4 Experiences With Information Contained in the Patient Alert Cards

The vast majority (85%) of physicians reported that they discussed the information in the patient alert cards with their patients when first prescribing rivaroxaban (85%). This was consistent across countries ranging from 79% in France to 92% in Germany. Approximately one-third of physicians reported that they discussed the information in the patient alert cards at each of the other times outlined in this question: "when a patient is facing an invasive procedure or surgical intervention" (34%), "when a patient has bleeding complications" (31%), and "when a patient has a Xarelto related adverse event" (30%) (Annex 3, Table A-6; Question 23).

10.4.5 Other Analyses

None

10.5 Adverse Events/Adverse Reactions

No adverse events were reported during the wave 2 survey.

11 Discussion

11.1 Key Results

One of the most important factors when dealing with anticoagulation is understanding the risks associated with each product and how to mitigate these risks. In general, physicians' knowledge of the key safety information in the educational materials for rivaroxaban was high.

Physicians' knowledge was particularly high for questions related to the risks of side effects with rivaroxaban treatment and use of rivaroxaban with special populations. Almost all physicians (94%) correctly reported that bleeding is the most important risk associated with rivaroxaban. Physicians' knowledge of patient populations at risk of experiencing serious side effects ranged from 69% to 94% correct for individual response options, and physicians' knowledge of contraindications ranged from 73% to 92% correct for individual response options.

Sixty-two percent of physicians were aware that rivaroxaban should be taken with food.

While almost all physicians (95%) knew that routine coagulation monitoring is not required for patients taking rivaroxaban, knowledge was lower for situations that require INR monitoring, ranging from 58% to 76% on individual response options. Knowledge was also lower regarding procedures for converting from VKA to rivaroxaban and for converting from rivaroxaban to VKA (ranging from 36%-66% for individual response options) and for converting from parenteral anticoagulants to rivaroxaban (ranging from 51%-54% for individual response options).

Physician knowledge was high for questions related to invasive procedures and medically important bleeding. Eighty percent of physicians correctly reported that rivaroxaban treatment should be suspended at least 24 hours before an invasive procedure or surgical intervention. Physicians' knowledge of the most appropriate actions to take if a patient taking rivaroxaban presents with a medically important bleeding complication ranged from 59% to 81% correct for individual response options.

Physicians' knowledge of dosing recommendations varied by question. Of physicians who prescribed for SPAF, 75% correctly indicated that 20 mg taken once daily was the standard recommended dose for this indication. A lower proportion of physicians (58%) selected the correct recommended dose for SPAF patients with moderate or severe renal impairment. Sixty-two percent of physicians who prescribed for DVT and secondary prevention selected the correct recommended dose for this indication.

For most questions, physician knowledge levels were consistent across countries. Physicians who reported specialities in cardiology and haematology had higher proportions of correct responses than physicians in other speciality categories for most of the knowledge questions, and oncologists tended to have lower proportions of correct responses. Physicians responsible for initiating rivaroxaban treatment or converting treatment from or to rivaroxaban had a higher proportion of correct responses than those who were responsible for maintenance treatment only. Physicians who reported receiving the prescriber guide for rivaroxaban also consistently provided more correct responses than those who did not report receiving the guide.

Physicians' knowledge was remarkably similar between waves 1 and 2. The differences in the proportions of correct responses were less than 5% for almost all of the questions in the survey. Annex 5 provides a graphic comparison of wave 1 and 2 results.

More than half of physicians reported that they received the prescriber guide for rivaroxaban (57%), ranging from 32% in the UK to 73% in Germany. The source of information about rivaroxaban reported most frequently by physicians was a company representative (59%), followed by the prescriber guide, and the summary of product characteristics (58%). Of the physicians who reported using the prescriber guide, most (80%) found it helpful or extremely helpful. Most physicians reported that they discussed the information on the patient alert cards with their patients when first prescribing rivaroxaban (85%).

11.2 Strengths

A key strength of the study is diversity of physician participants. The targeted number of physicians (approximately 300 per country) was achieved. The distribution of physicians by speciality, practice type, and rivaroxaban-prescribing practices represented a broad diversity of physicians across four countries.

The wave 2 survey was conducted approximately 2 years following wave 1, during which time physicians would have gained additional experience prescribing rivaroxaban for prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (SPAF) and DVT treatment and secondary prevention.

Accuracy of responses among physicians was facilitated through formal cognitive pretesting of the questionnaire before wave 1. The wording of the questions and response choices should have been easily understood by the respondents.

11.3 Limitations

As with all voluntary studies, some limitations are inherent. Many methodologic and operational challenges are well recognised.(6) Although the study was designed to ensure the selection of a diverse and generally representative sample of prescribers to participate in this study, there was no exhaustive list of all rivaroxaban prescribers from which to draw a sample; hence, it was impossible to select a random sample of all prescribers. Therefore, although participants were diverse in characteristics, the study participants may not necessarily represent all relevant prescribers. In addition, as is true with most surveys, it was possible that respondents who completed the questionnaire differed from non-respondents in characteristics measured in the questionnaire (e.g., knowledge, reading, and use of the educational materials). The direction and magnitude of such potential respondent bias is not known. A comparison of participants and non-participants was not possible because physicians who did not wish to participate in the survey did not respond to the invitation and characteristics of the invited physicians were not otherwise available. We could not compare physician and practice characteristics of the physician participants with what is known about the overall prescribing population because that information was not available to us.

11.4 Interpretation

Little information is in the public domain to set thresholds for acceptable levels of knowledge and behaviour related to risk-minimisation measures. A recent publication(7) reported on patient understanding of medication guides from a review of 66 assessment reports submitted to the United States Food and Drug Administration. Few of the studies (30%) achieved an 80% knowledge level (percentage correct) for the single most important risk communicated in the medication guide. The mean knowledge level was 63.8%. In this study, 94% of physicians responded accurately to the question of the most important risk.

Knowledge and behaviour reflect many factors, including availability and access to information, literacy and numeracy, beliefs, and motivation.

Knowledge varied across categories of information, with higher knowledge associated with the most important information (e.g., greatest risk, populations at increased risk, and contraindications) and lower knowledge associated with procedures, such as treatment switching, which might require physicians to refer to guidance documents. However, awareness of the need to take rivaroxaban with food was surprisingly low.

There is limited information in the public domain to be able to compare the percentage of physicians who report receipt of educational materials based on results from post-authorisation safety studies. A recent publication(8) reported the results of a multinational survey of 800 European physicians that assessed the receipt of educational materials. For that study, physicians' reported receipt of the educational materials ranged from 16% to 69% across the participating countries.

Physicians who reported receiving the prescriber guide for rivaroxaban displayed higher knowledge than those who did not report receiving the guide. These findings suggest that the educational materials are effectively communicating the desired information. The reported receipt of the physician prescriber guide ranged from 32% in the UK to 73% in Germany and ranged from 51% among general/internal medicine physicians to 78% among haematologists. Low levels of reported receipt of educational materials may reflect poor recall—if the material had indeed been received—or barriers to the receipt of the material. Variability across countries could reflect (1) the different distributions of specialists prescribing initial and maintenance therapy; (2) inherent differences in physician behaviour; (3) variations in prescribing guidelines/practices across country-specific health care systems; (4) differences in distribution practices for educational materials; or (5) different intensity of the educational efforts.

11.5 Generalisability

As noted in Section 11.2, the study achieved great diversity in physician characteristics within the four countries, allowing for stratification of results by those characteristics. We saw heterogeneity of most results by country; it is unknown how well these results would relate to other countries.

12 Other Information

Not applicable.

13 Conclusion

The study met its objectives to evaluate whether physicians receive the educational materials for rivaroxaban and to assess physician knowledge and understanding of key safety information, as well as use of the materials.

In general, the observed patterns of knowledge among the physicians are as expected—with greatest knowledge on the most important risks emphasised in the educational material and other product information and lower knowledge on more complex aspects of safe use (e.g., concepts related to dosing, converting to/from rivaroxaban, and patient monitoring) for which we would assume that physicians would consult the label and/or prescriber guide rather than relying on recall.

The results of the wave 1 and 2 surveys were remarkably similar, suggesting that the knowledge patterns were maintained approximately 2 years after the wave 1 survey. The knowledge retention suggests that the existing channels of educational communication are effective.

14 References

1. Xarelto summary of product characteristics—EU. Berlin: Bayer AG; 2017. Available at: https://www.xarelto.com/en/spc/. Accessed 18 Dec 2017.

2. European Network of Centres of Pharmacoepidemiology and Pharmacovigilance (ENCePP). The European Union Electronic Register of Post-Authorisation Studies (EU PAS Register). 15 July 2016. http://www.encepp.eu/encepp_studies/indexRegister.shtml. Accessed: 29 November 2017.

3. International Society for Pharmacoepidemiology (ISPE). Guidelines for good pharmacoepidemiology practices (GPP). Revision 3. June 2015. Available at: http://www.pharmacoepi.org/resources/guidelines_08027.cfm. Accessed 29 November 2017.

4. European Medicines Agency (EMA). Guideline on good pharmacovigilance practices (GVP). Module VIII – Post-authorisation safety studies (Rev 3). European Medicines Agency; 09 October 2017a. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129137.pdf Accessed: 29 November 2017.

5. European Network of Centres of Pharmacoepidemiology and Pharmacovigilance (ENCePP). Guide on methodological standards in pharmacoepidemiology (revision 6). EMA/95098/2010. 2017b. Available at: http://www.encepp.eu/standards_and_guidances/methodologicalGuide.shtml. Accessed 21 December 2017.

6. Arias A, DiSantostefano R, Gilsenan A, Madison T, Matus D, Primatesta P, et al. Evaluating the effectiveness of additional risk minimisation measures via surveys in Europe: challenges and recommendations. 2016. Available at: https://pharmacoepi.org/pub/f46953df-de69-31e7-8f74-725bd7fa685f. Accessed 15 May 2017.

7. Knox CA, Hampp C, Willy M, Winterstein AG, Dal Pan G. Patient understanding of drug risks: an evaluation of medication guide assessments. Pharmacoepidemiol Drug Saf. 2015;24:518-25.

8. Brody RS, Liss CL, Wray H, Iovin R, Michaylira C, Muthutantri A, et al. Effectiveness of a risk-minimization activity involving physician education on metabolic monitoring of patients receiving quetiapine: results from two postauthorization safety studies. Int Clin Psychopharmacol. 2016 Jan;31(1):34-41.

Appendices

Annex 1. List of Stand-Alone Documents

Signature Pages

Signature Page – Bayer AG

Title	Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)
Report version and date	Version 1.0, 24 May 2018
IMPACT study number	16167
Study type / Study phase	PASS Joint PASS: ☐ YES ☒ NO
EU PAS register number	EUPAS3911
Medicinal product / Active substance	Xarelto (rivaroxaban) / INN: Rivaroxaban; ATC code: B01AF01
Study Initiator and Funder	Bayer AG

The undersigned confirms that s/he has read this report and confirms that to the best of her/his knowledge it accurately describes the conduct and results of the study.

Print Name: PPD

Bayer AG

PPD

Date, Signature: June 6th, 2018

PPD

Signature Page – PPD

Title	Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)
Report version and date	Version 1.0, 24 May 2018
IMPACT study number	16167
Study type / Study phase	PASS Joint PASS: ☐ YES ☒ NO
EU PAS register number	EUPAS3911
Medicinal product / Active substance	Xarelto (rivaroxaban) / INN: Rivaroxaban; ATC code: B01AF01
Study Initiator and Funder	Bayer AG

The undersigned confirms that s/he has read this report and confirms that to the best of her/his knowledge it accurately describes the conduct and results of the study.

Print Name: PPD

Date, Signature: PPD

4 June 2018

Signature Page – PPD

Title	Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)
Report version and date	Version 1.0, 24 May 2018
IMPACT study number	16167
Study type / Study phase	PASS Joint PASS: ☐ YES ☒ NO
EU PAS register number	EUPAS3911
Medicinal product / Active substance	Xarelto (rivaroxaban) / INN: Rivaroxaban; ATC code: B01AF01
Study Initiator and Funder	Bayer AG

The undersigned confirms that s/he has read this report and confirms that to the best of her/his knowledge it accurately describes the conduct and results of the study.

Print Name: PPD

Date, Signature: 29 May 2018,

PPD

Signature Page – Bayer AG

Title	Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)
Report version and date	Version 1.0, 24 May 2018
IMPACT study number	16167
Study type / Study phase	PASS Joint PASS: ☐ YES ☒ NO
EU PAS register number	EUPAS3911
Medicinal product / Active substance	Xarelto (rivaroxaban) / INN: Rivaroxaban; ATC code: B01AF01
Study Initiator and Funder	Bayer AG

The undersigned confirms that s/he has read this report and confirms that to the best of her/his knowledge it accurately describes the conduct and results of the study.

Print Name: PPD

Bayer AG

Date, Signature: 24 May 2018, PPD

_____

Signature Page – Bayer AG

Title	Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)
Report version and date	Version 1.0, 24 May 2018
IMPACT study number	16167
Study type / Study phase	PASS Joint PASS: ☐ YES ☒ NO
EU PAS register number	EUPAS3911
Medicinal product / Active substance	Xarelto (rivaroxaban) / INN: Rivaroxaban; ATC code: B01AF01
Study Initiator and Funder	Bayer AG

The undersigned confirms that s/he has read this report and confirms that to the best of her/his knowledge it accurately describes the conduct and results of the study.

Print Name: PPD

Bayer AG

PPD

Date, Signature: PPD 4.05. PPD 8

PPD

Signature Page – Bayer AG

Title	Xarelto (Rivaroxaban) Risk-Minimisation Plan Evaluation: Patient and Physician Knowledge of Key Safety Messages (Wave 2)
Report version and date	Version 1.0, 24 May 2018
IMPACT study number	16167
Study type / Study phase	PASS Joint PASS: ☐ YES ☒ NO
EU PAS register number	EUPAS3911
Medicinal product / Active substance	Xarelto (rivaroxaban) / INN: Rivaroxaban; ATC code: B01AF01
Study Initiator and Funder	Bayer AG

The undersigned confirms that s/he has read this report and confirms that to the best of her/his knowledge it accurately describes the conduct and results of the study.

Print Name: PPD

Bayer AG

Date, Signature: 28.05.2018,

PPD

Annex 2. Physician Questionnaire

Physician Questionnaire

Xarelto Risk Minimisation Study

Study Introduction and Informed Consent

PPD an independent, nonprofit research firm engaging in numerous health and medicine research studies, is conducting a research study on behalf of Bayer AG (Bayer) and would like to invite you to participate. This study is being conducted as part of the ongoing safety and risk management process for Xarelto (rivaroxaban). This is not a marketing survey, but a scientific study conducted at the request of the European Medicines Agency (EMA), the drug regulatory body in the European Union (EU). The purpose of the study is to assess prescribers' understanding of and compliance with the safe use of Xarelto for the following two chronic indications:

- Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation
- Treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism following an acute deep vein thrombosis in adults. (This indication will be referred to as "**deep vein thrombosis treatment and secondary prevention"** throughout the questionnaire.)

You have been identified as a potential participant for this evaluation because you are a physician who treats patients who have, or who are at risk for developing these conditions. This questionnaire which takes 10 to 15 minutes to complete is being administered to approximately 1,500 physicians across five countries within the EU.

Any personal identifying information you provide to us is confidential, and we will employ the legally required technical and physical safeguards to protect your privacy. Your survey responses will be used only for statistical purposes and will not be disclosed or used in any personally-identifiable form, unless required by law.

Your responses to this survey (not including your name and contact information) will be shared with PPD researchers in the United States (US) for data analysis and storage purposes. Your survey responses will not be linked to your name in any report or publication. The risk of participation in this study relates to data security and is minimal, given the strict confidentiality and security procedures in place.

Your willingness to take part in this study will help us ensure that the key safety information about Xarelto is being effectively communicated to you and other physicians.

You will be compensated for your participation in this study. Per the code of conduct set by the European Federation of Pharmaceutical Industries and Associations (EFPIA), Bayer will post a

summary of payments provided to physicians who participated in this study to a public website. No personal identifying physician information will be reported.

We respect any requirements your employer might have for your participation in research studies and ask that you please ensure that any relevant approvals have been given prior to completing the survey.

By completing and submitting this survey, you indicate that you have read the information provided above and voluntarily agree to participate in this study.

C1. Do you agree to participate in the study?

- ☐ Yes, I agree to participate in this study.
- ☐ No, I do not agree to participate in this study.

[IF C1 = "No, I do not agree to participate in this study."
THEN DISPLAY "You have indicated that you do not agree to participate in the study. Thank you for your time." TERMINATE SURVEY].

To confirm your eligibility to participate in this brief assessment, please answer the following question:

S1. In the past 6 months, have you prescribed Xarelto (rivaroxaban) to patients for either of the following indications?

(Tick all that apply.)

- ☐ Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation
- ☐ Deep vein thrombosis treatment and secondary prevention in adults
- ☐ I have not prescribed Xarelto for either of these indications

[IF S1 = "I have not prescribed Xarelto for either of these indications",
THEN DISPLAY "It does not appear that you qualify for the survey. Thank you for your time and interest." AND TERMINATE SURVEY
ELSE DISPLAY "We have confirmed that you are eligible. We will now continue with the survey questions].

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

Physician Questionnaire

This questionnaire is designed to gain a better understanding of prescribers' knowledge about Xarelto for only the following two approved indications:

- Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation
- Deep vein thrombosis treatment and secondary prevention

Additionally, this assessment will be used to determine if the education materials regarding Xarelto, including the Prescriber Guide, are accurately understood and whether there are aspects of these materials that could be improved.

The first set of questions asks about your prescribing practices.

Q1. In the past 6 months, for how many patients have you prescribed Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation?

- ☐ 1 to 10
- ☐ 11 to 20
- ☐ 21 or more
- ☐ I have not prescribed Xarelto for this indication

Q2. In the past 6 months, for how many patients have you prescribed Xarelto for deep vein thrombosis treatment and secondary prevention?

- ☐ 1 to 10
- ☐ 11 to 20
- ☐ 21 or more
- ☐ I have not prescribed Xarelto for this indication

[IF Q1 = "I have not prescribed Xarelto for this indication" AND Q2 = "I have not prescribed Xarelto for this indication", THEN DISPLAY "It does not appear that you qualify for the survey. Thank you for your time and interest." AND TERMINATE SURVEY.]

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

Q3. When did you write your <u>most recent</u> prescription for Xarelto for either of these indications?

(Tick one.)

- ☐ Less than 1 month ago
- ☐ 1 to 3 months ago
- ☐ 4 to 6 months ago
- ☐ I don't know

Q4. Which of the following Xarelto treatment activities are you responsible for?

(Tick all that apply.)

- ☐ I initiate Xarelto treatment or convert treatment from or to Xarelto
- ☐ I write follow up (maintenance) prescriptions for Xarelto

The next questions ask about the use of Xarelto for prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation and deep vein thrombosis treatment and secondary prevention.

Q5. What is the most important risk associated with taking Xarelto?

(Tick one.)

- ☐ Neoplasia
- ☐ Hypertension
- ☐ Risk of bleeding*
- ☐ Immunosuppression
- ☐ I don't know

Q6. Which of the following populations are at an increased risk of experiencing serious side effect(s) associated with Xarelto?

(Tick Yes, No, or I don't know for each patient population listed)

Population	Yes, at higher risk	No, not at higher risk	I don't know
Patients with moderate or severe renal impairment	☐ *	☐	☐
Patients taking products that affect haemostasis such as NSAIDS, acetylsalicylic acid, platelet aggregation inhibitors	☐ *	☐	☐
Patients at risk of bleeding	☐ *	☐	☐
Patients with chronic constipation	☐	☐	☐

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

Q7. To which patient groups is Xarelto contraindicated?

(Tick all that apply.)

- ☐ Patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child-Pugh class B and C*
- ☐ Patients who are pregnant or breastfeeding*
- ☐ Patients receiving concomitant treatment with any other anticoagulant such as unfractionated heparin (UFH), low molecular weight heparins, heparin derivatives or oral anticoagulants except when switching therapy to or from Xarelto or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter*
- ☐ Patients with clinically significant active bleeding*
- ☐ I don't know

Q8. Xarelto (15 or 20 mg) must be taken….?

(Tick one.)

- ☐ On an empty stomach
- ☐ With food/on a full stomach*
- ☐ I don't know

Q9. Is routine coagulation monitoring required for patients taking Xarelto for these indications?

- ☐ Yes
- ☐ No*
- ☐ I don't know

Q10. In which of the following situations is INR monitoring needed?

(Tick all that apply.)

- ☐ When converting from vitamin K antagonist (VKA) (e.g., warfarin) to Xarelto*
- ☐ When converting from Xarelto to VKA*
- ☐ Continual INR monitoring is required for all patients taking Xarelto
- ☐ I don't know

Q11. Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto?

(Tick all that apply.)

- ☐ Stop VKA without measuring INR
- ☐ For patients treated for prevention of stroke and systemic embolism, stop VKA and initiate Xarelto when INR is $\leq$ 3*
- ☐ For patients treated for deep vein thrombosis and secondary prevention, stop VKA and initiate Xarelto when INR is $\leq$ 2.5*
- ☐ I don't know

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

Q12. Which of the following steps should be taken when converting patients from Xarelto to VKA (e.g., warfarin)?

(Tick all that apply.)

- ☐ Overlap the two drugs until INR is ≥ 2.0*
- ☐ Measure INR but make sure it has been longer than 24 hours since the last dose of Xarelto*
- ☐ Stop Xarelto at any time
- ☐ Measure INR at any time of the day
- ☐ I don't know

Q13. Which of the following are true when converting from parenteral anticoagulants to Xarelto…?

(Tick all that apply.)

- ☐ Stop parenteral anticoagulants for a week prior to starting Xarelto
- ☐ For patients with continuously administered parenteral anticoagulants such as intravenous unfractionated heparin, Xarelto should be started at time of drug discontinuation*
- ☐ For patients with parenteral drug on a fixed dosing scheme such as low molecular weight heparin (LMWH), Xarelto should be started 0 to 2 hours before the next scheduled drug administration*
- ☐ I don't know

Q14. If an invasive procedure or surgical intervention is required, when should treatment with Xarelto (15 to 20 mg) be suspended (if possible, based upon clinical judgement of physician)?

(Tick one.)

- ☐ One week prior to the procedure or surgical intervention
- ☐ At least 24 hours prior to the procedure or surgical intervention*
- ☐ It is not necessary to stop Xarelto for these procedures
- ☐ I don't know

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

Q15. What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication?

(Tick all that apply.)

- ☐ Provide symptomatic treatment (e.g., mechanical compression, surgery)*
- ☐ Delay the next administration of Xarelto or discontinue Xarelto as appropriate*
- ☐ Provide haemodynamic support (e.g., blood transfusion)*
- ☐ Administer procoagulant reversal agent (for life-threatening bleeding)*
- ☐ Refer the patient to emergency care*
- ☐ None of the above
- ☐ I don't know

[IF Q1 = "I have not prescribed Xarelto for this indication", SKIP TO intro text preceding Q18.

The following questions are about the indication for prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation.

Q16. What is the standard recommended dose of Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation?

(Tick one.)

- ☐ 20 mg taken once a day*
- ☐ 15 mg taken once a day
- ☐ 10 mg taken once a day
- ☐ None of the above
- ☐ I don't know

Q17. What is the recommended dose for patients with moderate or severe renal impairment (creatinine clearance of 15-49 mL/min) receiving Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation?

(Tick one.)

- ☐ 20 mg taken once a day
- ☐ 15 mg taken once a day*
- ☐ 10 mg taken once a day
- ☐ None of the above
- ☐ I don't know

[IF Q2 = "I have not prescribed Xarelto for this indication", SKIP TO intro text preceding Q19.

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

The following question is about the indication for deep vein thrombosis treatment and secondary prevention in adult patients.

Q18. What is the standard recommended dose for patients receiving Xarelto for deep vein thrombosis treatment and secondary prevention?

(Tick one.)

- ☐ 20 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day
- ☐ 15 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day*
- ☐ 10 mg once a day
- ☐ None of the above
- ☐ I don't know

In this next section, please tell us about any information you have received about Xarelto.

Q19. Which of the following sources of information about Xarelto did you receive?

(Tick all that apply.)

- ☐ Xarelto Prescriber Guide
- ☐ Briefing from a company representative
- ☐ Discussion with a clinical expert
- ☐ The Summary of Product Characteristics for Xarelto
- ☐ Clinical trials published in the medical literature
- ☐ Other
- ☐ None of the above

Q20. How helpful were these sources to you in treating and educating your patients?

[ONLY DISPLAY RESPONSES THAT WERE CHECKED IN Q19; IF Q19 = "NONE OF THE ABOVE", SKIP TO Q23.]

	1 Not at all helpful	2 Slightly helpful	3 Somewhat helpful	4 Very helpful	5 Extremely helpful
Xarelto Prescriber Guide	☐	☐	☐	☐	☐
Briefing from a company representative	☐	☐	☐	☐	☐
Discussion with a clinical expert	☐	☐	☐	☐	☐
Summary of Product Characteristics	☐	☐	☐	☐	☐
Medical Publications	☐	☐	☐	☐	☐
Other	☐	☐	☐	☐	☐

Q23[1]. When would you discuss the information on the Patient Alert Card with your patients taking Xarelto? The Patient Alert Card is part of the Xarelto product packaging and explains the need for treatment compliance, taking medication with food, signs and symptoms of bleeding, and when to seek medical attention.

(Tick all that apply.)

- ☐ When first prescribing Xarelto
- ☐ When a patient is facing an invasive procedure or surgical intervention
- ☐ When a patient has bleeding complications
- ☐ When a patient has a Xarelto related adverse event
- ☐ Other

[1] Question numbering from the wave 1 questionnaire has been maintained to facilitate programming of the wave 2 questionnaire. Physicians will not see numbering in final online survey.

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

In this next section, please tell us a little about yourself and your clinical practice.

Q24. Which of the following best describes your specialty?

- ☐ General medicine (including GPs)
- ☐ Internal medicine
- ☐ Neurology
- ☐ Cardiology
- ☐ Haematology
- ☐ Accident & Emergency medicine
- ☐ Oncology
- ☐ Pulmonology
- ☐ Other

Q25. How many years have you been practicing medicine?

- ☐ 5 years or less
- ☐ 6 to 10 years
- ☐ 11 to 15 years
- ☐ 16 to 20 years
- ☐ 21 to 25 years
- ☐ More than 25 years

Q26. Are you…?

- ☐ Male
- ☐ Female

Q27. How would you characterise your practice?

(Tick all that apply.)

- ☐ General practice
- ☐ Hospital-based clinic
- ☐ Nursing home
- ☐ Other

Thank you for completing the questionnaire!

Reporting adverse events - Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Bayer plc. Tel.:PPD **Fax:**PPD **Email:**PPD

If you would like additional information or have any questions about the prescribing guidelines or safety information related to Xarelto, please click to the link below to access the Xarelto Prescriber Guide.

[INSERT LINK]

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

Additions for other countries:

France:

Non-English Text

Italy:

Non- English Text

***Indicates a correct response to a knowledge question and should not be shown in EDC.**

Annex 3. Results Tables, Overall and by Country

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-1. Physician and Practice Characteristics by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
Which of the following best describe your specialty? (Q24)					
General medicine (Including GPs)	186 (60)	120 (39)	135 (44)	112 (36)	553 (45)
Neurology	10 (3)	35 (12)	35 (12)	32 (10)	112 (9)
Cardiology	29 (9)	44 (14)	57 (19)	52 (17)	182 (15)
Haematology	16 (5)	4 (1)	6 (2)	29 (9)	55 (4)
Accident & Emergency medicine	6 (2)	11 (4)	16 (5)	6 (2)	39 (3)
Oncology	31 (10)	4 (1)	7 (2)	23 (7)	65 (5)
Other	13 (4)	6 (2)	15 (5)	3 (1)	37 (3)
Internal medicine	14 (5)	75 (25)	19 (6)	32 (10)	140 (11)
Pulmonology	2 (1)	3 (1)	10 (3)	16 (5)	31 (3)
No answer	3 (1)	2 (1)	4 (1)	3 (1)	12 (1)
How many years have you been practicing medicine? (Q25)					
5 years or less	1 (<.5)	1 (<.5)	2 (1)	1 (<.5)	5 (<.5)
6 to 10 years	24 (8)	13 (4)	18 (6)	33 (11)	88 (7)
11 to 15 years	59 (19)	51 (17)	50 (16)	67 (22)	227 (19)
16 to 20 years	96 (31)	74 (24)	63 (21)	70 (23)	303 (25)
21 to 25 years	65 (21)	74 (24)	65 (21)	59 (19)	263 (21)
More than 25 years	62 (20)	89 (29)	102 (34)	75 (24)	328 (27)
No answer	3 (1)	2 (1)	4 (1)	3 (1)	12 (1)

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-1. Physician and Practice Characteristics by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
Are you...? (Q26)					
Male	214 (69)	246 (81)	240 (79)	206 (67)	906 (74)
Female	93 (30)	56 (18)	60 (20)	99 (32)	308 (25)
No answer	3 (1)	2 (1)	4 (1)	3 (1)	12 (1)
How would you characterise your practice? (Q27) (Tick all that apply)					
General practice	191 (62)	230 (76)	164 (54)	191 (62)	776 (63)
Hospital-based clinic	117 (38)	81 (27)	133 (44)	175 (57)	506 (41)
Nursing home	0	5 (2)	15 (5)	8 (3)	28 (2)
Other	3 (1)	3 (1)	4 (1)	4 (1)	14 (1)
No answer	3 (1)	2 (1)	4 (1)	3 (1)	12 (1)

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-2. Physician Prescribing Practices by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
In the past 6 months, for how many patients have you prescribed Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q1)					
1 to 10	152 (49)	73 (24)	115 (38)	147 (48)	487 (40)
11 to 20	89 (29)	107 (35)	104 (34)	92 (30)	392 (32)
21 or more	54 (17)	123 (40)	81 (27)	62 (20)	320 (26)
I have not prescribed Xarelto for this indication	15 (5)	1 (<.5)	4 (1)	7 (2)	27 (2)
In the past 6 months, for how many patients have you prescribed Xarelto for deep vein thrombosis treatment and secondary prevention? (Q2)					
1 to 10	163 (53)	151 (50)	151 (50)	156 (51)	621 (51)
11 to 20	49 (16)	80 (26)	75 (25)	43 (14)	247 (20)
21 or more	38 (12)	54 (18)	50 (16)	31 (10)	173 (14)
I have not prescribed Xarelto for this indication	60 (19)	19 (6)	28 (9)	78 (25)	185 (15)
When did you write your most recent prescription for Xarelto for either of these indications? (Q3) (Tick one)					
Less than 1 month ago	240 (77)	255 (84)	255 (84)	223 (72)	973 (79)
1 to 3 months ago	54 (17)	37 (12)	37 (12)	72 (23)	200 (16)
4 to 6 months ago	10 (3)	10 (3)	8 (3)	9 (3)	37 (3)
I don't know	6 (2)	2 (1)	3 (1)	4 (1)	15 (1)
No answer	0 (0)	0 (0)	1 (<.5)	0 (0)	1 (<.5)

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-2. Physician Prescribing Practices by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
Which of the following Xarelto treatment activities are you responsible for? (Q4) (Tick all that apply)					
I initiate Xarelto treatment or convert treatment from or to Xarelto	250 (81)	287 (94)	271 (89)	266 (86)	1074 (88)
I write follow up (maintenance) prescriptions for Xarelto	239 (77)	228 (75)	216 (71)	174 (56)	857 (70)

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
What is the most important risk associated with taking Xarelto? (Q5) (Tick one)					
Neoplasia	2 (1)	3 (1)	3 (1)	7 (2)	15 (1)
Hypertension	1 (<.5)	3 (1)	4 (1)	7 (2)	15 (1)
Risk of bleeding*	303 (98) (95 - 99)	290 (95) (92 - 97)	283 (93) (90 - 96)	280 (91) (87 - 94)	1156 (94) (93 - 96)
Immunosuppression	0 (0)	2 (1)	3 (1)	1 (<.5)	6 (<.5)
I don't know	4 (1)	6 (2)	11 (4)	13 (4)	34 (3)
Which of the following populations are at an increased risk of experiencing serious side effect(s) associated with Xarelto? (Q6) Patients with moderate or severe renal impairment					
Yes, at higher risk*	248 (80) (75 - 84)	243 (80) (75 - 84)	234 (77) (72 - 82)	246 (80) (75 - 84)	971 (79) (77 - 81)
No, not at higher risk	31 (10)	48 (16)	55 (18)	46 (15)	180 (15)
I don't know	29 (9)	13 (4)	12 (4)	13 (4)	67 (5)
No answer	2 (1)	0 (0)	3 (1)	3 (1)	8 (1)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
Patients taking products that affect hemostasis such as NSAIDS, acetylsalicylic acid, platelet aggregation inhibitors					
Yes, at higher risk*	281 (91) (87 - 94)	278 (91) (88 - 94)	266 (88) (83 - 91)	262 (85) (81 - 89)	1087 (89) (87 - 90)
No, not at higher risk	16 (5)	20 (7)	27 (9)	39 (13)	102 (8)
I don't know	13 (4)	6 (2)	7 (2)	4 (1)	30 (2)
No answer	0 (0)	0 (0)	4 (1)	3 (1)	7 (1)
Patients at risk of bleeding					
Yes, at higher risk*	299 (96) (94 - 98)	294 (97) (94 - 98)	277 (91) (87 - 94)	282 (92) (88 - 94)	1152 (94) (92 - 95)
No, not at higher risk	9 (3)	7 (2)	17 (6)	20 (6)	53 (4)
I don't know	1 (<.5)	2 (1)	7 (2)	3 (1)	13 (1)
No answer	1 (<.5)	1 (<.5)	3 (1)	3 (1)	8 (1)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
Patients with chronic constipation					
Yes, at higher risk	30 (10)	21 (7)	16 (5)	21 (7)	88 (7)
No, not at higher risk*	174 (56) (50 - 62)	241 (79) (74 - 84)	220 (72) (67 - 77)	206 (67) (61 - 72)	841 (69) (66 - 71)
I don't know	103 (33)	41 (13)	64 (21)	78 (25)	286 (23)
No answer	3 (1)	1 (<.5)	4 (1)	3 (1)	11 (1)
To which patient groups is Xarelto contraindicated? (Q7) (Tick all that apply)					
Patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child-Pugh class B and C*	252 (81)	257 (85)	258 (85)	263 (85)	1030 (84)
Patients who are pregnant or breastfeeding*	252 (81)	248 (82)	261 (86)	259 (84)	1020 (83)
Patients receiving concomitant treatment with any other anticoagulant such as unfractionated heparin (UFH), low molecular weight heparins, heparin derivatives or oral anticoagulants except when switching therapy to or from Xarelto or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter*	219 (71)	213 (70)	244 (80)	222 (72)	898 (73)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
To which patient groups is Xarelto contraindicated? (Q7) (Tick all that apply)					
Patients with clinically significant active bleeding*	291 (94)	279 (92)	276 (91)	286 (93)	1132 (92)
I don't know	10 (3)	5 (2)	6 (2)	6 (2)	27 (2)
No answer	0 (0)	0 (0)	2 (1)	2 (1)	4 (<.5)
Selected all four of the correct responses	176 (57) (51 - 62)	167 (55) (49 - 61)	198 (65) (59 - 70)	190 (62) (56 - 67)	731 (60) (57 - 62)
Selected at least three of the four correct responses	254 (82) (77 - 86)	247 (81) (76 - 85)	259 (85) (81 - 89)	260 (84) (80 - 88)	1020 (83) (81 - 85)
Selected at least two of the four correct responses	284 (92) (88 - 94)	284 (93) (90 - 96)	286 (94) (91 - 96)	280 (91) (87 - 94)	1134 (92) (91 - 94)
Selected at least one of the four correct responses	300 (97) (94 - 98)	299 (98) (96 - 99)	296 (97) (95 - 99)	300 (97) (95 - 99)	1195 (97) (96 - 98)
Xarelto (15 or 20 mg) must be taken….? (Q8) (Tick one)					
On an empty stomach	22 (7)	50 (16)	39 (13)	66 (21)	177 (14)
With food on a full stomach*	149 (48) (42 - 54)	209 (69) (63 - 74)	206 (68) (62 - 73)	190 (62) (56 - 67)	754 (62) (59 - 64)
I don't know	139 (45)	45 (15)	56 (18)	50 (16)	290 (24)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
Xarelto (15 or 20 mg) must be taken….? (Q8) (Tick one)					
No answer	0 (0)	0 (0)	3 (1)	2 (1)	5 (<.5)
Is routine coagulation monitoring required for patients taking Xarelto for these indications? (Q9)					
Yes	9 (3)	9 (3)	12 (4)	20 (6)	50 (4)
No*	300 (97) (94 - 98)	293 (96) (94 - 98)	287 (94) (91 - 97)	281 (91) (88 - 94)	1161 (95) (93 - 96)
I don't know	1 (<.5)	2 (1)	2 (1)	3 (1)	8 (1)
No answer	0 (0)	0 (0)	3 (1)	4 (1)	7 (1)
In which of the following situations is INR monitoring needed? (Q10) (Tick all that apply)					
When converting from vitamin K antagonist (VKA) (e.g., warfarin) to Xarelto*	194 (63)	200 (66)	162 (53)	151 (49)	707 (58)
When converting from Xarelto to VKA*	229 (74)	246 (81)	260 (86)	198 (64)	933 (76)
Continual INR monitoring is required for all patients taking Xarelto	6 (2)	10 (3)	11 (4)	18 (6)	45 (4)
I don't know	17 (5)	4 (1)	0 (0)	11 (4)	32 (3)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
In which of the following situations is INR monitoring needed? (Q10) (Tick all that apply)					
No answer	0 (0)	0 (0)	3 (1)	2 (1)	5 (<.5)
Selected both of the correct responses	132 (43) (37 - 48)	151 (50) (44 - 55)	122 (40) (35 - 46)	69 (22) (18 - 27)	474 (39) (36 - 41)
Selected at least one of the two correct responses	291 (94) (91 - 96)	295 (97) (94 - 99)	300 (99) (97 - 100)	280 (91) (87 - 94)	1166 (95) (94 - 96)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)					
Stop VKA without measuring INR	22 (7)	56 (18)	74 (24)	44 (14)	196 (16)
For patients treated for prevention of stroke and systemic embolism, stop VKA and initiate Xarelto when INR is ≤ 3*	161 (52)	150 (49)	154 (51)	177 (57)	642 (52)
For patients treated for deep vein thrombosis and secondary prevention, stop VKA and initiate Xarelto when INR is ≤ 2.5*	201 (65)	221 (73)	202 (66)	182 (59)	806 (66)
I don't know	51 (16)	13 (4)	15 (5)	20 (6)	99 (8)
No answer	0 (0)	0 (0)	3 (1)	2 (1)	5 (<.5)
Selected both of the correct responses	119 (38) (33 - 44)	123 (40) (35 - 46)	117 (38) (33 - 44)	109 (35) (30 - 41)	468 (38) (35 - 41)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)					
Selected at least one of the two correct responses	243 (78) (73 - 83)	248 (82) (77 - 86)	239 (79) (74 - 83)	250 (81) (76 - 85)	980 (80) (78 - 82)
Which of the following steps should be taken when converting patients from Xarelto to VKA (e.g., warfarin)? (Q12) (Tick all that apply)					
Overlap the two drugs until INR is ≥ 2.0*	207 (67)	188 (62)	206 (68)	157 (51)	758 (62)
Measure INR but make sure it has been longer than 24 hours since the last dose of Xarelto*	71 (23)	139 (46)	109 (36)	126 (41)	445 (36)
Stop Xarelto at any time	13 (4)	21 (7)	23 (8)	29 (9)	86 (7)
Measure INR at any time of the day	10 (3)	23 (8)	16 (5)	6 (2)	55 (4)
I don't know	58 (19)	19 (6)	13 (4)	23 (7)	113 (9)
No answer	0 (0)	0 (0)	3 (1)	2 (1)	5 (<.5)
Selected both of the correct responses	36 (12) (8 - 16)	58 (19) (15 - 24)	44 (14) (11 - 19)	22 (7) (5 - 11)	160 (13) (11 - 15)
Selected at least one of the two correct responses	242 (78) (73 - 83)	269 (88) (84 - 92)	271 (89) (85 - 92)	261 (85) (80 - 89)	1043 (85) (83 - 87)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
Which of the following are true when converting from parenteral anticoagulants to Xarelto…? (Q13) (Tick all that apply)					
Stop parenteral anticoagulants for a week prior to starting Xarelto	8 (3)	9 (3)	10 (3)	7 (2)	34 (3)
For patients with continuously administered parenteral anticoagulants such as intravenous unfractionated heparin, Xarelto should be started at time of drug discontinuation*	125 (40)	168 (55)	173 (57)	157 (51)	623 (51)
For patients with parenteral drug on a fixed dosing scheme such as low molecular weight heparin (LMWH), Xarelto should be started 0 to 2 hours before the next scheduled drug administration*	127 (41)	174 (57)	175 (58)	183 (59)	659 (54)
I don't know	116 (37)	32 (11)	38 (13)	31 (10)	217 (18)
No answer	1 (<.5)	0 (0)	4 (1)	2 (1)	7 (1)
Selected both of the correct responses	63 (20) (16 - 25)	75 (25) (20 - 30)	90 (30) (25 - 35)	67 (22) (17 - 27)	295 (24) (22 - 27)
Selected at least one of the two correct responses	189 (61) (55 - 66)	267 (88) (84 - 91)	258 (85) (80 - 89)	273 (89) (85 - 92)	987 (81) (78 - 83)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
If an invasive procedure or surgical intervention is required, when should treatment with Xarelto (15 to 20 mg) be suspended (if possible, based upon clinical judgement of physician)? (Q14) (Tick one)					
One week prior to the procedure or surgical intervention	23 (7)	14 (5)	54 (18)	25 (8)	116 (9)
At least 24 hours prior to the procedure or surgical intervention*	236 (76) (71 - 81)	275 (90) (87 - 94)	211 (69) (64 - 75)	254 (82) (78 - 87)	976 (80) (77 - 82)
It is not necessary to stop Xarelto for these procedures	6 (2)	11 (4)	18 (6)	21 (7)	56 (5)
I don't know	44 (14)	4 (1)	18 (6)	6 (2)	72 (6)
No answer	1 (<.5)	0 (0)	3 (1)	2 (1)	6 (<.5)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)					
Provide symptomatic treatment (e.g., mechanical compression, surgery)*	233 (75)	257 (85)	221 (73)	216 (70)	927 (76)
Delay the next administration of Xarelto or discontinue Xarelto as appropriate*	226 (73)	252 (83)	221 (73)	232 (75)	931 (76)
Provide hemodynamic support (e.g., blood transfusion)*	228 (74)	222 (73)	201 (66)	220 (71)	871 (71)
Administer procoagulant reversal agent (for life-threatening bleeding)*	160 (52)	212 (70)	159 (52)	198 (64)	729 (59)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)					
Refer the patient to emergency care*	272 (88)	251 (83)	247 (81)	223 (72)	993 (81)
None of the above	0 (0)	1 (<.5)	2 (1)	2 (1)	5 (<.5)
I don't know	2 (1)	2 (1)	5 (2)	8 (3)	17 (1)
No answer	2 (1)	0 (0)	3 (1)	3 (1)	8 (1)
Selected all five of the correct responses	124 (40) (35 - 46)	154 (51) (45 - 56)	108 (36) (30 - 41)	131 (43) (37 - 48)	517 (42) (39 - 45)
Selected at least four of the five correct responses	200 (65) (59 - 70)	215 (71) (65 - 76)	171 (56) (50 - 62)	196 (64) (58 - 69)	782 (64) (61 - 66)
Selected at least three of the five correct responses	233 (75) (70 - 80)	249 (82) (77 - 86)	223 (73) (68 - 78)	223 (72) (67 - 77)	928 (76) (73 - 78)
Selected at least two of the five correct responses	256 (83) (78 - 87)	275 (90) (87 - 94)	253 (83) (79 - 87)	244 (79) (74 - 84)	1028 (84) (82 - 86)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)					
Selected at least one of the five correct responses	306 (99) (97 - 100)	301 (99) (97 - 100)	294 (97) (94 - 98)	295 (96) (93 - 98)	1196 (98) (97 - 98)
What is the standard recommended dose of Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q16) (Tick one)					
20 mg taken once a day*	221 (75) (70 - 80)	249 (82) (77 - 86)	217 (72) (67 - 77)	208 (69) (64 - 74)	895 (75) (72 - 77)
15 mg taken once a day	38 (13)	28 (9)	36 (12)	40 (13)	142 (12)
10 mg taken once a day	15 (5)	16 (5)	37 (12)	38 (13)	106 (9)
None of the above	1 (<.5)	7 (2)	5 (2)	10 (3)	23 (2)
I don't know	18 (6)	3 (1)	2 (1)	2 (1)	25 (2)
No answer	2 (1)	0 (0)	3 (1)	3 (1)	8 (1)
Not applicable skip pattern - Q1 (Have not prescribed Xarelto for this indication)	15	1	4	7	27

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
What is the recommended dose for patients with moderate or severe renal impairment (creatinine clearance of 15-49 mL/min) receiving Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q17) (Tick one)					
20 mg taken once a day	11 (4)	4 (1)	22 (7)	12 (4)	49 (4)
15 mg taken once a day*	164 (56) (50 - 61)	211 (70) (64 - 75)	153 (51) (45 - 57)	172 (57) (51 - 63)	700 (58) (56 - 61)
10 mg taken once a day	66 (22)	73 (24)	90 (30)	93 (31)	322 (27)
None of the above	7 (2)	10 (3)	22 (7)	13 (4)	52 (4)
I don't know	44 (15)	5 (2)	10 (3)	8 (3)	67 (6)
No answer	3 (1)	0 (0)	3 (1)	3 (1)	9 (1)
Not applicable skip pattern - Q1 (Have not prescribed Xarelto for this indication)	15	1	4	7	27
What is the standard recommended dose for patients receiving Xarelto for deep vein thrombosis treatment and secondary prevention? (Q18) (Tick one)					
20 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day	36 (14)	59 (21)	56 (20)	47 (20)	198 (19)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-3. Knowledge Questions by Country and Overall

Question	UK N=310 n (%) (95% CI)	Germany N=304 n (%) (95% CI)	France N=304 n (%) (95% CI)	Spain N=308 n (%) (95% CI)	Overall N=1226 n (%) (95% CI)
What is the standard recommended dose for patients receiving Xarelto for deep vein thrombosis treatment and secondary prevention? (Q18) (Tick one)					
15 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day*	168 (67) (61 - 73)	182 (64) (58 - 69)	172 (62) (56 - 68)	122 (53) (46 - 60)	644 (62) (59 - 65)
10 mg once a day	18 (7)	29 (10)	33 (12)	40 (17)	120 (12)
None of the above	1 (<.5)	4 (1)	5 (2)	11 (5)	21 (2)
I don't know	25 (10)	9 (3)	7 (3)	7 (3)	48 (5)
No answer	2 (1)	2 (1)	3 (1)	3 (1)	10 (1)
Not applicable skip pattern - Q2 (Have not prescribed Xarelto for this indication)	60	19	28	78	185

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: Exact 95% Confidence Intervals (95% CI) for the proportion of correct responses (denoted by asterisks) for select questionnaire items were computed using the Clopper-Pearson method.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-4. Sources of Information About Xarelto by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
Which of the following sources of information about Xarelto did you receive? (Q19) (Tick all that apply)					
Xarelto Prescriber Guide	100 (32)	222 (73)	179 (59)	200 (65)	701 (57)
Briefing from a company representative	124 (40)	222 (73)	205 (67)	177 (57)	728 (59)
Discussion with a clinical expert	59 (19)	82 (27)	63 (21)	95 (31)	299 (24)
The Summary of Product Characteristics for Xarelto	120 (39)	258 (85)	164 (54)	172 (56)	714 (58)
Clinical trials published in the medical literature	69 (22)	176 (58)	87 (29)	137 (44)	469 (38)
Other	26 (8)	23 (8)	22 (7)	18 (6)	89 (7)
None of the above	51 (16)	7 (2)	14 (5)	9 (3)	81 (7)
No answer	3 (1)	2 (1)	4 (1)	3 (1)	12 (1)

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-5. Ratings of Sources of Information About Xarelto by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
How helpful were these sources to you in treating and educating your patients? (Q20)					
Xarelto Prescriber Guide					
Not at all helpful	0 (0)	0 (0)	1 (1)	0 (0)	1 (<.5)
Slightly helpful	8 (8)	0 (0)	10 (6)	2 (1)	20 (3)
Somewhat helpful	13 (13)	49 (22)	24 (13)	31 (16)	117 (17)
Very helpful	57 (57)	135 (61)	114 (64)	127 (64)	433 (62)
Extremely helpful	22 (22)	38 (17)	30 (17)	40 (20)	130 (19)
Not applicable skip pattern (Q19 item was not ticked)	210	82	125	108	525
Briefing from a company representative					
Not at all helpful	0 (0)	1 (<.5)	2 (1)	2 (1)	5 (1)
Slightly helpful	9 (7)	8 (4)	5 (2)	14 (8)	36 (5)
Somewhat helpful	42 (34)	47 (21)	43 (21)	51 (29)	183 (25)
Very helpful	61 (49)	111 (50)	113 (55)	91 (51)	376 (52)
Extremely helpful	12 (10)	55 (25)	42 (20)	19 (11)	128 (18)
Not applicable skip pattern (Q19 item was not ticked)	186	82	99	131	498

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-5. Ratings of Sources of Information About Xarelto by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
Discussion with a clinical expert					
Not at all helpful	0 (0)	1 (1)	0 (0)	0 (0)	1 (<.5)
Slightly helpful	1 (2)	0 (0)	1 (2)	1 (1)	3 (1)
Somewhat helpful	14 (24)	14 (17)	13 (21)	18 (19)	59 (20)
Very helpful	32 (54)	38 (46)	30 (48)	54 (57)	154 (52)
Extremely helpful	12 (20)	29 (35)	19 (30)	22 (23)	82 (27)
Not applicable skip pattern (Q19 item was not ticked)	251	222	241	213	927
Summary of Product Characteristics					
Not at all helpful	1 (1)	1 (<.5)	2 (1)	0 (0)	4 (1)
Slightly helpful	1 (1)	3 (1)	3 (2)	5 (3)	12 (2)
Somewhat helpful	41 (34)	40 (16)	36 (22)	42 (24)	159 (22)
Very helpful	62 (52)	138 (53)	93 (57)	107 (62)	400 (56)
Extremely helpful	15 (13)	76 (29)	30 (18)	18 (10)	139 (19)
Not applicable skip pattern (Q19 item was not ticked)	190	46	140	136	512

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-5. Ratings of Sources of Information About Xarelto by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
Medical Publications					
Not at all helpful	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Slightly helpful	3 (4)	2 (1)	1 (1)	0 (0)	6 (1)
Somewhat helpful	14 (20)	32 (18)	12 (14)	17 (12)	75 (16)
Very helpful	42 (61)	98 (56)	46 (53)	83 (61)	269 (57)
Extremely helpful	10 (14)	44 (25)	28 (32)	37 (27)	119 (25)
Not applicable skip pattern (Q19 item was not ticked)	241	128	217	171	757
Other					
Not at all helpful	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Slightly helpful	2 (8)	2 (9)	1 (5)	1 (6)	6 (7)
Somewhat helpful	7 (27)	6 (26)	4 (18)	10 (56)	27 (30)
Very helpful	14 (54)	11 (48)	9 (41)	7 (39)	41 (46)
Extremely helpful	3 (12)	4 (17)	8 (36)	0 (0)	15 (17)
Not applicable skip pattern (Q19 item was not ticked)	284	281	282	290	1137

PPD Project 0304565

Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment

Table A-6. Physician's Experiences with Information Contained in the Patient Alert Cards by Country and Overall

Question	UK N=310 n (%)	Germany N=304 n (%)	France N=304 n (%)	Spain N=308 n (%)	Overall N=1226 n (%)
When would you discuss the information on the Patient Alert Card with your patients taking Xarelto? The Patient Alert Card is part of the Xarelto product packaging and explains the need for treatment compliance, taking medication with food, signs and symptoms of bleeding, and when to seek medical attention. (Q23) (Tick all that apply)					
When first prescribing Xarelto	267 (86)	281 (92)	240 (79)	258 (84)	1046 (85)
When a patient is facing an invasive procedure or surgical intervention	93 (30)	123 (40)	106 (35)	95 (31)	417 (34)
When a patient has bleeding complications	84 (27)	118 (39)	84 (28)	91 (30)	377 (31)
When a patient has a Xarelto related adverse event	96 (31)	102 (34)	82 (27)	88 (29)	368 (30)
Other	14 (5)	10 (3)	20 (7)	13 (4)	57 (5)
No answer	4 (1)	2 (1)	4 (1)	3 (1)	13 (1)

Annex 4. Results Tables, by Other Stratifications

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
What is the most important risk associated with taking Xarelto? (Q5) (Tick one)						
Neoplasia	7 (1)	0 (0)	1 (1)	1 (2)	6 (9)	0 (0)
Hypertension	6 (1)	1 (1)	3 (2)	0 (0)	4 (6)	1 (1)
Risk of bleeding*	656 (95)	110 (98)	175 (96)	51 (93)	50 (77)	103 (96)
Immunosuppression	3 (<.5)	0 (0)	1 (1)	2 (4)	0 (0)	0 (0)
I don't know	21 (3)	1 (1)	2 (1)	1 (2)	5 (8)	3 (3)
Which of the following populations are at an increased risk of experiencing serious side effect(s) associated with Xarelto? (Q6) Patients with moderate or severe renal impairment						
Yes, at higher risk*	540 (78)	90 (80)	164 (90)	47 (85)	42 (65)	80 (75)
No, not at higher risk	109 (16)	14 (13)	17 (9)	5 (9)	15 (23)	20 (19)
I don't know	44 (6)	7 (6)	1 (1)	2 (4)	7 (11)	6 (6)
No answer	0 (0)	1 (1)	0 (0)	1 (2)	1 (2)	1 (1)
Patients taking products that affect hemostasis such as NSAIDS, acetylsalicylic acid, platelet aggregation inhibitors						
Yes, at higher risk*	622 (90)	101 (90)	168 (92)	47 (85)	53 (82)	88 (82)
No, not at higher risk	53 (8)	5 (4)	11 (6)	8 (15)	11 (17)	14 (13)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
Patients taking products that affect hemostasis such as NSAIDS, acetylsalicylic acid, platelet aggregation inhibitors						
I don't know	16 (2)	5 (4)	3 (2)	0 (0)	1 (2)	5 (5)
No answer	2 (<.5)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
Patients at risk of bleeding						
Yes, at higher risk*	648 (94)	107 (96)	177 (97)	51 (93)	60 (92)	101 (94)
No, not at higher risk	33 (5)	4 (4)	3 (2)	4 (7)	4 (6)	5 (5)
I don't know	11 (2)	0 (0)	2 (1)	0 (0)	0 (0)	0 (0)
No answer	1 (<.5)	1 (1)	0 (0)	0 (0)	1 (2)	1 (1)
Patients with chronic constipation						
Yes, at higher risk	46 (7)	6 (5)	13 (7)	7 (13)	12 (18)	3 (3)
No, not at higher risk*	464 (67)	89 (79)	135 (74)	33 (60)	35 (54)	79 (74)
I don't know	181 (26)	16 (14)	34 (19)	14 (25)	16 (25)	24 (22)
No answer	2 (<.5)	1 (1)	0 (0)	1 (2)	2 (3)	1 (1)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
To which patient groups is Xarelto contraindicated? (Q7) (Tick all that apply)						
Patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child-Pugh class B and C*	580 (84)	98 (88)	162 (89)	47 (85)	48 (74)	90 (84)
Patients who are pregnant or breastfeeding*	582 (84)	84 (75)	166 (91)	50 (91)	45 (69)	88 (82)
Patients receiving concomitant treatment with any other anticoagulant such as unfractionated heparin (UFH), low molecular weight heparins, heparin derivatives or oral anticoagulants except when switching therapy to or from Xarelto or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter*	487 (70)	93 (83)	145 (80)	43 (78)	45 (69)	80 (75)
Patients with clinically significant active bleeding*	635 (92)	106 (95)	173 (95)	50 (91)	59 (91)	102 (95)
I don't know	18 (3)	0 (0)	1 (1)	2 (4)	2 (3)	3 (3)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
To which patient groups is Xarelto contraindicated? (Q7) (Tick all that apply)						
Selected all four of the correct responses	391 (56)	70 (63)	130 (71)	39 (71)	36 (55)	61 (57)
Selected at least three of the four correct responses	572 (83)	93 (83)	162 (89)	47 (85)	46 (71)	95 (89)
Selected at least two of the four correct responses	646 (93)	106 (95)	173 (95)	51 (93)	52 (80)	100 (93)
Selected at least one of the four correct responses	675 (97)	112 (100)	181 (99)	53 (96)	63 (97)	104 (97)
Xarelto (15 or 20 mg) must be taken….? (Q8) (Tick one)						
On an empty stomach	108 (16)	14 (13)	26 (14)	8 (15)	7 (11)	13 (12)
With food on a full stomach*	398 (57)	74 (66)	134 (74)	37 (67)	34 (52)	72 (67)
I don't know	187 (27)	24 (21)	22 (12)	10 (18)	24 (37)	22 (21)
Is routine coagulation monitoring required for patients taking Xarelto for these indications? (Q9)						
Yes	20 (3)	2 (2)	8 (4)	4 (7)	10 (15)	4 (4)
No*	669 (97)	109 (97)	174 (96)	50 (91)	52 (80)	102 (95)
I don't know	3 (<.5)	1 (1)	0 (0)	0 (0)	3 (5)	1 (1)
No answer	1 (<.5)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
In which of the following situations is INR monitoring needed? (Q10) (Tick all that apply)						
When converting from vitamin K antagonist (VKA) (e.g., warfarin) to Xarelto*	398 (57)	65 (58)	123 (68)	40 (73)	34 (52)	44 (41)
When converting from Xarelto to VKA*	534 (77)	92 (82)	133 (73)	39 (71)	42 (65)	88 (82)
Continual INR monitoring is required for all patients taking Xarelto	24 (3)	3 (3)	4 (2)	4 (7)	5 (8)	4 (4)
I don't know	18 (3)	0 (0)	1 (1)	0 (0)	9 (14)	3 (3)
Selected both of the correct responses	269 (39)	46 (41)	77 (42)	26 (47)	23 (35)	31 (29)
Selected at least one of the two correct responses	663 (96)	111 (99)	179 (98)	53 (96)	53 (82)	101 (94)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)						
Stop VKA without measuring INR	115 (17)	18 (16)	18 (10)	5 (9)	7 (11)	31 (29)
For patients treated for prevention of stroke and systemic embolism, stop VKA and initiate Xarelto when INR is ≤ 3*	361 (52)	58 (52)	102 (56)	33 (60)	33 (51)	50 (47)
For patients treated for deep vein thrombosis and secondary prevention, stop VKA and initiate Xarelto when INR is ≤ 2.5*	458 (66)	64 (57)	135 (74)	42 (76)	35 (54)	68 (64)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)						
I don't know	65 (9)	11 (10)	5 (3)	3 (5)	10 (15)	5 (5)
Selected both of the correct responses	274 (40)	36 (32)	70 (38)	27 (49)	20 (31)	38 (36)
Selected at least one of the two correct responses	545 (79)	86 (77)	167 (92)	48 (87)	48 (74)	80 (75)
Which of the following steps should be taken when converting patients from Xarelto to VKA (e.g., warfarin)? (Q12) (Tick all that apply)						
Overlap the two drugs until INR is ≥ 2.0*	419 (60)	71 (63)	123 (68)	40 (73)	37 (57)	66 (62)
Measure INR but make sure it has been longer than 24 hours since the last dose of Xarelto*	236 (34)	46 (41)	69 (38)	24 (44)	23 (35)	44 (41)
Stop Xarelto at any time	50 (7)	4 (4)	16 (9)	1 (2)	6 (9)	8 (7)
Measure INR at any time of the day	38 (5)	1 (1)	6 (3)	2 (4)	3 (5)	4 (4)
I don't know	81 (12)	10 (9)	4 (2)	0 (0)	10 (15)	7 (7)
Selected both of the correct responses	85 (12)	18 (16)	24 (13)	9 (16)	8 (12)	16 (15)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
Which of the following steps should be taken when converting patients from Xarelto to VKA (e.g., warfarin)? (Q12) (Tick all that apply)						
Selected at least one of the two correct responses	570 (82)	99 (88)	168 (92)	55 (100)	52 (80)	94 (88)
Which of the following are true when converting from parenteral anticoagulants to Xarelto…? (Q13) (Tick all that apply)						
Stop parenteral anticoagulants for a week prior to starting Xarelto	18 (3)	2 (2)	5 (3)	2 (4)	3 (5)	4 (4)
For patients with continuously administered parenteral anticoagulants such as intravenous unfractionated heparin, Xarelto should be started at time of drug discontinuation*	331 (48)	67 (60)	104 (57)	31 (56)	27 (42)	59 (55)
For patients with parenteral drug on a fixed dosing scheme such as low molecular weight heparin (LMWH), Xarelto should be started 0 to 2 hours before the next scheduled drug administration*	325 (47)	65 (58)	129 (71)	41 (75)	34 (52)	61 (57)
I don't know	163 (24)	12 (11)	12 (7)	2 (4)	17 (26)	10 (9)
No answer	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)
Selected both of the correct responses	135 (19)	32 (29)	65 (36)	19 (35)	14 (22)	27 (25)
Selected at least one of the two correct responses	521 (75)	100 (89)	168 (92)	53 (96)	47 (72)	93 (87)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
If an invasive procedure or surgical intervention is required, when should treatment with Xarelto (15 to 20 mg) be suspended (if possible, based upon clinical judgement of physician)? (Q14) (Tick one)						
One week prior to the procedure or surgical intervention	61 (9)	13 (12)	10 (5)	6 (11)	8 (12)	18 (17)
At least 24 hours prior to the procedure or surgical intervention*	533 (77)	94 (84)	164 (90)	47 (85)	50 (77)	83 (78)
It is not necessary to stop Xarelto for these procedures	43 (6)	2 (2)	5 (3)	1 (2)	2 (3)	2 (2)
I don't know	56 (8)	3 (3)	3 (2)	1 (2)	5 (8)	4 (4)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)						
Provide symptomatic treatment (e.g., mechanical compression, surgery)*	482 (70)	94 (84)	163 (90)	48 (87)	49 (75)	87 (81)
Delay the next administration of Xarelto or discontinue Xarelto as appropriate*	483 (70)	92 (82)	168 (92)	47 (85)	51 (78)	87 (81)
Provide hemodynamic support (e.g., blood transfusion)*	437 (63)	88 (79)	159 (87)	49 (89)	49 (75)	86 (80)
Administer procoagulant reversal agent (for life-threatening bleeding)*	362 (52)	77 (69)	134 (74)	45 (82)	35 (54)	75 (70)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)						
Refer the patient to emergency care*	587 (85)	87 (78)	140 (77)	41 (75)	50 (77)	84 (79)
None of the above	4 (1)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)
I don't know	7 (1)	1 (1)	1 (1)	0 (0)	3 (5)	5 (5)
Selected all five of the correct responses	243 (35)	57 (51)	107 (59)	33 (60)	27 (42)	50 (47)
Selected at least four of the five correct responses	391 (56)	82 (73)	141 (77)	43 (78)	43 (66)	79 (74)
Selected at least three of the five correct responses	484 (70)	90 (80)	163 (90)	47 (85)	49 (75)	91 (85)
Selected at least two of the five correct responses	551 (80)	99 (88)	172 (95)	52 (95)	53 (82)	97 (91)
Selected at least one of the five correct responses	682 (98)	110 (98)	181 (99)	55 (100)	62 (95)	102 (95)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
What is the standard recommended dose of Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q16) (Tick one)						
20 mg taken once a day*	522 (76)	85 (77)	163 (90)	39 (75)	29 (51)	54 (57)
15 mg taken once a day	81 (12)	9 (8)	13 (7)	8 (15)	9 (16)	21 (22)
10 mg taken once a day	60 (9)	11 (10)	5 (3)	5 (10)	11 (19)	14 (15)
None of the above	12 (2)	4 (4)	0 (0)	0 (0)	4 (7)	3 (3)
I don't know	16 (2)	1 (1)	1 (1)	0 (0)	4 (7)	3 (3)
Not applicable skip pattern - Q1 (Have not prescribed Xarelto for this indication)	2	2	0	3	8	12
What is the recommended dose for patients with moderate or severe renal impairment (creatinine clearance of 15-49 mL/min) receiving Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q17) (Tick one)						
20 mg taken once a day	27 (4)	4 (4)	5 (3)	2 (4)	6 (11)	5 (5)
15 mg taken once a day*	384 (56)	66 (60)	147 (81)	37 (71)	19 (33)	44 (46)
10 mg taken once a day	210 (30)	29 (26)	24 (13)	12 (23)	16 (28)	31 (33)
None of the above	25 (4)	7 (6)	4 (2)	1 (2)	8 (14)	7 (7)
I don't know	45 (7)	4 (4)	2 (1)	0 (0)	8 (14)	8 (8)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
What is the recommended dose for patients with moderate or severe renal impairment (creatinine clearance of 15-49 mL/min) receiving Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q17) (Tick one)						
Not applicable skip pattern - Q1 (Have not prescribed Xarelto for this indication)	2	2	0	3	8	12
What is the standard recommended dose for patients receiving Xarelto for deep vein thrombosis treatment and secondary prevention? (Q18) (Tick one)						
20 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day	118 (20)	11 (17)	26 (17)	12 (24)	14 (22)	17 (16)
15 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day*	366 (62)	33 (51)	115 (75)	32 (63)	33 (52)	64 (62)
10 mg once a day	67 (11)	13 (20)	7 (5)	7 (14)	9 (14)	17 (16)
None of the above	9 (2)	3 (5)	2 (1)	0 (0)	4 (6)	3 (3)
I don't know	32 (5)	5 (8)	4 (3)	0 (0)	4 (6)	3 (3)
No answer	1 (<.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Not applicable skip pattern - Q2 (Have not prescribed Xarelto for this indication)	100	47	28	4	1	3
Which of the following sources of information about Xarelto did you receive? (Q19) (Tick all that apply.)						
Xarelto Prescriber Guide	356 (51)	74 (66)	127 (70)	43 (78)	36 (55)	65 (61)
Briefing from a company representative	426 (61)	63 (56)	143 (79)	33 (60)	15 (23)	48 (45)
Discussion with a clinical expert	156 (23)	21 (19)	68 (37)	16 (29)	4 (6)	34 (32)

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-8. Knowledge Questions by Specialty

Question	General / Internal medicine N=693 n (%)	Neurology N=112 n (%)	Cardiology N=182 n (%)	Haema-tology N=55 n (%)	Oncology N=65 n (%)	Other[a] N=107 n (%)
The Summary of Product Characteristics for Xarelto	387 (56)	65 (58)	127 (70)	41 (75)	28 (43)	66 (62)
Clinical trials published in the medical literature	195 (28)	54 (48)	134 (74)	25 (45)	18 (28)	43 (40)
Other	59 (9)	3 (3)	11 (6)	1 (2)	2 (3)	13 (12)
None of the above	57 (8)	9 (8)	0 (0)	2 (4)	6 (9)	7 (7)

[a]Includes the following response categories: Accident & Emergency Medicine, Pulmonology, and Other.
Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 24 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
What is the most important risk associated with taking Xarelto? (Q5) (Tick one)		
Neoplasia	13 (1)	2 (1)
Hypertension	12 (1)	3 (2)
Risk of bleeding*	1018 (95)	138 (91)
Immunosuppression	6 (1)	0 (0)
I don't know	25 (2)	9 (6)
Which of the following populations are at an increased risk of experiencing serious side effect(s) associated with Xarelto? (Q6) Patients with moderate or severe renal impairment		
Yes, at higher risk*	855 (80)	116 (76)
No, not at higher risk	160 (15)	20 (13)
I don't know	51 (5)	16 (11)
No answer	8 (1)	0 (0)
Patients taking products that affect hemostasis such as NSAIDS, acetylsalicylic acid, platelet aggregation inhibitors		
Yes, at higher risk*	961 (89)	126 (83)
No, not at higher risk	84 (8)	18 (12)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
Patients taking products that affect hemostasis such as NSAIDS, acetylsalicylic acid, platelet aggregation inhibitors		
I don't know	22 (2)	8 (5)
No answer	7 (1)	0 (0)
Patients at risk of bleeding		
Yes, at higher risk*	1013 (94)	139 (91)
No, not at higher risk	43 (4)	10 (7)
I don't know	10 (1)	3 (2)
No answer	8 (1)	0 (0)
Patients with chronic constipation		
Yes, at higher risk	81 (8)	7 (5)
No, not at higher risk*	742 (69)	99 (65)
I don't know	240 (22)	46 (30)
No answer	11 (1)	0 (0)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
To which patient groups is Xarelto contraindicated? (Q7) (Tick all that apply)		
Patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child-Pugh class B and C*	902 (84)	128 (84)
Patients who are pregnant or breastfeeding*	897 (84)	123 (81)
Patients receiving concomitant treatment with any other anticoagulant such as unfractionated heparin (UFH), low molecular weight heparins, heparin derivatives or oral anticoagulants except when switching therapy to or from Xarelto or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter*	793 (74)	105 (69)
Patients with clinically significant active bleeding*	992 (92)	140 (92)
I don't know	21 (2)	6 (4)
No answer	4 (<.5)	0 (0)
Selected all four of the correct responses	640 (60)	91 (60)
Selected at least three of the four correct responses	899 (84)	121 (80)
Selected at least two of the four correct responses	996 (93)	138 (91)
Selected at least one of the four correct responses	1049 (98)	146 (96)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
Xarelto (15 or 20 mg) must be taken….? (Q8) (Tick one)		
On an empty stomach	159 (15)	18 (12)
With food on a full stomach*	682 (64)	72 (47)
I don't know	228 (21)	62 (41)
No answer	5 (<.5)	0 (0)
Is routine coagulation monitoring required for patients taking Xarelto for these indications? (Q9)		
Yes	43 (4)	7 (5)
No*	1019 (95)	142 (93)
I don't know	6 (1)	2 (1)
No answer	6 (1)	1 (1)
In which of the following situations is INR monitoring needed? (Q10) (Tick all that apply)		
When converting from vitamin K antagonist (VKA) (e.g., warfarin) to Xarelto*	637 (59)	70 (46)
When converting from Xarelto to VKA*	823 (77)	110 (72)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
In which of the following situations is INR monitoring needed? (Q10) (Tick all that apply)		
Continual INR monitoring is required for all patients taking Xarelto	37 (3)	8 (5)
I don't know	19 (2)	13 (9)
No answer	5 (<.5)	0 (0)
Selected both of the correct responses	427 (40)	47 (31)
Selected at least one of the two correct responses	1033 (96)	133 (88)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)		
Stop VKA without measuring INR	178 (17)	18 (12)
For patients treated for prevention of stroke and systemic embolism, stop VKA and initiate Xarelto when INR is ≤ 3*	572 (53)	70 (46)
For patients treated for deep vein thrombosis and secondary prevention, stop VKA and initiate Xarelto when INR is ≤ 2.5*	726 (68)	80 (53)
I don't know	62 (6)	37 (24)
No answer	5 (<.5)	0 (0)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)		
Selected both of the correct responses	417 (39)	51 (34)
Selected at least one of the two correct responses	881 (82)	99 (65)
Which of the following steps should be taken when converting patients from Xarelto to VKA (e.g., warfarin)? (Q12) (Tick all that apply)		
Overlap the two drugs until INR is ≥ 2.0*	670 (62)	88 (58)
Measure INR but make sure it has been longer than 24 hours since the last dose of Xarelto*	390 (36)	55 (36)
Stop Xarelto at any time	80 (7)	6 (4)
Measure INR at any time of the day	48 (4)	7 (5)
I don't know	85 (8)	28 (18)
No answer	5 (<.5)	0 (0)
Selected both of the correct responses	137 (13)	23 (15)
Selected at least one of the two correct responses	923 (86)	120 (79)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
Which of the following are true when converting from parenteral anticoagulants to Xarelto…? (Q13) (Tick all that apply)		
Stop parenteral anticoagulants for a week prior to starting Xarelto	31 (3)	3 (2)
For patients with continuously administered parenteral anticoagulants such as intravenous unfractionated heparin, Xarelto should be started at time of drug discontinuation*	576 (54)	47 (31)
For patients with parenteral drug on a fixed dosing scheme such as low molecular weight heparin (LMWH), Xarelto should be started 0 to 2 hours before the next scheduled drug administration*	604 (56)	55 (36)
I don't know	152 (14)	65 (43)
No answer	7 (1)	0 (0)
Selected both of the correct responses	278 (26)	17 (11)
Selected at least one of the two correct responses	902 (84)	85 (56)
If an invasive procedure or surgical intervention is required, when should treatment with Xarelto (15 to 20 mg) be suspended (if possible, based upon clinical judgement of physician)? (Q14) (Tick one)		
One week prior to the procedure or surgical intervention	98 (9)	18 (12)
At least 24 hours prior to the procedure or surgical intervention*	877 (82)	99 (65)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
If an invasive procedure or surgical intervention is required, when should treatment with Xarelto (15 to 20 mg) be suspended (if possible, based upon clinical judgement of physician)? (Q14) (Tick one)		
It is not necessary to stop Xarelto for these procedures	45 (4)	11 (7)
I don't know	48 (4)	24 (16)
No answer	6 (1)	0 (0)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)		
Provide symptomatic treatment (e.g., mechanical compression, surgery)*	824 (77)	103 (68)
Delay the next administration of Xarelto or discontinue Xarelto as appropriate*	829 (77)	102 (67)
Provide hemodynamic support (e.g., blood transfusion)*	777 (72)	94 (62)
Administer procoagulant reversal agent (for life-threatening bleeding)*	660 (61)	69 (45)
Refer the patient to emergency care*	869 (81)	124 (82)
None of the above	4 (<.5)	1 (1)
I don't know	12 (1)	5 (3)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)		
No answer	8 (1)	0 (0)
Selected all five of the correct responses	471 (44)	46 (30)
Selected at least four of the five correct responses	704 (66)	78 (51)
Selected at least three of the five correct responses	824 (77)	104 (68)
Selected at least two of the five correct responses	910 (85)	118 (78)
Selected at least one of the five correct responses	1050 (98)	146 (96)
What is the standard recommended dose of Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q16) (Tick one)		
20 mg taken once a day*	802 (76)	93 (62)
15 mg taken once a day	122 (12)	20 (13)
10 mg taken once a day	85 (8)	21 (14)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
What is the standard recommended dose of Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q16) (Tick one)		
None of the above	16 (2)	7 (5)
I don't know	16 (2)	9 (6)
No answer	8 (1)	0 (0)
Not applicable skip pattern - Q1 (Have not prescribed Xarelto for this indication)	25	2
What is the recommended dose for patients with moderate or severe renal impairment (creatinine clearance of 15-49 mL/min) receiving Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q17) (Tick one)		
20 mg taken once a day	43 (4)	6 (4)
15 mg taken once a day*	647 (62)	53 (35)
10 mg taken once a day	270 (26)	52 (35)
None of the above	40 (4)	12 (8)
I don't know	40 (4)	27 (18)
No answer	9 (1)	0 (0)
Not applicable skip pattern - Q1 (Have not prescribed Xarelto for this indication)	25	2

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-9. Knowledge Questions by Whether or not Physicians is Responsible for Initiating Rivaroxaban Treatment or Converting Treatment From or to Rivaroxaban

Question	Yes N=1074 n (%)	No N=152 n (%)
What is the standard recommended dose for patients receiving Xarelto for deep vein thrombosis treatment and secondary prevention? (Q18) (Tick one)		
20 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day	187 (20)	11 (11)
15 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day*	587 (62)	57 (56)
10 mg once a day	103 (11)	17 (17)
None of the above	16 (2)	5 (5)
I don't know	37 (4)	11 (11)
No answer	10 (1)	0 (0)
Not applicable skip pattern - Q2 (Have not prescribed Xarelto for this indication)	134	51

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
What is the most important risk associated with taking Xarelto? (Q5) (Tick one)		
Neoplasia	13 (2)	2 (<.5)
Hypertension	10 (1)	5 (1)
Risk of bleeding*	658 (94)	487 (95)
Immunosuppression	6 (1)	0 (0)
I don't know	14 (2)	19 (4)
Which of the following populations are at an increased risk of experiencing serious side effect(s) associated with Xarelto? (Q6) Patients with moderate or severe renal impairment		
Yes, at higher risk*	570 (81)	393 (77)
No, not at higher risk	99 (14)	81 (16)
I don't know	29 (4)	38 (7)
No answer	3 (<.5)	1 (<.5)
Patients taking products that affect hemostasis such as NSAIDS, acetylsalicylic acid, platelet aggregation inhibitors		
Yes, at higher risk*	627 (89)	452 (88)
No, not at higher risk	58 (8)	44 (9)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
Patients taking products that affect hemostasis such as NSAIDS, acetylsalicylic acid, platelet aggregation inhibitors		
I don't know	14 (2)	16 (3)
No answer	2 (<.5)	1 (<.5)
Patients at risk of bleeding		
Yes, at higher risk*	663 (95)	481 (94)
No, not at higher risk	30 (4)	23 (4)
I don't know	6 (1)	7 (1)
No answer	2 (<.5)	2 (<.5)
Patients with chronic constipation		
Yes, at higher risk	57 (8)	30 (6)
No, not at higher risk*	492 (70)	343 (67)
I don't know	148 (21)	137 (27)
No answer	4 (1)	3 (1)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
To which patient groups is Xarelto contraindicated? (Q7) (Tick all that apply)		
Patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child-Pugh class B and C*	612 (87)	413 (81)
Patients who are pregnant or breastfeeding*	598 (85)	417 (81)
Patients receiving concomitant treatment with any other anticoagulant such as unfractionated heparin (UFH), low molecular weight heparins, heparin derivatives or oral anticoagulants except when switching therapy to or from Xarelto or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter*	538 (77)	355 (69)
Patients with clinically significant active bleeding*	656 (94)	469 (91)
I don't know	10 (1)	16 (3)
Selected all four of the correct responses	447 (64)	280 (55)
Selected at least three of the four correct responses	604 (86)	411 (80)
Selected at least two of the four correct responses	662 (94)	466 (91)
Selected at least one of the four correct responses	691 (99)	497 (97)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
Xarelto (15 or 20 mg) must be taken….? (Q8) (Tick one)		
On an empty stomach	106 (15)	70 (14)
With food on a full stomach*	479 (68)	270 (53)
I don't know	116 (17)	173 (34)
Is routine coagulation monitoring required for patients taking Xarelto for these indications? (Q9)		
Yes	33 (5)	15 (3)
No*	661 (94)	495 (96)
I don't know	5 (1)	3 (1)
No answer	2 (<.5)	0 (0)
In which of the following situations is INR monitoring needed? (Q10) (Tick all that apply)		
When converting from vitamin K antagonist (VKA) (e.g., warfarin) to Xarelto*	427 (61)	277 (54)
When converting from Xarelto to VKA*	555 (79)	373 (73)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
In which of the following situations is INR monitoring needed? (Q10) (Tick all that apply)		
Continual INR monitoring is required for all patients taking Xarelto	28 (4)	16 (3)
I don't know	9 (1)	22 (4)
Selected both of the correct responses	302 (43)	170 (33)
Selected at least one of the two correct responses	680 (97)	480 (94)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)		
Stop VKA without measuring INR	104 (15)	90 (18)
For patients treated for prevention of stroke and systemic embolism, stop VKA and initiate Xarelto when INR is ≤ 3*	394 (56)	243 (47)
For patients treated for deep vein thrombosis and secondary prevention, stop VKA and initiate Xarelto when INR is ≤ 2.5*	500 (71)	302 (59)
I don't know	31 (4)	68 (13)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)		
Selected both of the correct responses	295 (42)	170 (33)
Selected at least one of the two correct responses	599 (85)	375 (73)
Which of the following steps should be taken when converting patients from Xarelto to VKA (e.g., warfarin)? (Q12) (Tick all that apply)		
Overlap the two drugs until INR is ≥ 2.0*	446 (64)	310 (60)
Measure INR but make sure it has been longer than 24 hours since the last dose of Xarelto*	289 (41)	153 (30)
Stop Xarelto at any time	48 (7)	37 (7)
Measure INR at any time of the day	34 (5)	20 (4)
I don't know	32 (5)	80 (16)
Selected both of the correct responses	101 (14)	59 (12)
Selected at least one of the two correct responses	634 (90)	404 (79)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
Which of the following are true when converting from parenteral anticoagulants to Xarelto…? (Q13) (Tick all that apply)		
Stop parenteral anticoagulants for a week prior to starting Xarelto	16 (2)	18 (4)
For patients with continuously administered parenteral anticoagulants such as intravenous unfractionated heparin, Xarelto should be started at time of drug discontinuation*	414 (59)	205 (40)
For patients with parenteral drug on a fixed dosing scheme such as low molecular weight heparin (LMWH), Xarelto should be started 0 to 2 hours before the next scheduled drug administration*	435 (62)	220 (43)
I don't know	62 (9)	154 (30)
No answer	1 (<.5)	0 (0)
Selected both of the correct responses	214 (31)	78 (15)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
Which of the following are true when converting from parenteral anticoagulants to Xarelto…? (Q13) (Tick all that apply)		
Selected at least one of the two correct responses	635 (91)	347 (68)
If an invasive procedure or surgical intervention is required, when should treatment with Xarelto (15 to 20 mg) be suspended (if possible, based upon clinical judgement of physician)? (Q14) (Tick one)		
One week prior to the procedure or surgical intervention	70 (10)	46 (9)
At least 24 hours prior to the procedure or surgical intervention*	580 (83)	391 (76)
It is not necessary to stop Xarelto for these procedures	28 (4)	27 (5)
I don't know	23 (3)	49 (10)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)		
Provide symptomatic treatment (e.g., mechanical compression, surgery)*	564 (80)	359 (70)
Delay the next administration of Xarelto or discontinue Xarelto as appropriate*	581 (83)	347 (68)
Provide hemodynamic support (e.g., blood transfusion)*	530 (76)	338 (66)
Administer procoagulant reversal agent (for life-threatening bleeding)*	475 (68)	253 (49)
Refer the patient to emergency care*	571 (81)	418 (81)
None of the above	2 (<.5)	3 (1)
I don't know	9 (1)	8 (2)

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)		
Selected all five of the correct responses	350 (50)	167 (33)
Selected at least four of the five correct responses	499 (71)	280 (55)
Selected at least three of the five correct responses	570 (81)	354 (69)
Selected at least two of the five correct responses	612 (87)	412 (80)
Selected at least one of the five correct responses	690 (98)	502 (98)
What is the standard recommended dose of Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q16) (Tick one)		
20 mg taken once a day*	534 (78)	358 (71)
15 mg taken once a day	74 (11)	67 (13)
10 mg taken once a day	57 (8)	49 (10)
None of the above	14 (2)	9 (2)
I don't know	7 (1)	18 (4)
Not applicable skip pattern - Q1 (Have not prescribed Xarelto for this indication)	15	12

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
What is the recommended dose for patients with moderate or severe renal impairment (creatinine clearance of 15-49 mL/min) receiving Xarelto for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation? (Q17) (Tick one)		
20 mg taken once a day	28 (4)	21 (4)
15 mg taken once a day*	451 (66)	246 (49)
10 mg taken once a day	160 (23)	162 (32)
None of the above	27 (4)	25 (5)
I don't know	20 (3)	47 (9)
Not applicable skip pattern - Q1 (Have not prescribed Xarelto for this indication)	15	12

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-10. Knowledge Questions by Whether or not Physicians Received Xarelto Prescriber Guide

Question	Yes N=701 n (%)	No N=513 n (%)
What is the standard recommended dose for patients receiving Xarelto for deep vein thrombosis treatment and secondary prevention? (Q18) (Tick one)		
20 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day	106 (18)	92 (22)
15 mg twice a day for the first three weeks of administration, followed by 20 mg taken once a day*	402 (67)	241 (56)
10 mg once a day	69 (11)	51 (12)
None of the above	11 (2)	10 (2)
I don't know	15 (2)	33 (8)
No answer	1 (<.5)	0 (0)
Not applicable skip pattern - Q2 (Have not prescribed Xarelto for this indication)	97	86

Note1: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.
Note2: 12 physicians who did not respond to Question 19 were excluded from this table.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-11. Knowledge Questions by Indication(s) for Which Physicians Prescribed Xarelto

Question	SPAF only N=301 n (%)	DVT only N=90 n (%)	SPAF and DVT N=835 n (%)
Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto? (Q11) (Tick all that apply)			
Stop VKA without measuring INR	38 (13)	15 (17)	143 (17)
For patients treated for prevention of stroke and systemic embolism, stop VKA and initiate Xarelto when INR is ≤ 3*	160 (53)	35 (39)	447 (54)
For patients treated for deep vein thrombosis and secondary prevention, stop VKA and initiate Xarelto when INR is ≤ 2.5*	166 (55)	59 (66)	581 (70)
I don't know	35 (12)	7 (8)	57 (7)
No answer	1 (<.5)	0 (0)	4 (<.5)
Selected both of the correct responses	93 (31)	23 (26)	352 (42)
Selected at least one of the two correct responses	233 (77)	71 (79)	676 (81)

SPAF = Stroke Prevention in Atrial Fibrillation, DVT = Deep Vein Thrombosis.
Note: Indication categories are from physician experiences in the past six months as reported per response to screening question S1.
Note: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-11. Knowledge Questions by Indication(s) for Which Physicians Prescribed Xarelto

Question	SPAF only N=301 n (%)	DVT only N=90 n (%)	SPAF and DVT N=835 n (%)
Which of the following steps should be taken when converting patients from Xarelto to VKA (e.g., warfarin)? (Q12) (Tick all that apply)			
Overlap the two drugs until INR is ≥ 2.0*	172 (57)	59 (66)	527 (63)
Measure INR but make sure it has been longer than 24 hours since the last dose of Xarelto*	101 (34)	27 (30)	317 (38)
Stop Xarelto at any time	14 (5)	7 (8)	65 (8)
Measure INR at any time of the day	8 (3)	2 (2)	45 (5)
I don't know	43 (14)	7 (8)	63 (8)
No answer	1 (<.5)	0 (0)	4 (<.5)
Selected both of the correct responses	28 (9)	8 (9)	124 (15)
Selected at least one of the two correct responses	245 (81)	78 (87)	720 (86)

SPAF = Stroke Prevention in Atrial Fibrillation, DVT = Deep Vein Thrombosis.
Note: Indication categories are from physician experiences in the past six months as reported per response to screening question S1.
Note: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

PPD Project 0304565
Bayer AG BHC RMS for Xarelto in Europe - 3 Year Assessment
Table A-11. Knowledge Questions by Indication(s) for Which Physicians Prescribed Xarelto

Question	SPAF only N=301 n (%)	DVT only N=90 n (%)	SPAF and DVT N=835 n (%)
Which of the following are true when converting from parenteral anticoagulants to Xarelto…? (Q13) (Tick all that apply)			
Stop parenteral anticoagulants for a week prior to starting Xarelto	3 (1)	5 (6)	26 (3)
For patients with continuously administered parenteral anticoagulants such as intravenous unfractionated heparin, Xarelto should be started at time of drug discontinuation*	137 (46)	43 (48)	443 (53)
For patients with parenteral drug on a fixed dosing scheme such as low molecular weight heparin (LMWH), Xarelto should be started 0 to 2 hours before the next scheduled drug administration*	142 (47)	49 (54)	468 (56)
I don't know	78 (26)	16 (18)	123 (15)
No answer	2 (1)	0 (0)	5 (1)
Selected both of the correct responses	61 (20)	20 (22)	214 (26)
Selected at least one of the two correct responses	218 (72)	72 (80)	697 (83)

SPAF = Stroke Prevention in Atrial Fibrillation, DVT = Deep Vein Thrombosis.
Note: Indication categories are from physician experiences in the past six months as reported per response to screening question S1.
Note: For each question the percentages reported for the response items were calculated using a denominator of the number of physicians who faced the question; thus physicians who did not face a question because of the skip pattern were not included in the denominator for that question.

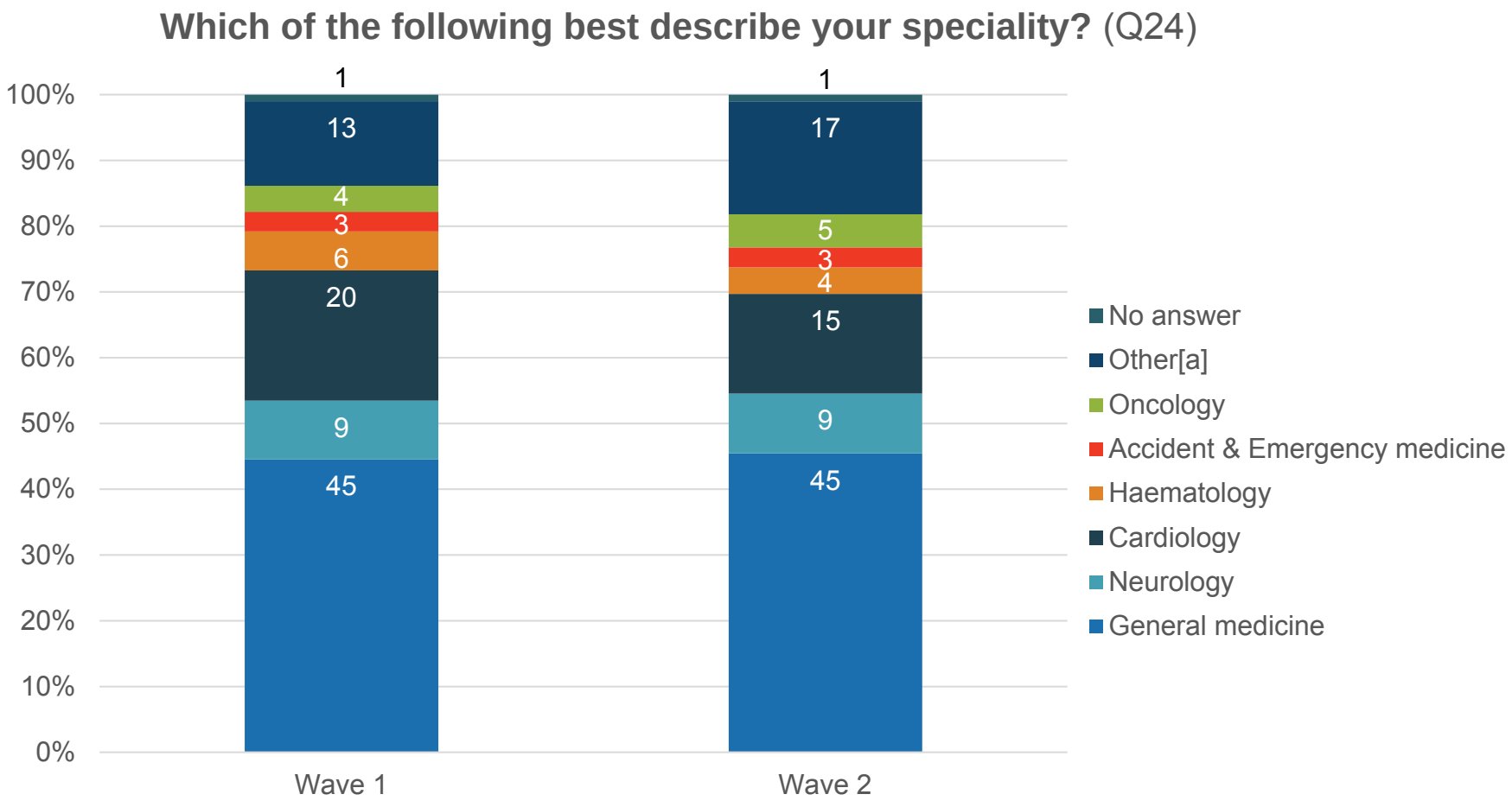
Annex 5. Graphic Comparison of Wave 1 and 2 Results

PPD

Xarelto Risk Minimisation Evaluation Plan: Comparison of Wave 1 and 2 Results From the Physician Assessment

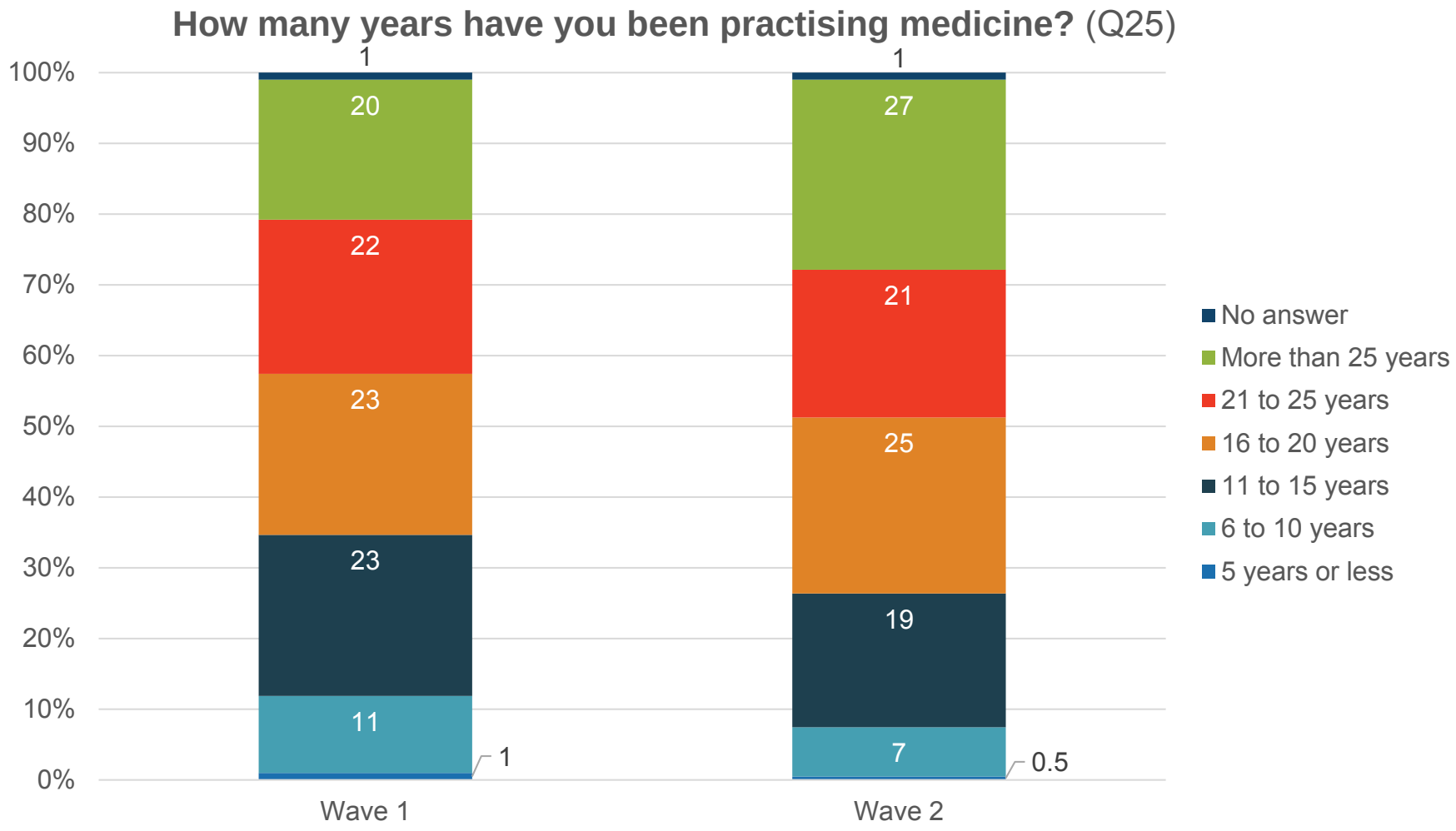
The power of **knowledge.**
The value of **understanding.**

Speciality

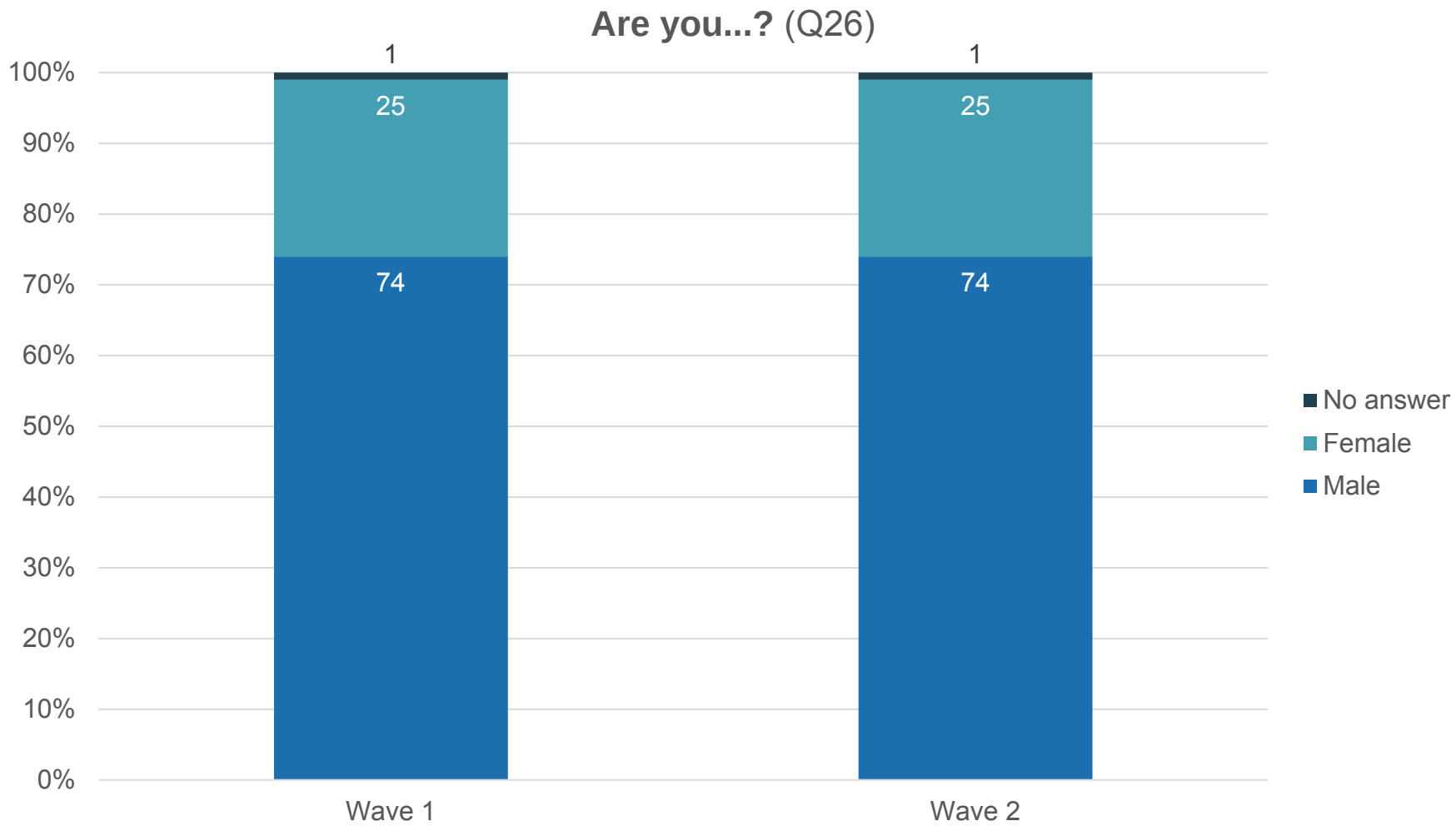


[a] Wave 2 contained two new options, “Internal medicine” and “Pulmonology.” These have been grouped into the “Other” category to make response categories comparable between waves.

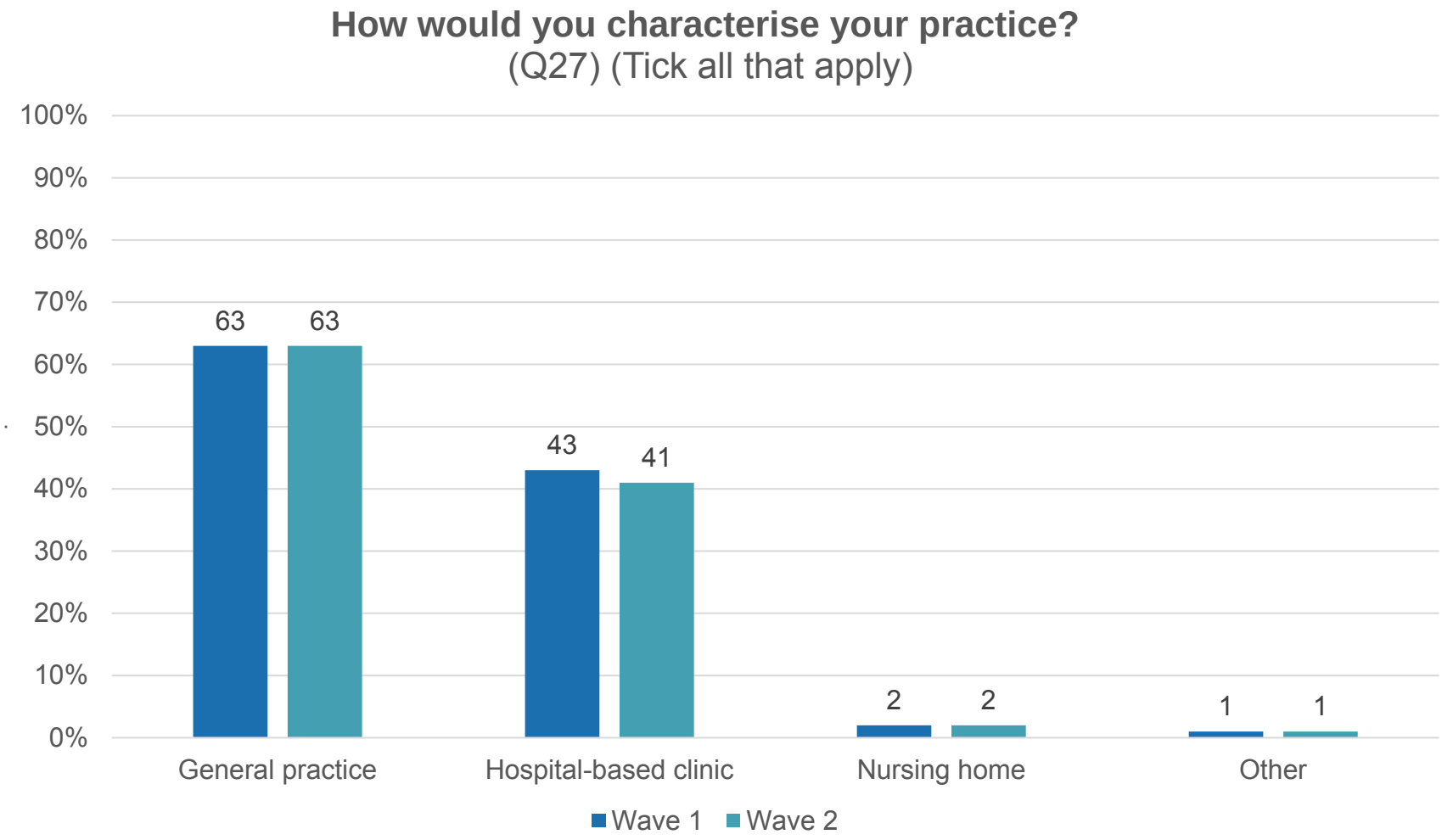
Years Practising Medicine



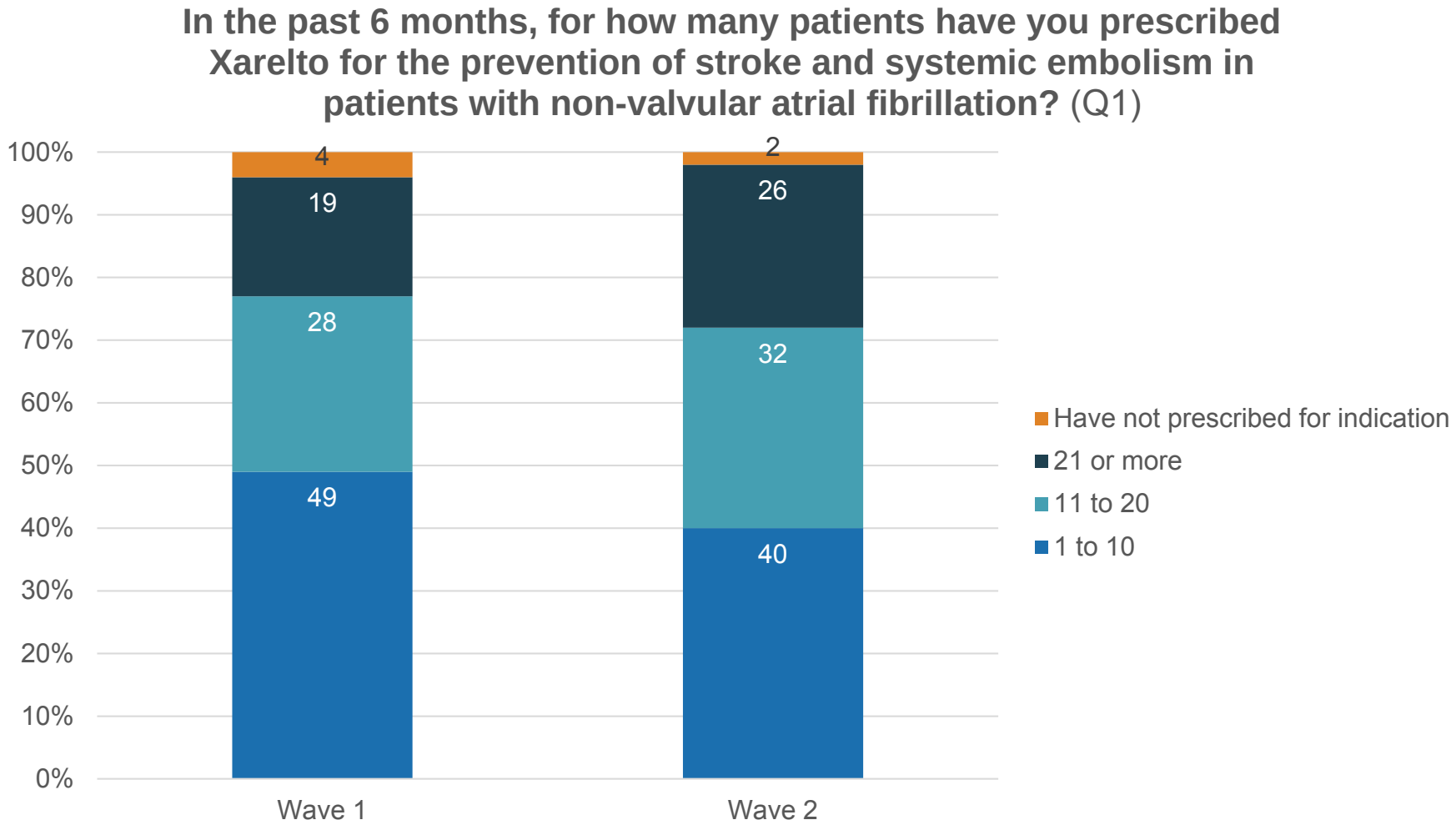
Sex



Practice Setting

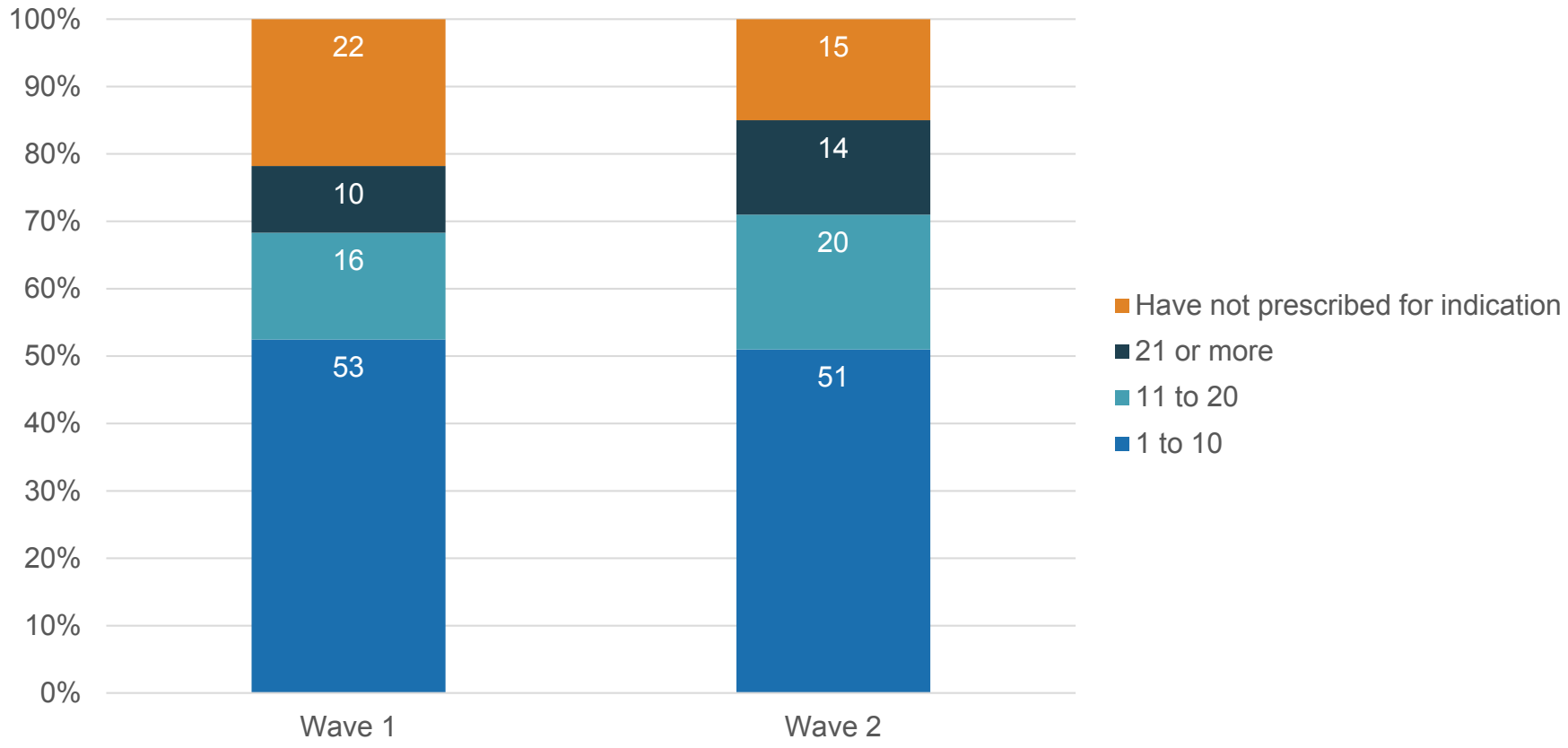


Prescribing Volume for Stroke and Systemic Embolism

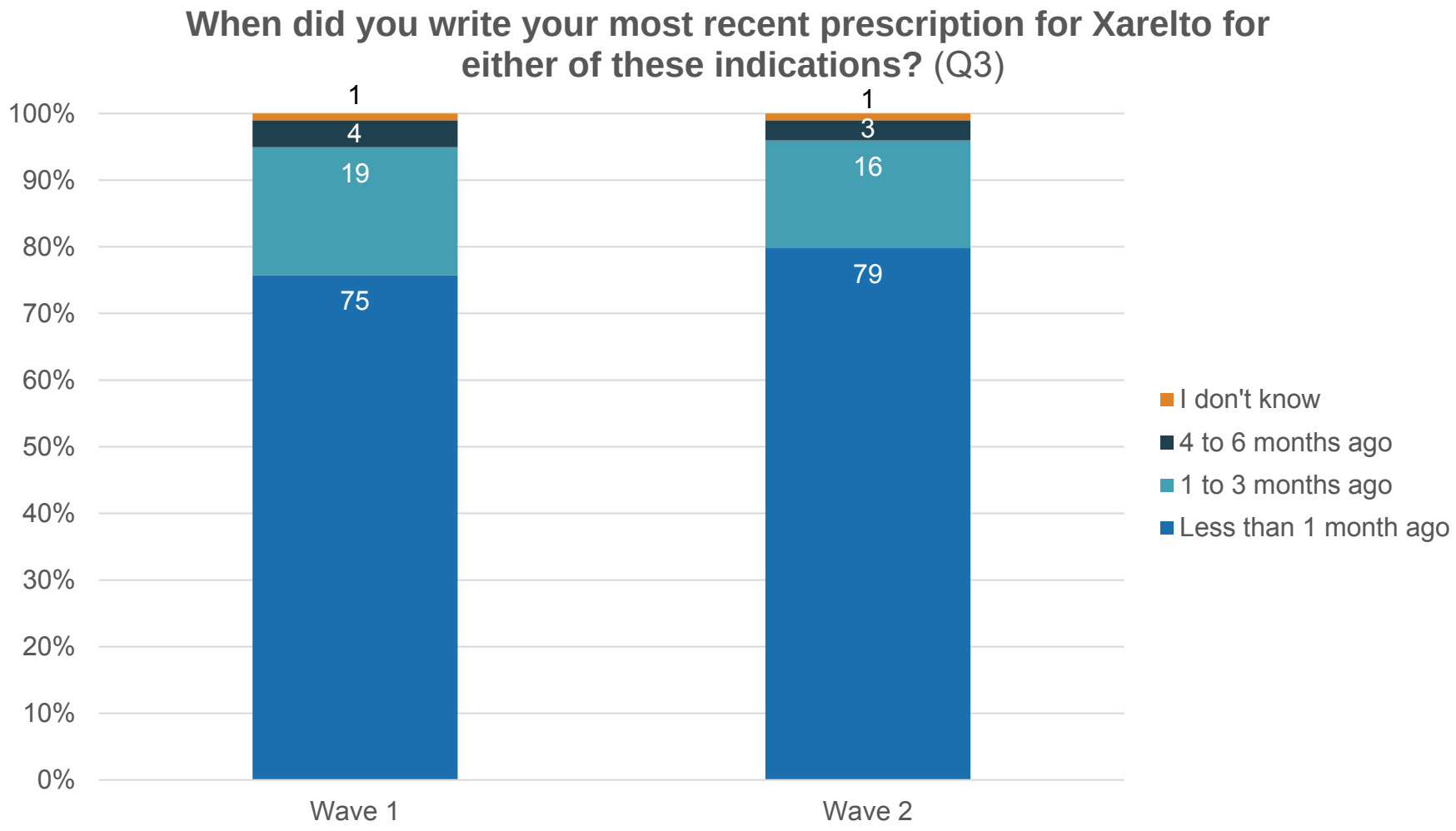


Prescribing Volume for DVT and Secondary Prevention

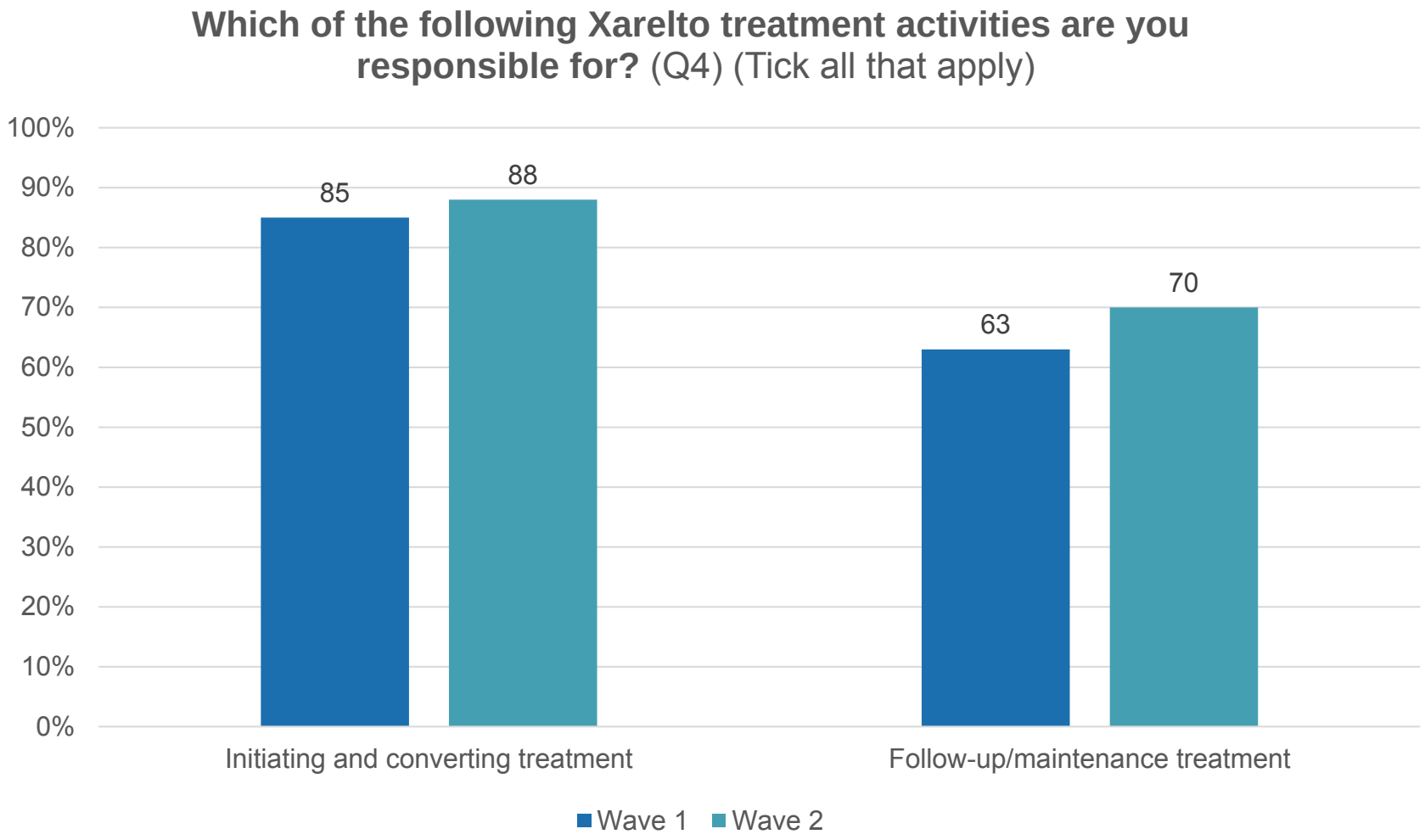
In the past 6 months, for how many patients have you prescribed Xarelto for deep vein thrombosis (DVT) treatment and secondary prevention? (Q2)



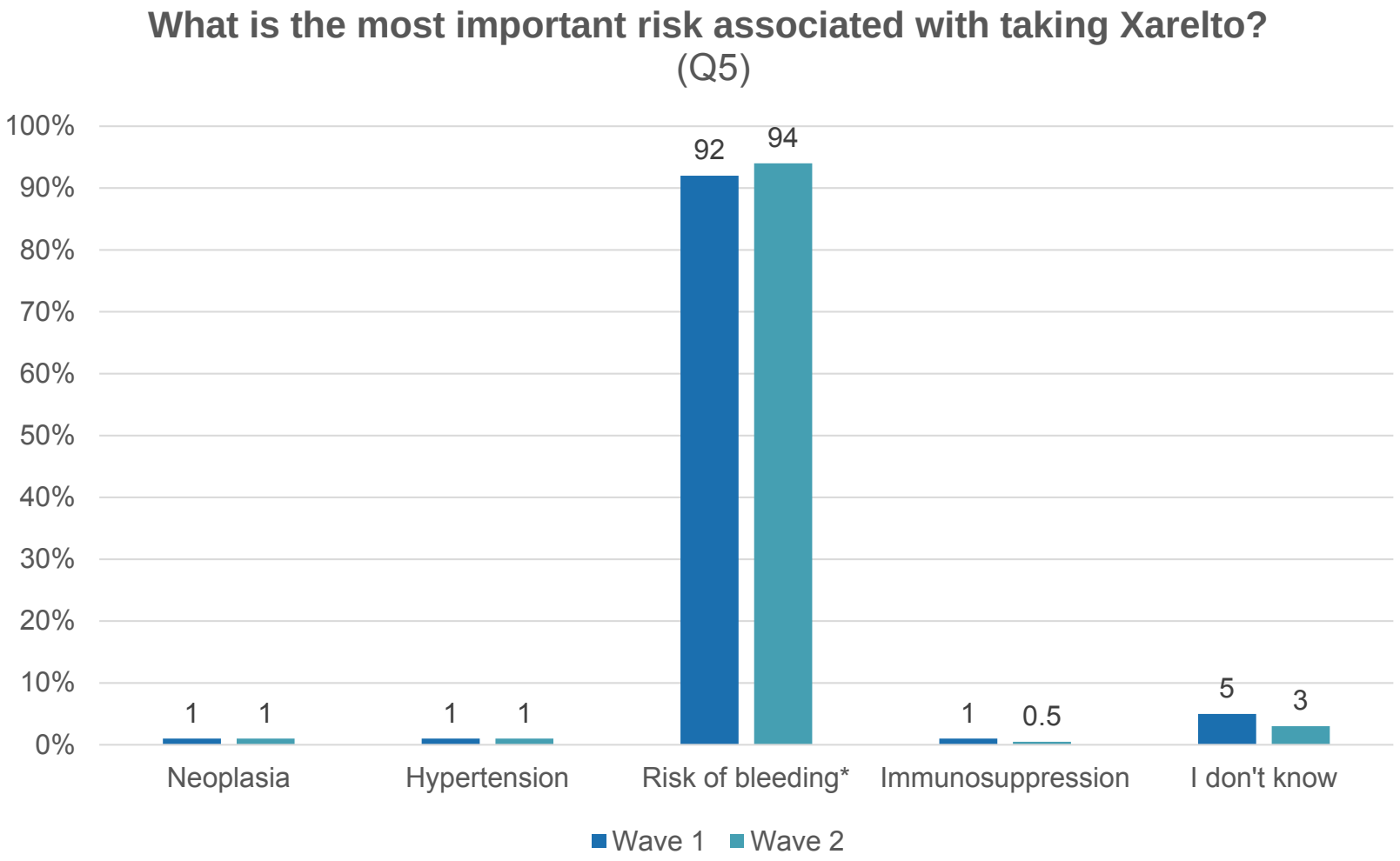
Most Recent Prescription Written



Treatment Responsibilities

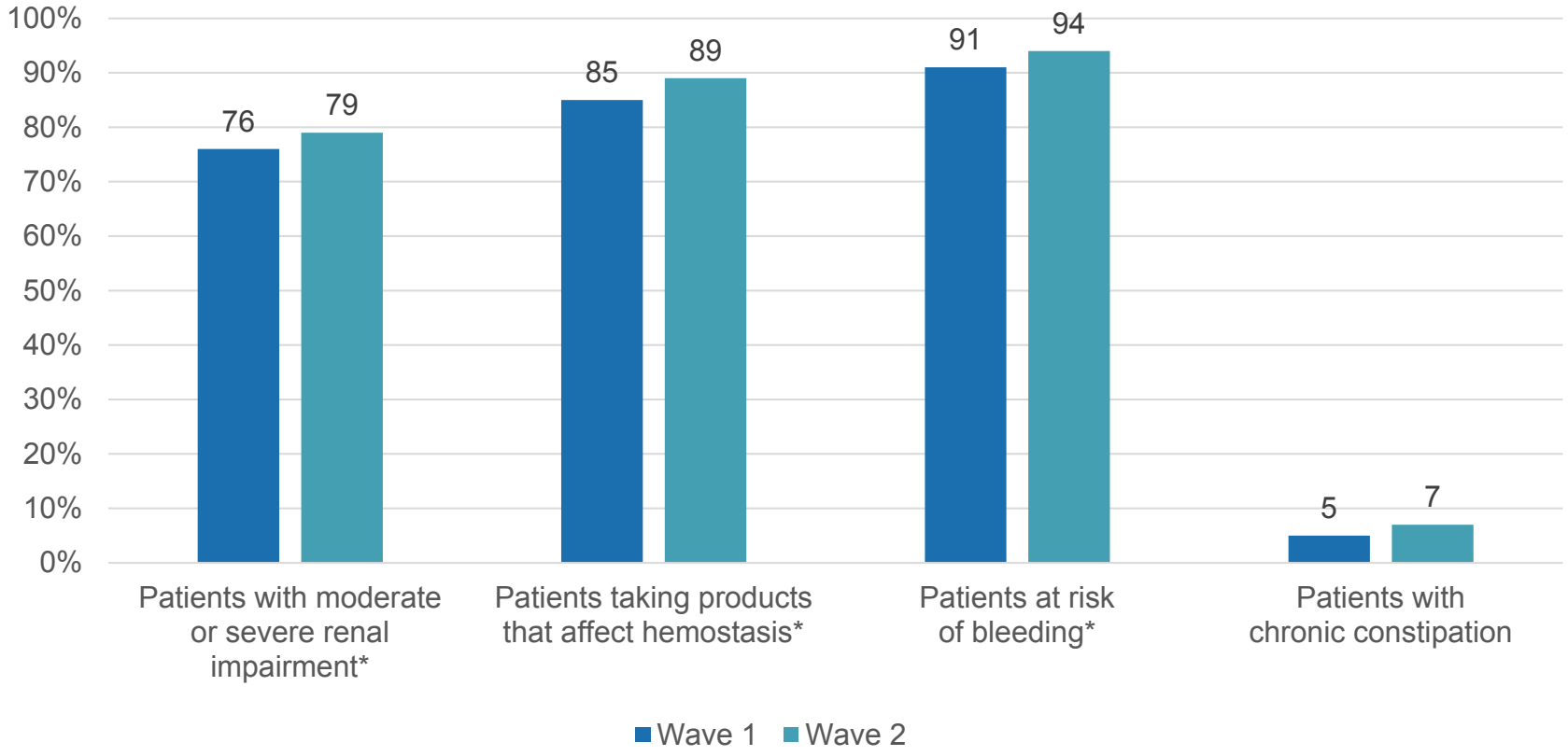


Most Important Risk

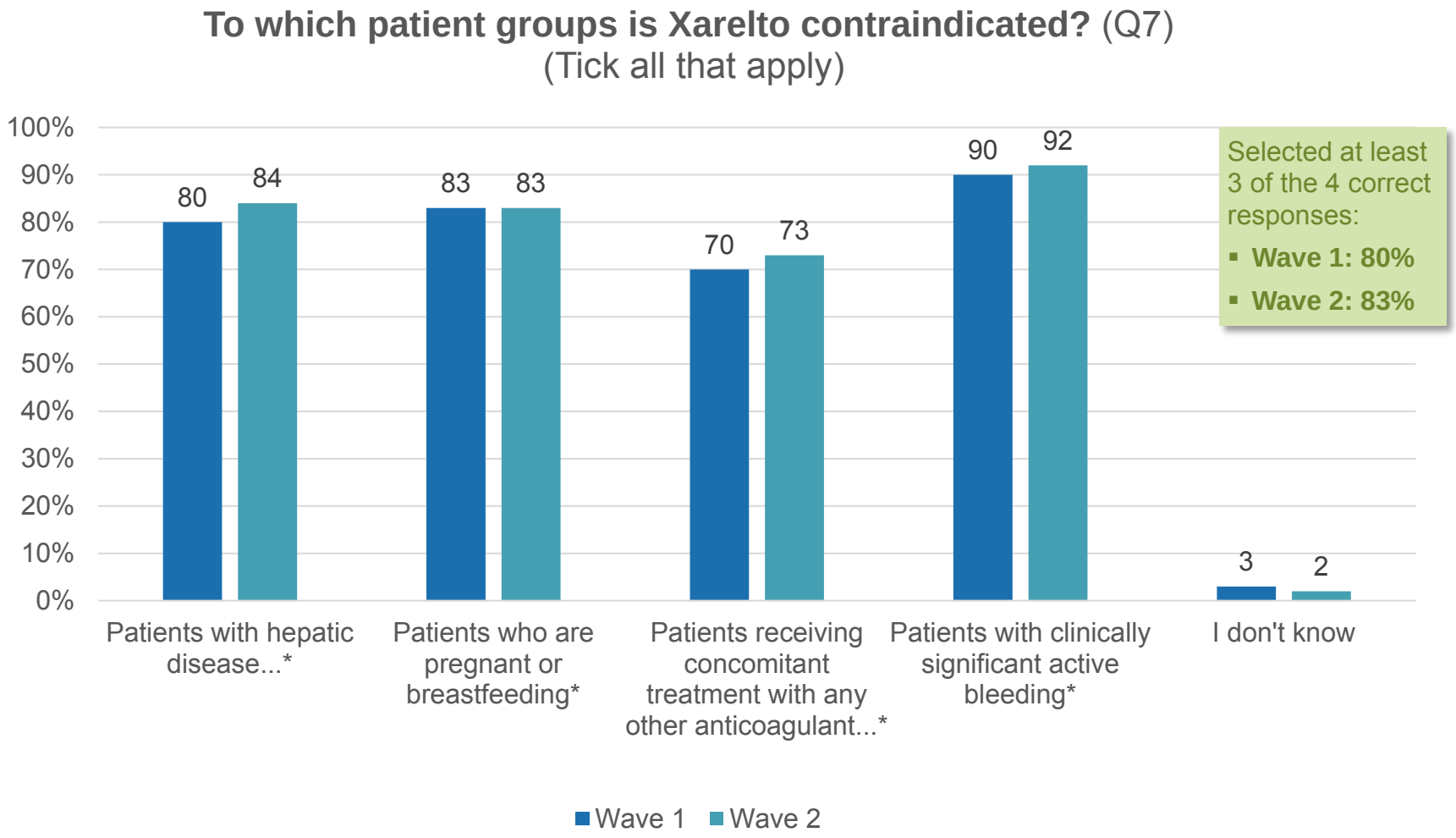


Patients at Increased Risk for Serious Side Effects

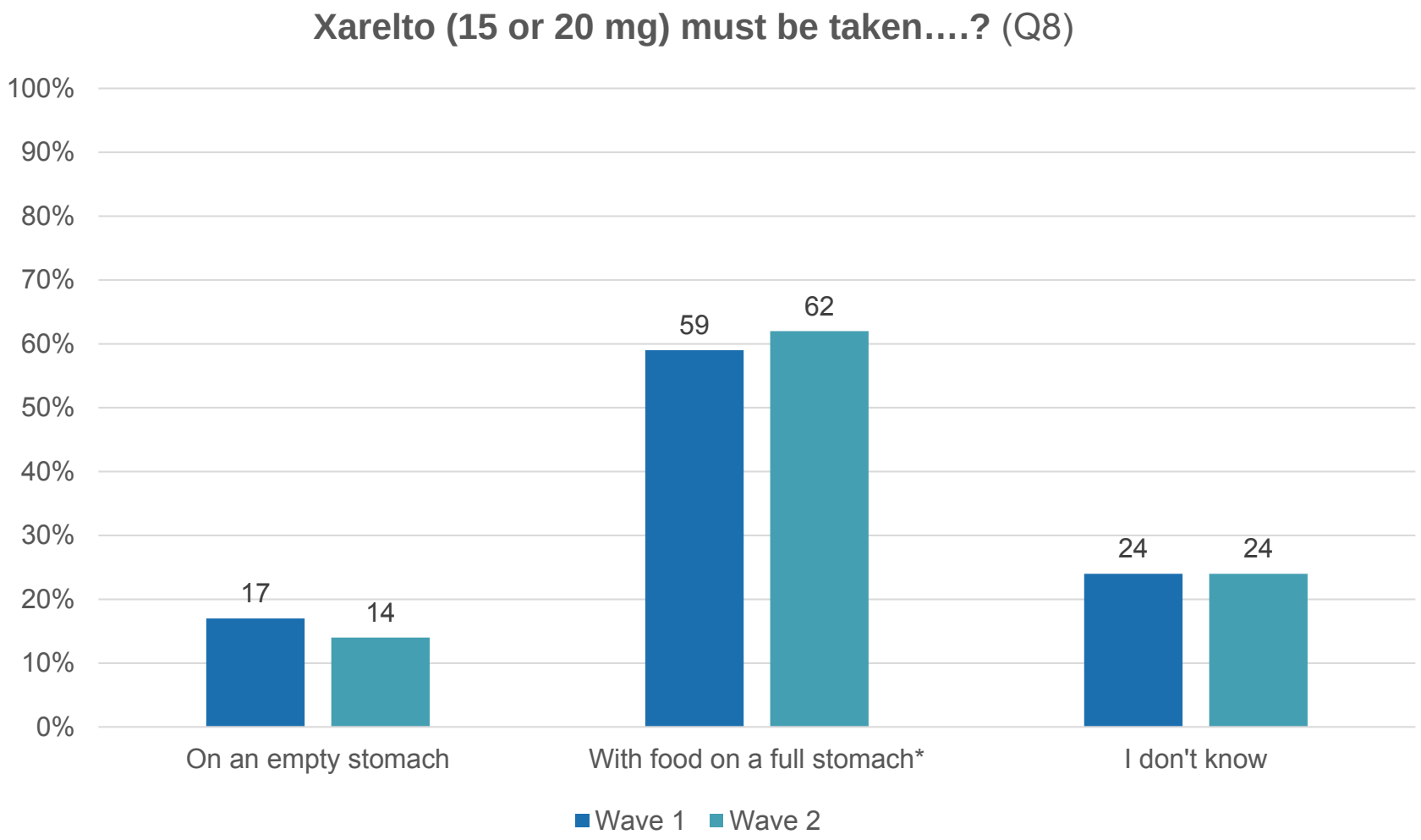
Which of the following populations are at an increased risk of experiencing serious side effect(s) associated with Xarelto? (Q6)
[Select "Yes," "No," or "I don't know" to each]



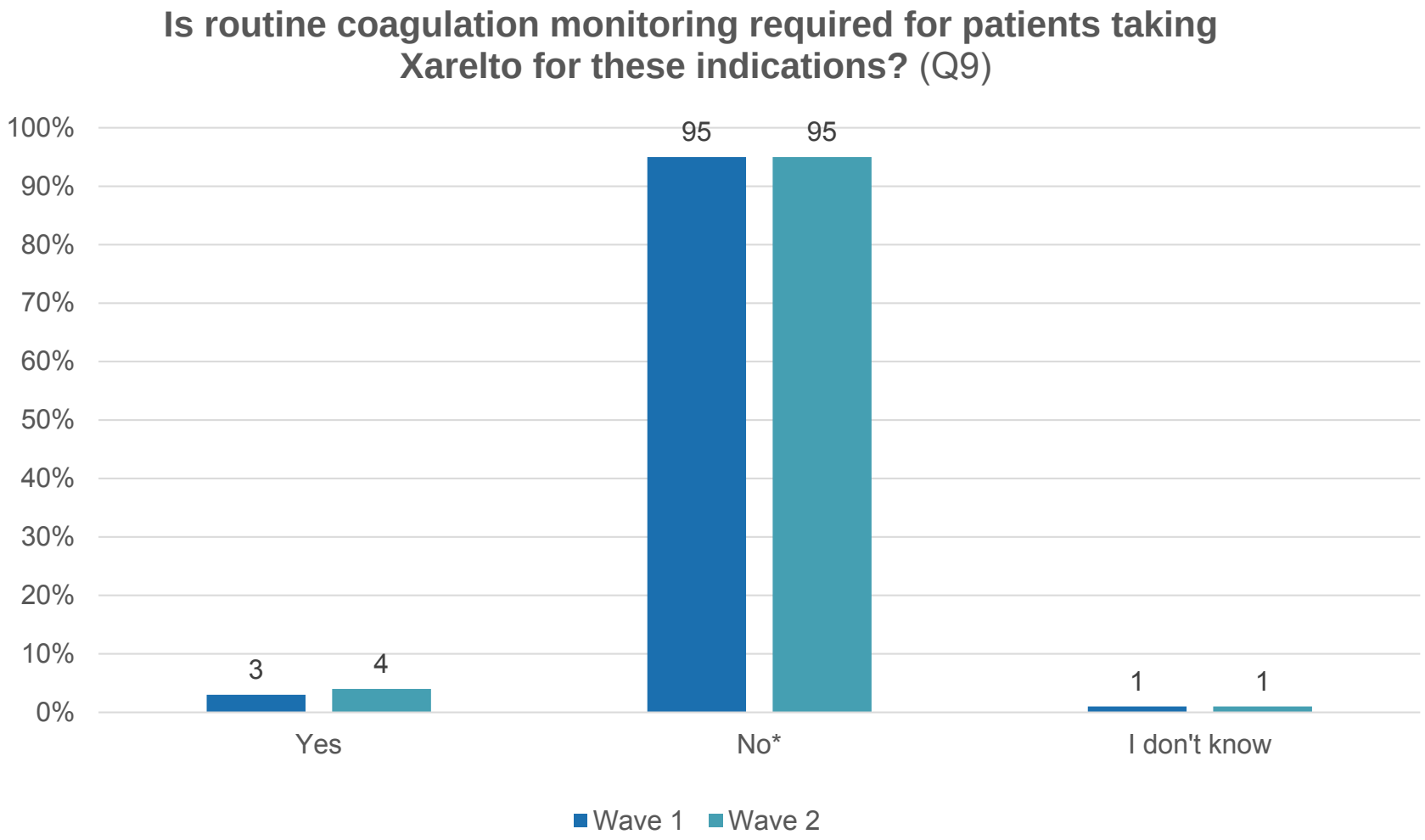
Contraindications



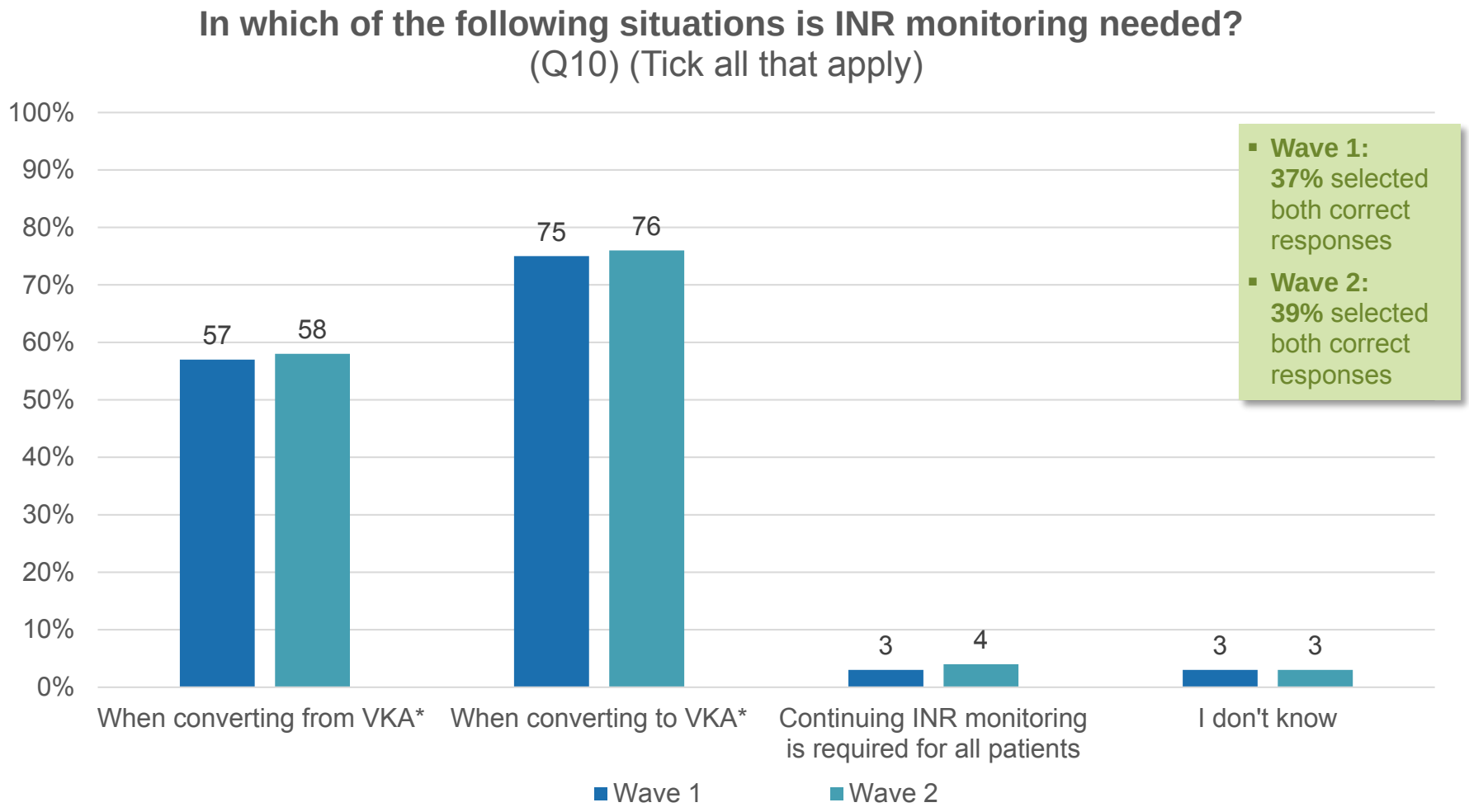
Xarelto With Food



Routine Coagulation Monitoring

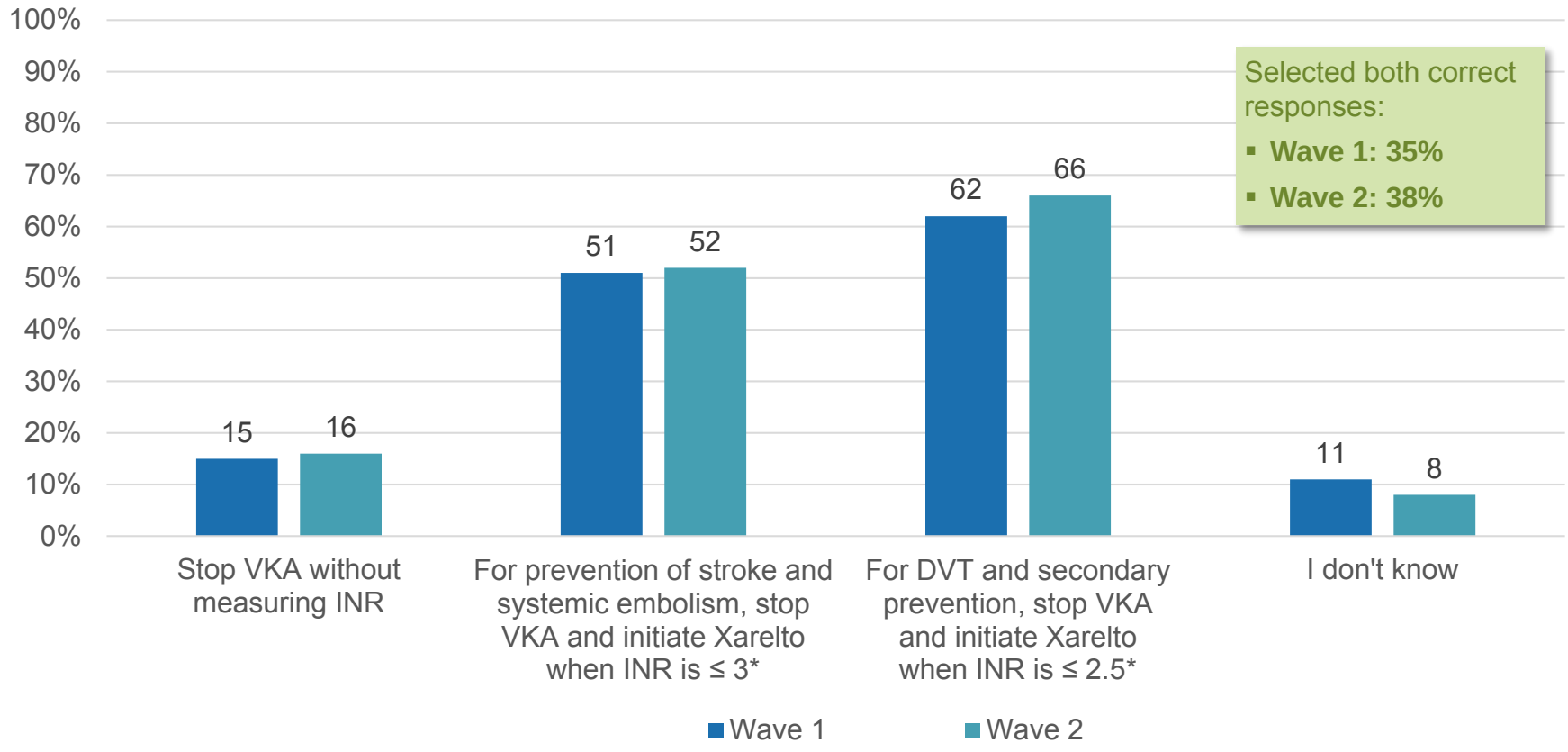


INR Monitoring



Converting from VKA to Xarelto

Which of the following steps should be taken when converting patients from VKA (e.g., warfarin) to Xarelto?
(Q11) (Tick all that apply)

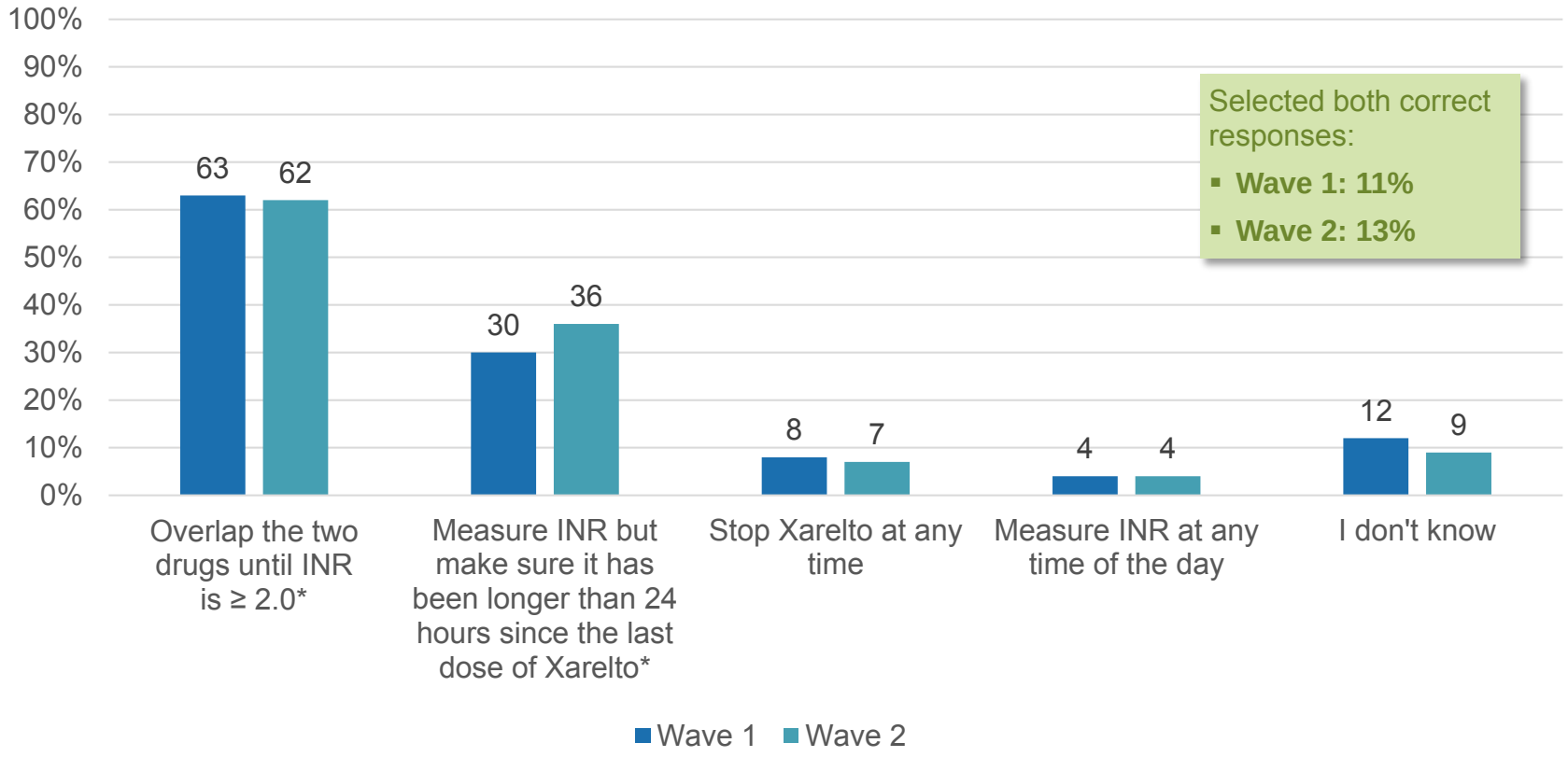


Selected both correct responses:

- **Wave 1: 35%**
- **Wave 2: 38%**

Converting from Xarelto to VKA

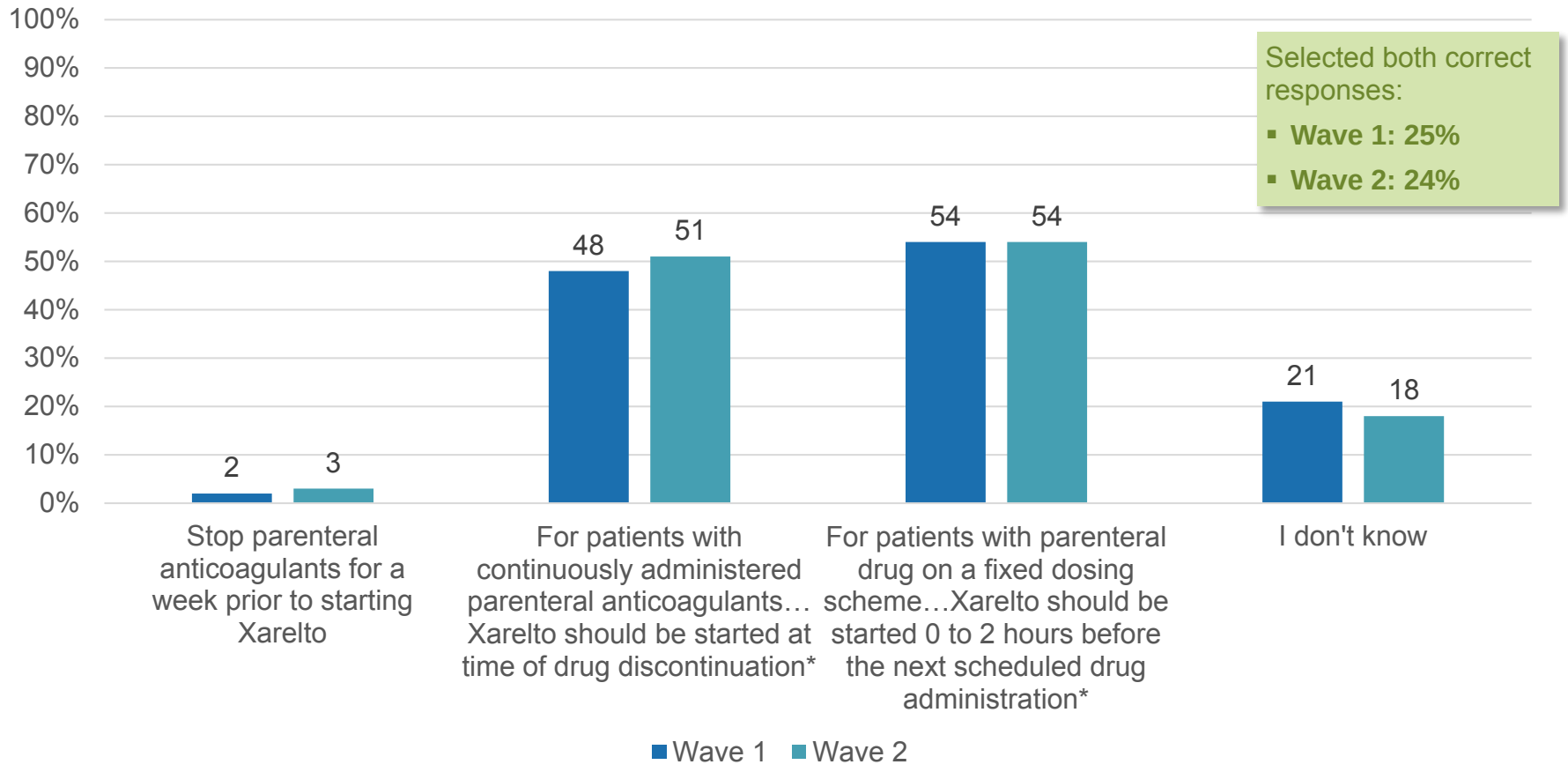
Which of the following steps should be taken when converting patients from Xarelto to VKA (e.g., warfarin)?
(Q12) (Tick all that apply)



PPD

Converting From Parenteral Anticoagulants to Xarelto

Which of the following are true when converting from parenteral anti coagulants to Xarelto…? (Q13) (Tick all that apply)

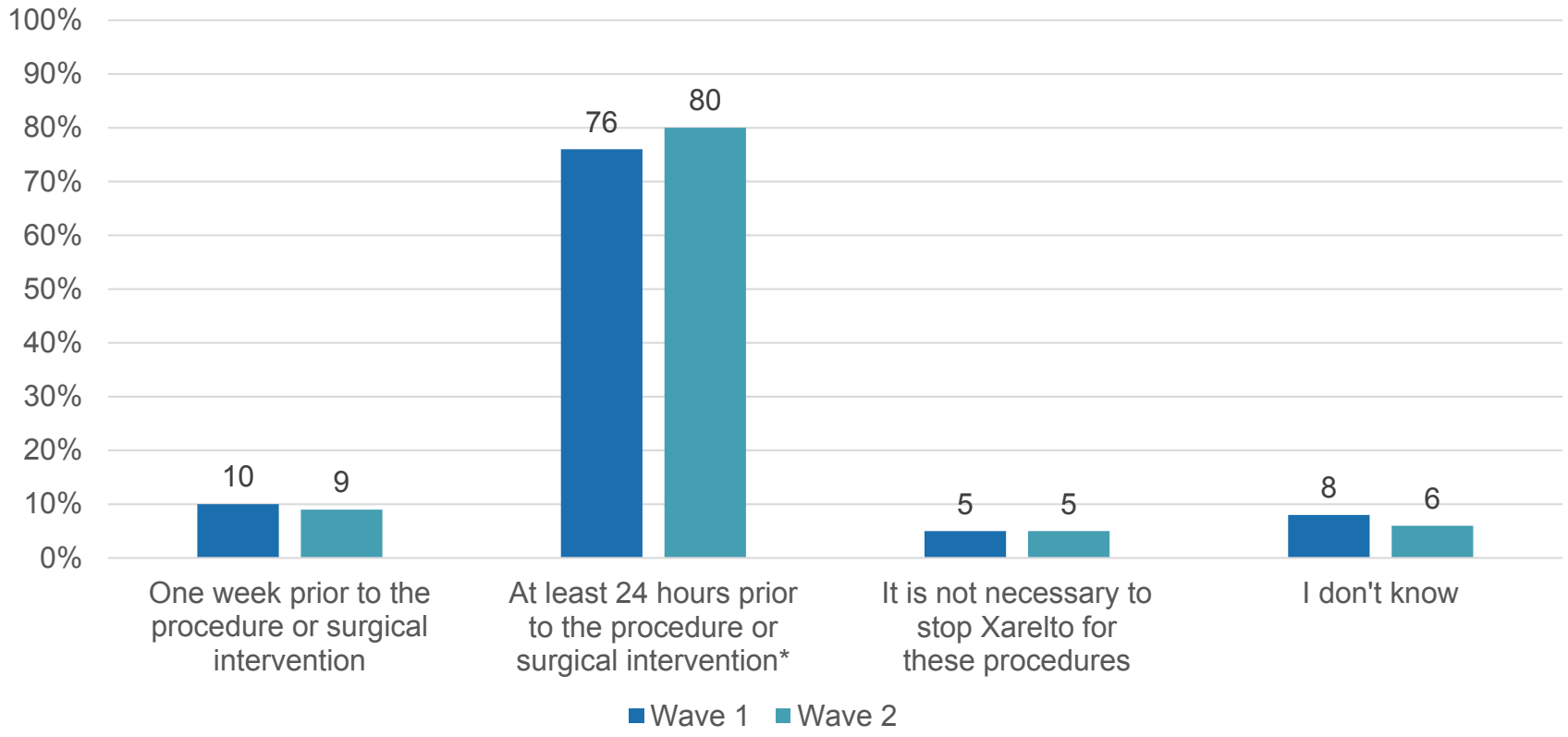


Selected both correct responses:

- **Wave 1: 25%**
- **Wave 2: 24%**

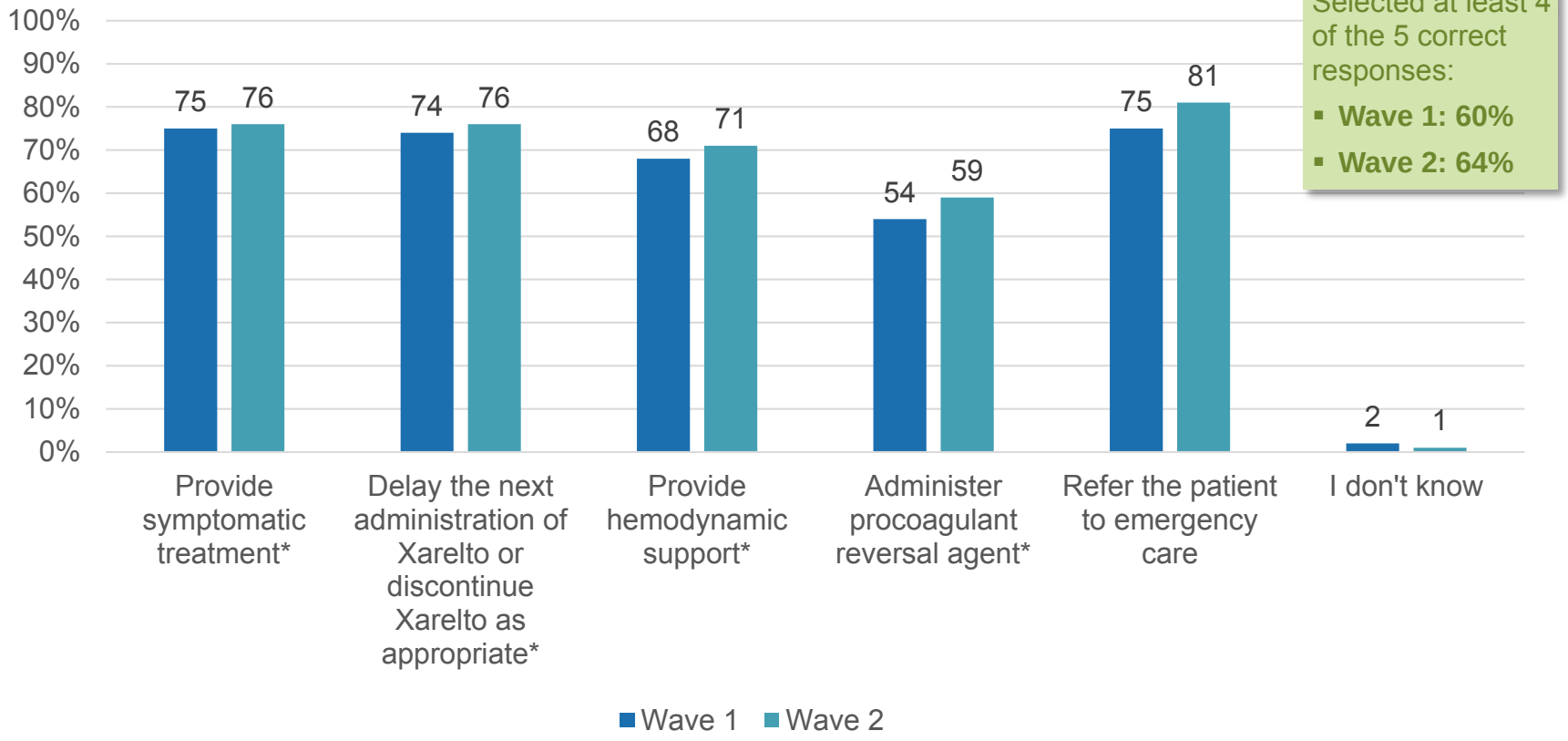
Invasive Procedure and Surgical Intervention

If an invasive procedure or surgical intervention is required, when should treatment with Xarelto (15 to 20 mg) be suspended (if possible, based upon clinical judgment of physician)? (Q14)



Medically Important Bleeding

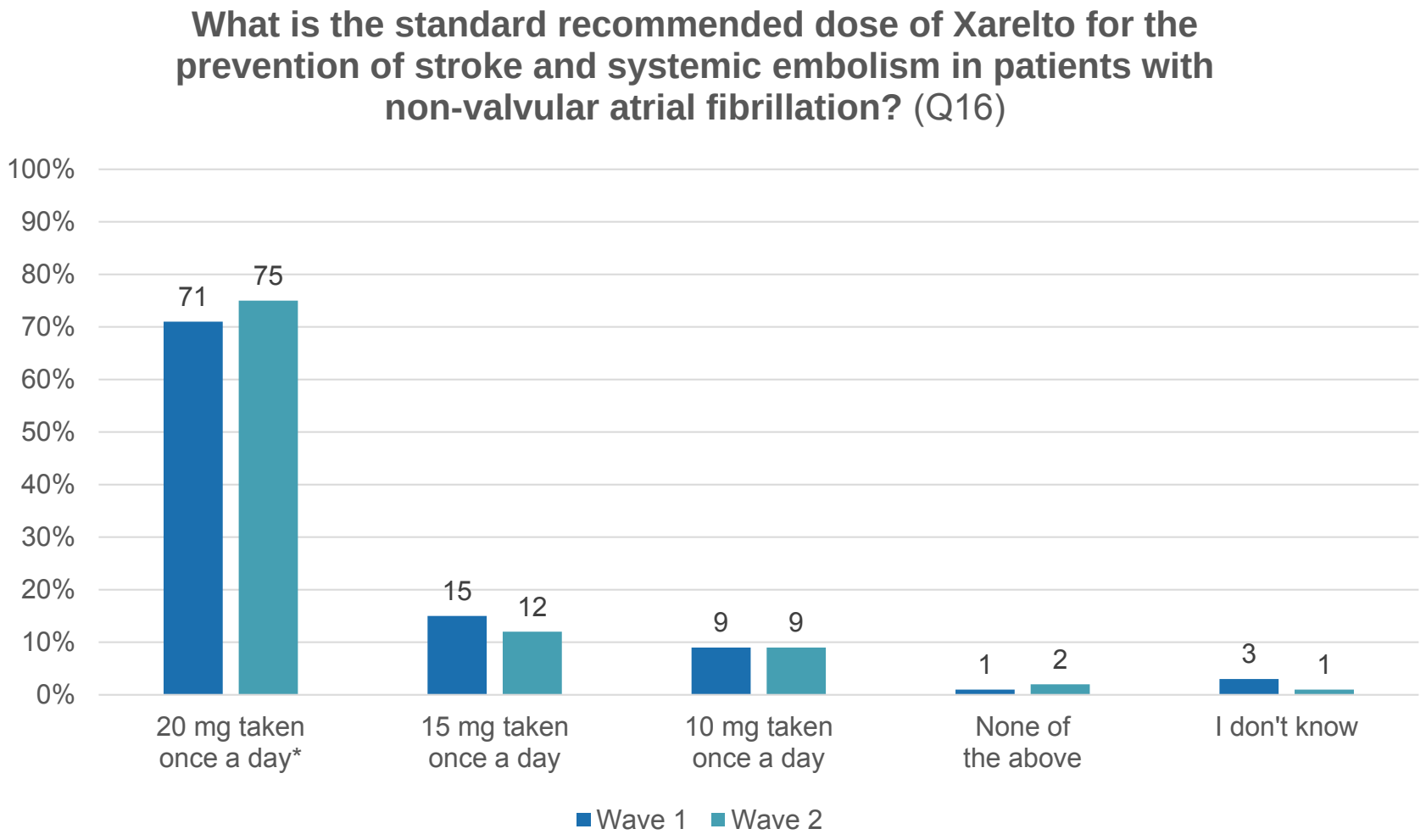
What are the most appropriate actions you should take if a patient taking Xarelto presents with a medically important bleeding complication? (Q15) (Tick all that apply)



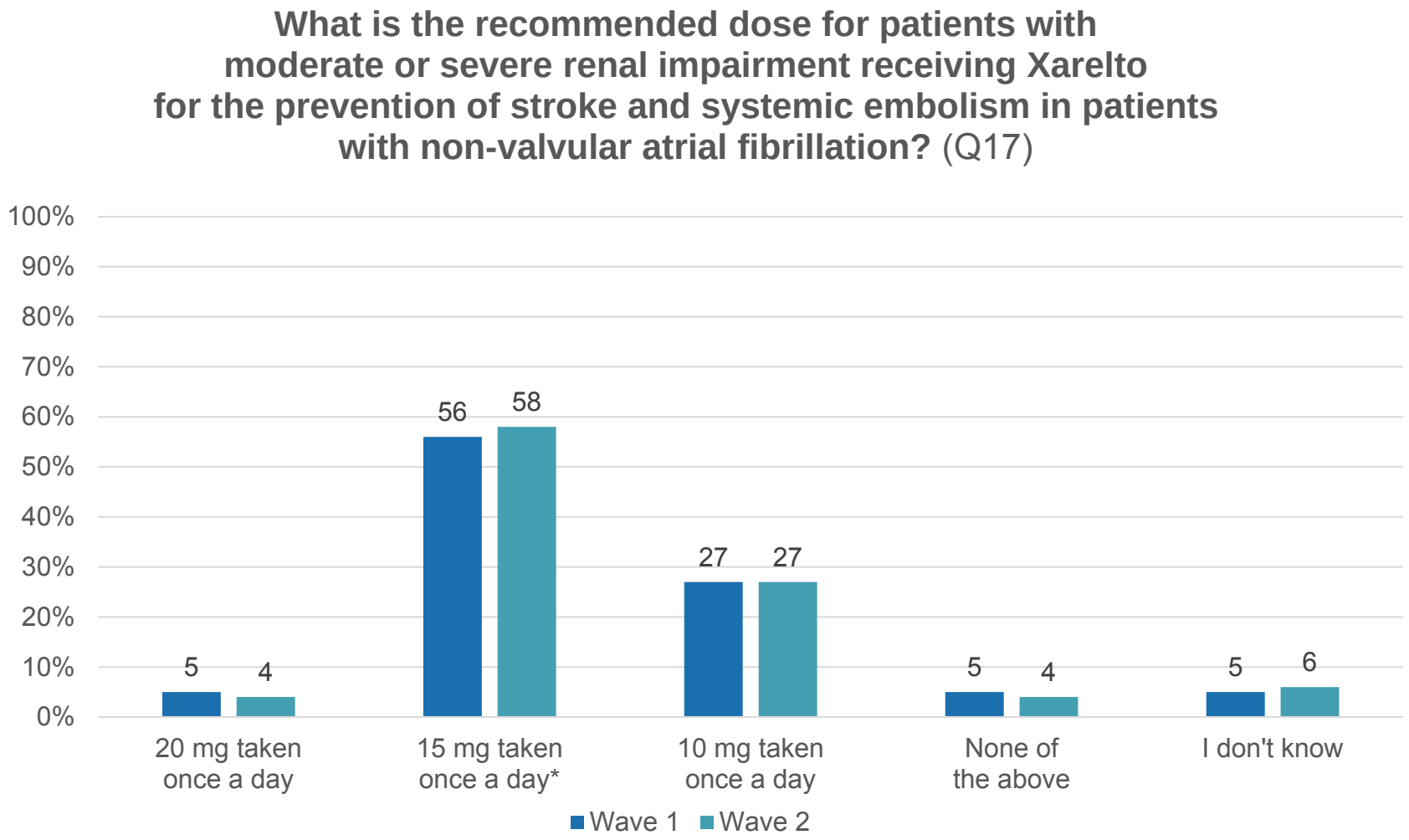
Selected at least 4 of the 5 correct responses:

- **Wave 1: 60%**
- **Wave 2: 64%**

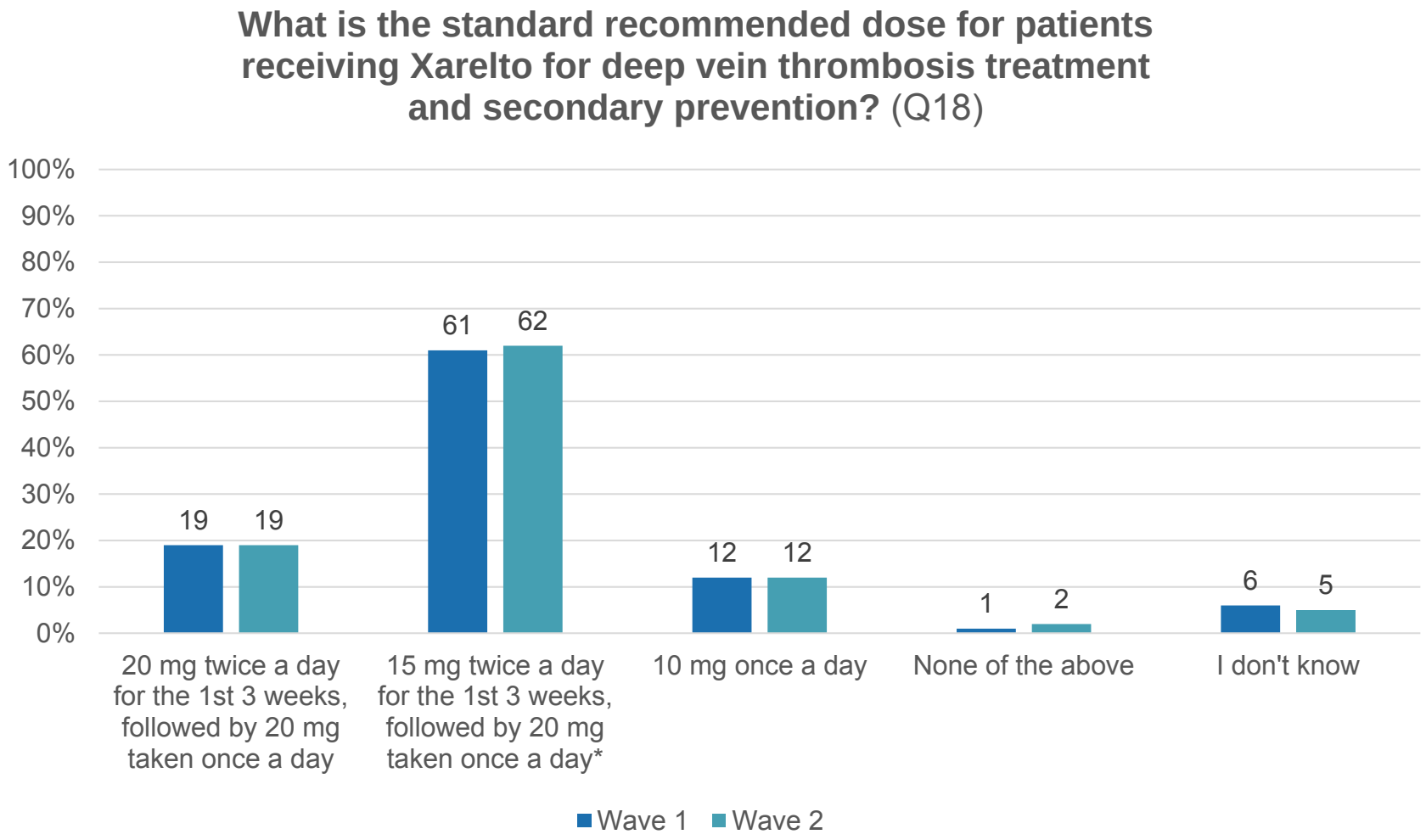
Dosing



Dosing (continued)

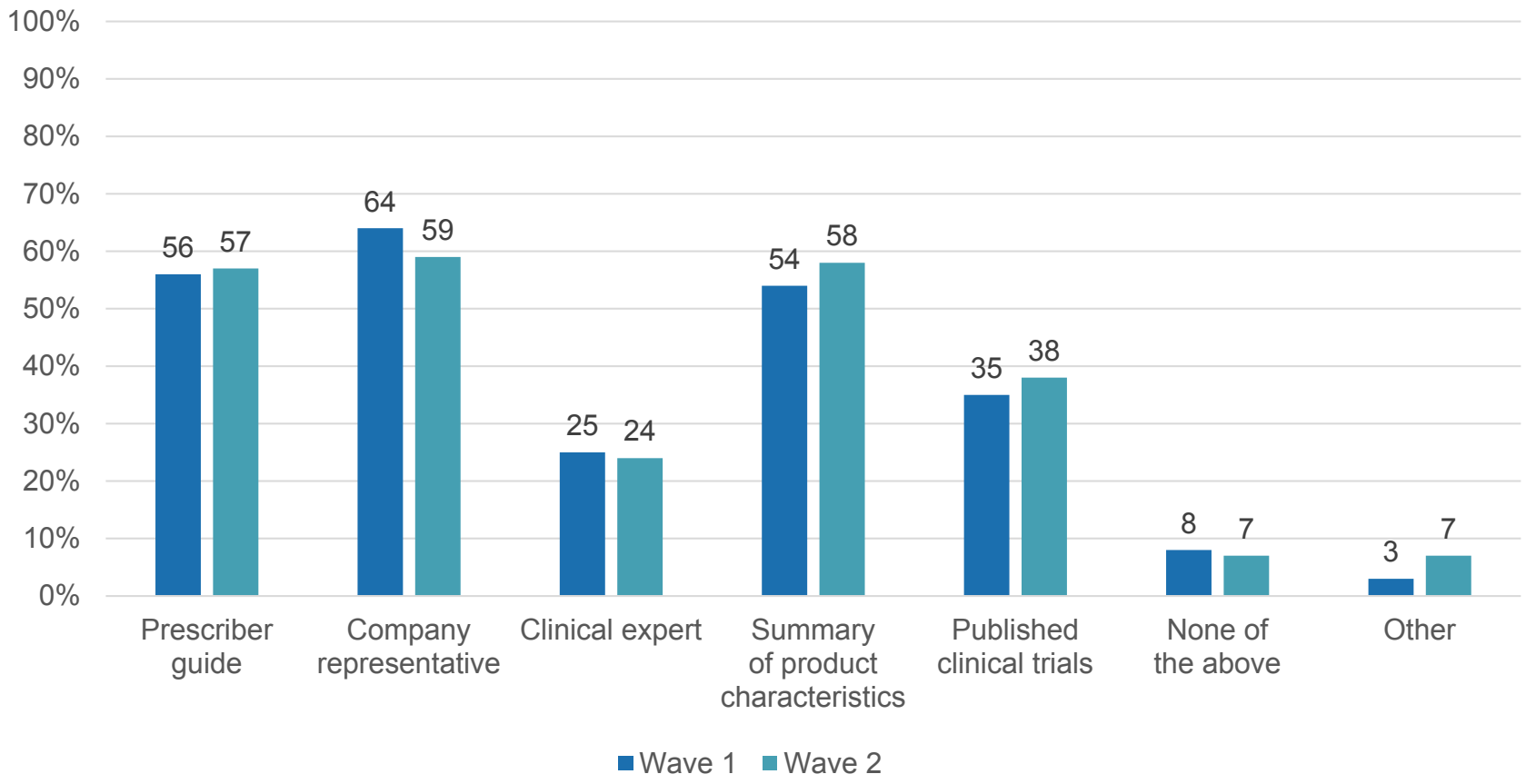


Dosing (continued)

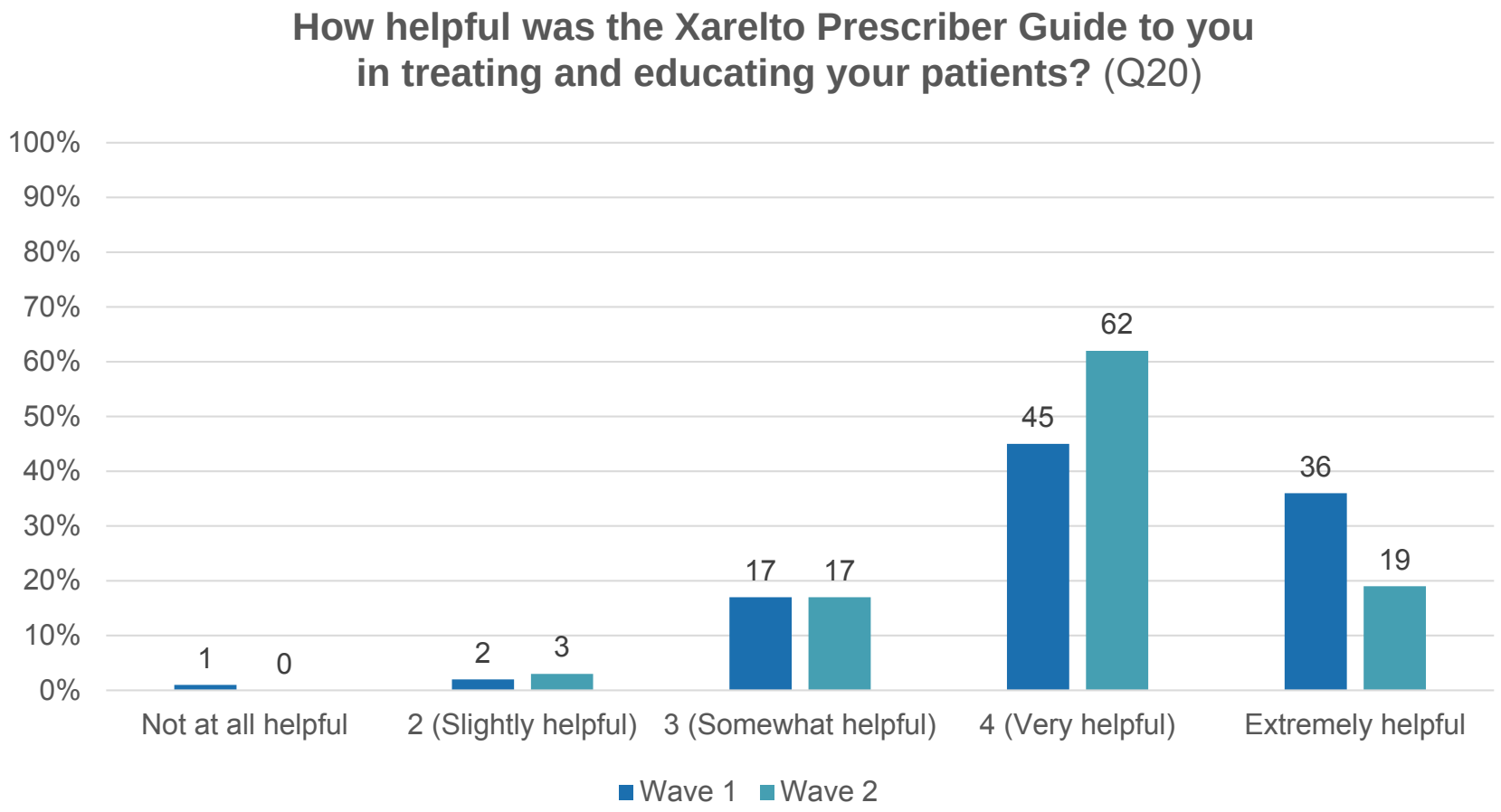


Sources of Information About Xarelto

From which of the following sources did you receive information about Xarelto? (Q19) (Tick all that apply)



Rating of Prescriber Guide Helpfulness



Note: Text describing meaning of response categories 2, 3, and 4 was added for Wave 2

Patient Alert Card Discussion With Patient

When would you discuss the information on the Patient Alert Card with your patients taking Xarelto? (Q23) (Tick all that apply)