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Prevalence and Knowledge of Potential Interactions between Over-the-Counter Products and Apixaban

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Abstract

Background: Direct-acting oral anticoagulants (DOACs) such as apixaban are the most commonly prescribed anticoagulants, with advantages in that they do not require routine monitoring. However, less frequent contact with health care professionals may contribute to poor patient knowledge about potential interactions between over-the-counter (OTC) products and DOACs.

Objective: Determine the prevalence of use of OTC products (OTC medications and dietary supplements) with potentially serious apixaban interactions, and assess patient knowledge of potential interactions.

Design: Cross-sectional survey.

Setting: Academic-affiliated outpatient medical practices in Northern and Southern California.

Participants: 791 English- or Spanish-speaking patients prescribed apixaban.

Measurements: Use and knowledge of OTC medications and dietary supplements with potentially serious apixaban interactions.

Results: Almost all respondents (n=771; 97.5%) reported OTC product use. Thirty-three percent (n=266) took at least 1 OTC product with potentially serious apixaban interactions daily/most days and 53 (6.7%) took multiple products (mean=2.6 [SD=2.6]). Aspirin was taken daily by 116 (14.7%; of which 75 (64.7%) also consumed other potentially interacting OTC products), and some days/as needed by an additional 82 (10.4%). Ibuprofen and naproxen were taken daily/most

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days by 14 (1.8%) and occasionally by 225 (28.5%). Dietary supplements with potentially serious interactions were taken daily/most days by 160 (20.2%). About 66% of respondents were either uncertain or incorrect about the potential for increased bleeding from combining NSAIDs and apixaban. Less knowledge about OTC products with potentially serious interactions was associated with greater OTC product use (OR=0.54; 95% CI 0.35–0.85).

Conclusion: Significant numbers of patients take OTC products (particularly dietary supplements) with potentially serious interactions with the DOAC apixaban, and appear to lack knowledge about potentially harmful interactions. Interventions are needed to educate patients and healthcare providers about potential dangers of taking interacting OTC products in combination with apixaban and data are needed on outcomes associated with concomitant apixaban-OTC product use.

Keywords

anticoagulants; apixaban; over-the-counter drugs; dietary supplements; patient medication knowledge

INTRODUCTION

Direct-acting oral anticoagulants (DOACs) are now the anticoagulants of choice for prevention of stroke in patients with non-valvular atrial fibrillation (NVAF) without mechanical valves or severe mitral valve, renal, or liver disease, and are replacing warfarin for treatment of venous thromboembolic disease in patients without cancer.[1, 2] DOACs have fewer food interactions, simplified dosing and monitoring regimens, and lower rates of intracranial hemorrhages compared to warfarin. They also have fewer medication interactions primarily limited to potent combined P-glycoprotein (P-gp) and cytochrome p-4503A4 (CYP3A4) inhibitors (azoles, clarithromycin and selected anti-retroviral agents) or inducers (carbamazepine, phenytoin, rifabutin, rifampin, ritonavir, St. John's wort) that might alter DOAC concentrations (Table 1). Antiplatelet agents or dietary supplements with anti-platelet activity can increase bleeding risk (Table 1).[1, 3–8]

The vast majority of patients receiving DOACs are not followed at monthly intervals by health care professionals or in specialized anticoagulation clinics. While less frequent monitoring and fewer healthcare professional visits may benefit patients, it may also result in decreased patient education and knowledge regarding interactions between anticoagulants and over-the-counter (OTC) medications or dietary supplements.

OTC products can be bought by patients without a prescription, and consist of: 1) OTC medications and 2) dietary supplements (vitamins, minerals, herbs or other botanicals, amino acids, or other substances used to supplement the diet).[9] It is known that one-third of patients taking warfarin consume non-vitamin non-mineral dietary supplements with reported warfarin interactions.[10] As DOACs replace warfarin for anticoagulation, it is likely that a significant fraction of DOAC patients also consume OTC products, but specific knowledge about patterns of over-the-counter (OTC) use is lacking.

Our goal was to determine the prevalence of use of OTC medications and dietary supplements with potentially serious interactions with apixaban, one of the most frequently prescribed DOACs,[11, 12] and to assess patient knowledge of potentially serious OTC product-apixaban interactions.

METHODS

Study procedures were approved by the University of California, Los Angeles Institutional Review Board (IRB), with the University of California, San Francisco relying on UCLA's IRB through the UC IRB Reliance Registry. Eligible patients were identified via data extractions by the UCLA and UCSF Clinical & Translational Science Institutes from the UCLA Integrated Clinical and Research Data Repository and UCSF electronic medical record systems. Data extractions generated lists of English and Spanish-speaking outpatients aged 18 years and older receiving at least one prescription for apixaban at UCLA (from January 2017-January 2018) or UCSF (from August 2016-February 2017 and June 2017-May 2018).

The survey was conducted from April to October 2018. All patients identified through database searches with an email address on file received electronic invitations to complete a one-time survey. Those without email addresses were mailed invitations via postal mail. All patients were given the opportunity to opt-out of participation. Those who did not opt-out were mailed a paper copy of the survey with a postage-paid return envelope or emailed a link to an online REDCap survey. REDCap (Research Electronic Data Capture) is a secure, HIPAA-compliant, web-based system for building and managing web-based research projects such as surveys and databases.[13]

Respondents completed an eligibility screen. We surveyed patients who reported taking apixaban for more than one month, and who noted no problems in the past 12 months with "memory or thinking that interferes with your ability to do things you regularly do such as taking care of your home, managing your finances, or keeping up with TV programs."[14] Participants received a $10 gift card for completing the survey.

Survey instrument

The English-language survey was translated into Spanish using forward and back translation. Cognitive testing of the survey was conducted in both English and Spanish. The survey questioned patients about how often they took a list of 3 OTC medications (aspirin, ibuprofen/naproxen (NSAIDs), acetaminophen) and 13 common dietary supplements (Gingko biloba, Chinese herbs excluding Gingko biloba, fish oil / omega-3 fatty acids / cod liver oil, flaxseed, ginger, herbal teas, melatonin, saw palmetto, St. John's wort, turmeric, multivitamin, vitamin D and/or calcium, and vitamin E) "while on Eliquis (apixaban)" (daily, most days, some days, as needed, never). Patients used their own discretion when selecting frequency of use; categories were not further specified. Patients also were asked to write in the names of other dietary supplements taken that were not listed. The survey queried patient knowledge about whether or not they "might bleed more easily" if they took apixaban with the following OTC products: aspirin, ibuprofen or naproxen, acetaminophen,

or St. John's wort (5-point Likert scale responses, ranging from "strongly disagree" to "strongly agree").

Patients were also asked if they talked to a healthcare provider about whether it was okay to take an OTC product with apixaban (yes/no), and if yes, who they spoke to (doctor, pharmacist, nurse, other healthcare provider). Other questions asked about demographics (age, sex, race/ethnicity, education level), number of prescription medications taken, self-rated health (5-point Likert scale), prior warfarin use (yes/no), and health literacy (confidence in filling out medical forms; assessed on 5-point Likert scale[15–17]).

The initial survey did not ask about knowledge regarding potential interactions between apixaban and Chinese herbs, ginger, gingko biloba, herbal tea, or turmeric, as these are not listed as interacting substances in the product label.[18] Since these products can have potentially serious interactions with apixaban,[19, 20] we subsequently surveyed respondents who reported taking at least one of these products 'every day' or 'most days' about whether they "might bleed more easily" if they took the product(s) they were on with apixaban (5-point Likert scale responses, ranging from "strongly disagree" to "strongly agree").

Classification of OTC products for potentially serious interactions with apixaban.

OTC medications and dietary supplements with potentially serious interactions with apixaban were identified from: the approved product package insert,[18] the reference database Lexicomp[19] and the Natural Medicines database (the most authoritative resource available on dietary supplements[20]), where products are classified as: avoid, consider therapy modification, monitor, or no interactions. Concordance between two sources was used to classify agents into categories of potentially clinically relevant (serious) interactions: avoid (St. John's wort), consider therapy modification (changing one of the treatments) (aspirin, Chinese herbs, herbal teas, ginger, gingko biloba, and turmeric), and monitor closely (NSAIDs such as ibuprofen or naproxen).[19, 20]

Knowledge Scores

Mean knowledge scores were generated to describe patient knowledge about interactions between apixaban and aspirin, NSAIDs, acetaminophen, and St. John's wort. Knowledge scores ranged from −1 to 1, with higher scores indicating more accurate knowledge; patients received a score of : +1 if they "strongly agreed" or "agreed" that the OTC product might make them bleed more easily if taken with apixaban; 0 if they were "uncertain;" and −1 if they "strongly disagreed" or "disagreed." Scoring for knowledge about acetaminophen was reversed, with higher scores correctly indicating that patients disagreed that potential interactions existed. Scores for the individual products were summed and divided by the number of products for which patients provided responses. Sensitivity analyses examined mean knowledge scores that included and excluded knowledge about acetaminophen, which does not interact with apixaban.

Data analysis.

STATA 16.0 (StataCorp, LLC) was used for all analyses. Data are presented as means and standard deviations, frequencies, or percentages.

Knowledge, use of OTC products, and knowledge source.—Unpaired t-tests were used to evaluate relationships between mean knowledge scores and regular (daily/most days) use of any OTC products with potentially serious interactions with apixaban (aspirin, NSAIDS, St. John's wort, Chinese herbs, herbal teas, ginger, gingko biloba, turmeric) (yes/no). Frequencies with which patients reported seeking information from healthcare providers were tabulated. T-tests were used to examine relationships between patient knowledge about potential OTC product-apixaban interactions on: 1) discussions with healthcare providers about whether it was okay to take an OTC product with apixaban; and 2) prior warfarin use.

Multivariable Analyses—Multivariable models using multiple logistic regression evaluated regular use (daily/most days) of: 1) aspirin, ibuprofen or naproxen; 2) dietary supplements; and 3) any OTC product with potentially serious interactions with apixaban (yes/no), as primary outcome variables, with the mean knowledge score as the primary predictor. We adjusted for other predictors including: patient age; gender; race/ethnicity; health literacy; total number of prescription medications taken; and prior history of warfarin use (yes/no). Sensitivity analyses examined the mean knowledge score without acetaminophen.

RESULTS

Patient and prescription medication use characteristics.

Participation invitations were distributed to 4006 outpatients (UCLA n=2006; UCSF n=2000). Of 1343 respondents, 55 opted-out of participation, and 518 were excluded because they were ineligible (deceased, no longer taking apixaban, had taken it for less than 1 month, or failed the cognitive screening), giving an eligibility rate of 59.8%. Data from two additional patients were excluded due to incomplete responses to OTC product use questions. A total of 791 patients completed the survey. Applying the eligibility rate to patients for whom we were unable to assess eligibility (n=4006−518−791 =2697) the net response rate was 32.9% (791/(791+[0.598 × 2697]). Almost 60% of the respondents were male, 75.3% were white, and the mean age was 71 years (SD=11.8) (Table 2). Almost all had at least some college education. Seventy-eight percent of the patients took apixaban for atrial fibrillation, 22.8% for blood clots, and 10.8% for stroke (some had more than one indication). Most had been on apixaban for more than 12 months, and 34.8% had previously been on warfarin.

Dietary supplement use

Daily or most days use of dietary supplements was reported by 618 patients (78.1%). The most common dietary supplements taken daily or on most days were vitamin D and/or calcium (n=421; 53.2%), followed by multivitamins (n=310; 39.2%). Other commonly used supplements were fish oil / omega-3 fatty acids / cod liver oil (n=176; 22.3%); B vitamins (n=100; 12.6%); vitamin E (n=82; 10.4%); vitamin C (n=59; 7.5%); magnesium, melatonin, and other herbal supplements (each with n=48; 6.1%); and coenzyme Q10 (n=41; 5.2%). All other dietary supplements were taken by fewer than 5% of respondents. The majority of patients n=709 (89.6%) reported at least occasional use of one or more dietary supplements; 618 (78.1%) reported daily use of at least one dietary supplement.

The most commonly taken dietary supplements with potential apixaban interactions of increased bleeding were herbal teas[21, 22] (n=88; 11.1%) and turmeric[23–26] (n=71; 9%) (Figure 1). Chinese herbs, ginger, gingko biloba were used in fewer than 5% of respondents. Use of St. John's wort was rare (<1%).

Aspirin and NSAID use

Aspirin was taken daily by 116 (14.7%) patients and some days or as needed by an additional 82 (10.4%). For 41 of the 116 daily aspirin users, aspirin was the only potentially serious interacting OTC product that they consumed (5.2% of the total sample). Twenty (17.2%) daily aspirin users had daily or most days use of at least one other OTC product with potentially serious interactions (either dietary supplements or NSAIDs). An additional 58 (50%) of daily aspirin users took apixaban in combination with another OTC product that increases bleeding risk some of the time or as needed. In total, 75 (64.7%) of daily aspirin users taking apixaban also at least occasionally consumed OTC products that are known to increase the risk of bleeding. Few took ibuprofen/naproxen daily (n=5; 0.6%) or most days (n=9; 1.1%), but 25 (3.2%) used them on some days and 200 (25.4%) as needed. Most people took acetaminophen as needed (n=403; 51.1%) or not at all (n=268; 34%).

Overall Use of OTC products (OTC medications and dietary supplements) with potentially serious interactions with apixaban.

One-third (n=266) of the respondents reported taking at least one OTC product with potentially serious interactions with apixaban either daily or most days. Two hundred and thirteen (27%) took only one product daily or most days; of these 95 (44.6%) took only aspirin. Forty-one (5.2%) took 2 OTC products daily or most days, 11 (1.4%) took 3, and 1 (0.13%) took 4. An additional 215 (27.2%) took an OTC product with potentially serious apixaban interactions some days or as needed. Twenty percent (n=160) of patients were regularly taking a dietary supplement with a potentially serious interaction with apixaban.

Knowledge about apixaban and potential apixaban-OTC product interactions

Patients who regularly (daily or most days) took any OTC product with potentially serious interactions with apixaban were less knowledgeable about potential OTC interactions than those not taking one regularly ($p<0.01$). Of all surveyed patients, 71% recognized that potential bleeding might occur with concurrent aspirin use, whereas only about half responded correctly to questions about potential interactions between apixaban and NSAIDs or acetaminophen. Two-thirds of respondents were either uncertain or incorrect about the potential increased bleeding risk with combined NSAIDs and apixaban.

Knowledge regarding interactions of aspirin with apixaban was significantly better in non-regular aspirin users than in regular users (74% compared to 55.5% with accurate knowledge; $p<0.001$), but 22 to 29% of each group were uncertain of whether aspirin increased bleeding risk (Figure 2). Differences in knowledge between regular NSAID users and non-regular users were similar to that for aspirin, with more non-regular users aware of the interaction compared to regular users (46% versus 28%, respectively; $p=0.01$) (Figure 2).

Of respondents taking St. John's wort, 10.5% incorrectly believed there was a potential increased risk of bleeding if it was combined with apixaban (the interaction results in decreased apixaban concentrations and potentially increases stroke risk), 79.8% were uncertain if there was an interaction and 9.7% believed there was no interaction. We asked 61 of 83 participants who were regularly taking Chinese herbs, ginger, gingko biloba, herbal teas, or turmeric (dietary supplements with potentially serious interactions with apixaban) about whether the product(s) they were taking might lead them to bleed more easily when taken with apixaban. Only 3 participants agreed that herbal teas might interact with apixaban, and 3 agreed that turmeric might interact. All others were either unsure, disagreed, or strongly disagreed that potential interactions might occur. No significant differences in knowledge were detected in patients reporting prior warfarin use compared to those without prior warfarin use.

Healthcare Professional Discussions regarding Potential OTC Product-Apixaban Interactions.

Two-thirds of the respondents reported talking to a health care professional(s) about whether it was okay to take an OTC with apixaban; 93% spoke with physicians, 46% with pharmacists, 16% with nurses, and 5% with other health care professionals. Those who reported discussing OTC products with healthcare providers were significantly more knowledgeable about potential interactions with NSAIDs than those who did not ($p<0.001$), but there were no significant differences in knowledge about potential interactions with aspirin, St. John's wort, or fish oil.

Relationship of Knowledge on Use of OTC Products with Potentially Serious Apixaban Interactions

Multivariable analyses revealed that regular use of aspirin and NSAIDs occurred significantly more often when respondents were less knowledgeable about whether potential interactions existed between apixaban and aspirin, NSAIDs, St. John's wort, or acetaminophen (OR 0.18; 95% CI=0.10–0.32), and when they were female (OR 0.37; 95% CI=0.23–0.60). Greater health literacy (OR 1.37; 95% CI=1.07–1.74), previous warfarin use (OR 1.61; 95% CI=1.06–2.44), and more prescription medication use (OR 1.12; 95% CI=1.05–1.20) were negatively associated with regular aspirin and NSAID use. Regular use of dietary supplements was not associated with knowledge about potential interactions. The only characteristic significantly associated with regular use of all assessed OTC products with potentially serious apixaban interactions was less knowledge about whether or not there were potential interactions between apixaban and aspirin, NSAIDs, St. John's wort, and acetaminophen (OR=0.54; 95% CI=0.35 – 0.85). Sensitivity analyses that excluded acetaminophen from the mean knowledge score gave similar results for all outcomes assessed.

DISCUSSION

In this cross-sectional study of apixaban patients, about one-third of respondents reported regular use of OTC products that may interact with apixaban to increase bleeding, and an additional 27% reported that they at least occasionally took these products. Twenty percent

of patients were regularly taking dietary supplements with potentially serious apixaban interactions. Knowledge about potential OTC product-apixaban interactions was a major factor associated with lower rates of use of potentially interacting OTC products, but explained only a small amount of the variation between users and non-users. Overall, knowledge regarding potential interactions was low.

The most commonly used OTC medication was aspirin. Over half of the patients taking aspirin on a regular basis accurately recognized its potential for increased bleeding when taken with apixaban, as did almost 30% of patients taking NSAIDs. We did not collect information about the reason for participants' aspirin use, but it is likely that some were taking aspirin daily for primary or secondary prevention of cardiovascular disease. Perhaps more importantly, almost two-thirds of daily aspirin users also consumed other OTC products that further increase the risk of bleeding in combination with apixaban. As emerging data on aspirin suggests that its use for primary prevention in older patients is controversial and may be associated with greater harm from bleeding than cardiovascular benefit,[27–29] additional considerations regarding aspirin use is important.

Regular NSAID use was very low in the patients surveyed. We do not know if providers told patients to avoid regular NSAID use, nor did we ask about the reasons for patient NSAID use. However, patients who reported talking to a healthcare provider about taking an OTC product with apixaban knew more about the potential for interactions between NSAIDs and apixaban. Knowledge about other potential interactions was unrelated to discussions with healthcare providers, suggesting that patients may not have asked about other OTC products. Potentially problematic OTC product-DOAC interactions may not be recognized by clinicians because patients typically do not tell their providers before or after they start taking OTC products,[30–39] either because patients take these products sporadically or because they believe that OTC products are safe.[39–41]

Patients who have taken OTC medications or dietary supplements without any problems prior to starting apixaban may not consider potential interactions, particularly if they ingest the supplements as part of their diet. For example, certain ethnic groups may regularly incorporate dietary supplements such as turmeric and Chinese herbs in their meals, and unless providers ask them, patients may not realize they are important to disclose. Information about potential interactions with more commonly used OTC products such as about turmeric, herbal teas, Chinese herbs, ginger, and gingko biloba is not on the FDA-approved prescribing information or package insert for apixaban, as opposed to St. John's wort,[18] which was rarely taken by patients. As provider queries about dietary supplements have been shown to be a primary driver of patient disclosure of supplement use,[30] it is important for providers to ask patients about their OTC product intake and provide information about potential interactions.

This study has several limitations. The response rate of 33% may limit the generalizability of the study. OTC product use was based on self-report and is limited by participant recall, and we asked only about use of selected dietary supplements. We also only asked about knowledge of potential interactions between selected OTC products and apixaban. We only asked a subset of participants about knowledge of all dietary supplements with potentially

serious interactions with apixaban, such as about Chinese herbs, garlic, ginger, gingko biloba, herbal teas, and turmeric. In addition, we did not assess the dosing of OTC products or the reasons for aspirin use. In many cases, aspirin may have been recommended by a provider, and would have been appropriate for the patient's clinical situation. Respondents were not asked what OTC products they discussed with their providers.

DOAC use is increasing, as is OTC medication and dietary supplement use. New OTC products are constantly being adopted by patients.[42] This study demonstrates that patients have limited knowledge about potential serious interactions between OTC products and apixaban. Finally, as our goal was to address OTC product use, we did not address potential interactions with prescription medications. Future work should explore the adverse events that may result from these potential interactions. Healthcare providers must screen patients for OTC product use, educate patients about the potential harms of taking certain OTC products with apixaban or other anticoagulants, and report adverse events resulting from concomitant use of these products.

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2. ***Author Contributions.*** Study concept and design: Drs. Tarn, Fang and Schwartz; acquisition of data: Drs. Tarn and Schwartz, Ms. Barrientos and Wang, and Mr. Ramaprasad; analysis and interpretation of data: Drs. Tarn and Schwartz, Ms. Barrientos; manuscript preparation and revisions: all authors.

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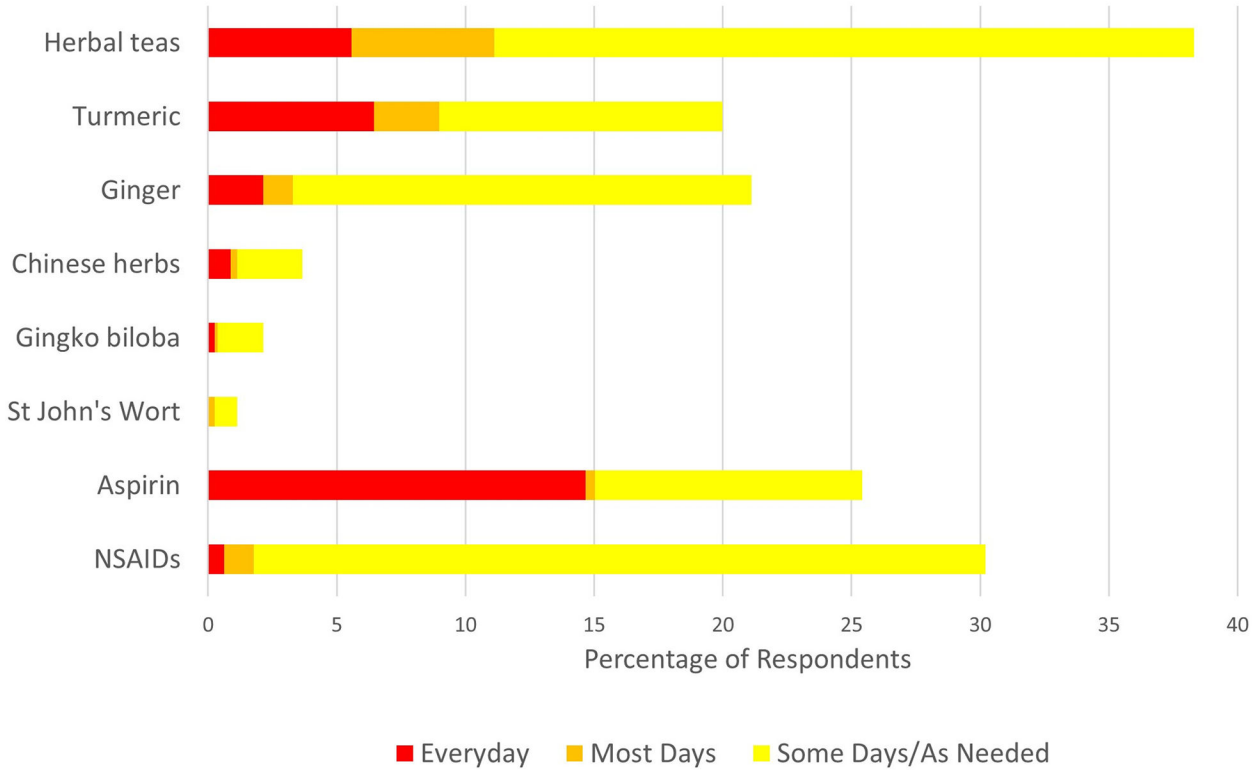

Figure 1. Frequency of Use of OTC Products with Potentially Serious Interactions with Apixaban.

Percentage of respondents (n=791) who used dietary supplements or OTC medications with potentially serious interactions with apixaban are shown with red indicating everyday use, orange indicating use on most days, and yellow representing use on some days or as needed.

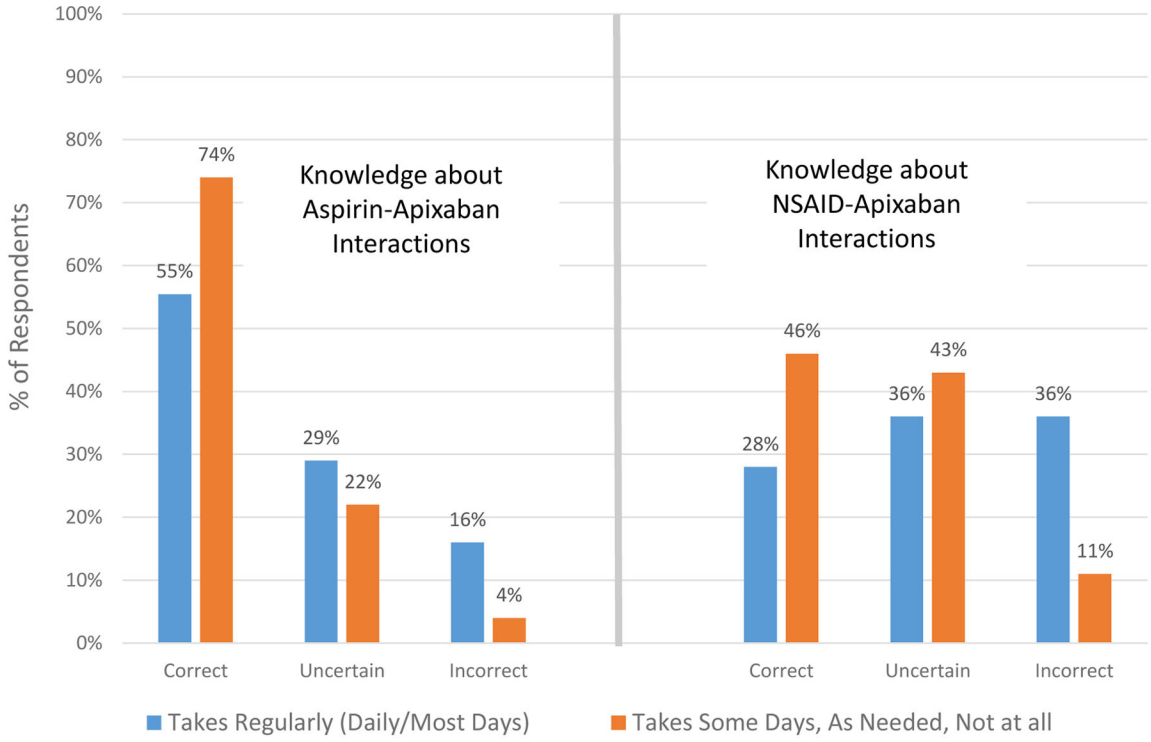

Figure 2. Knowledge about Potentially Serious Aspirin-Apixaban and NSAIDs-Apixaban Interactions in Relation to Respondent Use of Aspirin and NSAIDs.

The left panel presents respondent knowledge about aspirin-apixaban interactions and the right panel presents respondent knowledge about NSAID-apixaban interactions. Blue bars represent respondents who reported taking the OTC product with apixaban daily or on most days (n=119 for aspirin; n=14 for NSAIDs); orange bars represent respondents who reported they did not take the OTC product with apixaban or took it only some days or as needed (n=664 for aspirin; n=767 for NSAIDs).

Table 1.

Major potential over-the-counter product and apixaban interactions[19, 20]

	Potentially increases bleeding risk	Increases bleeding risk[e]	Decreases Effect	Database Recommendation[19, 20]	FDA approved Package Insert[18]
OTC Products					
Chinese Herbs[a]	x			Consider therapy modification	----
Ginger	x			Consider therapy modification	----
Gingko biloba	x			Consider therapy modification	----
Herbal Teas[b]	x			Consider therapy modification	----
St. John's wort			x	Avoid Concomitant Use	Avoid Concomitant Use
Turmeric	x			Consider therapy modification	----
Aspirin		x		Consider therapy modification	Increases bleeding risk
NSAIDs		x		Monitor closely	Increases bleeding risk
Prescription Medications					
Clopidogrel		x		Consider therapy modification	Increases bleeding risk
Mifepristone		x		Avoid Concomitant Use	----
Prasugrel, ticagralor		x		US: consider therapy modification: Canada: Avoid Concomitant Use	Increases bleeding risk
Progestins, higher dose estrogens			x	Consider therapy modification	----
SSRI, SNRI		x		Monitor	Increases bleeding risk
Vorapaxar		x		Avoid Concomitant Use	----
Other DOACs, heparins, warfarin, thrombolytics		x		Avoid Concomitant Use	Increases bleeding risk
Strong CYP3A4-Pgp Inducers[c]			x	Avoid Concomitant Use	Avoid Concomitant Use
Strong CYP3A4-PgP inhibitors[d]	x			Consider therapy modification	Reduce dose (NVAF)

SSRI=selective serotonin reuptake inhibitor, SNRI= selective serotonin and norepinephrine reuptake inhibitor.

[a]Chinese herbs include products such as danshen, dong quai and ginseng

[b]Herbal teas include green and chamomile tea

[c]Rifampin, rifabutin, phenytoin, carbamazepine

[d]Azoles, numerous retroviral agents (indinavir and ritonavir, lopinavir and ritonavir, paritaprevir and ritonavir, ombitasvir and/or dasabuvir, ritonavir, saquinavir and ritonavir, telaprevir danoprevir and ritonavir, elvitegravir and ritonavir, boceprevir), conivaptan, grapefruit juice, troleandomycin, cobicistat

[e]Herbs and supplements variably reported to increase bleeding risk: fish oil, vitamin E, flaxseed, melatonin, saw palmetto, alfalfa, anise, bilberry, bladderwrack, bromelain, cat's claw, celery, coleus, cordyceps, dong quai, evening primrose, fenugreek, feverfew, garlic, grape seed, guggul, horse chestnuts, horseradish, licorice, prickly ash, red clover, reishi mushroom, SAMe (S-adenosylmethionine), sweet clover, taurine, white willow. No interactions identified: vitamin D or calcium, acetaminophen, multivitamins

Table 2.

Patient and prescription medication use characteristics, n=791

Characteristic	
Age, mean (SD); range	71 (11.8); 25–99
Gender, n (%)	
Female sex	315 (39.8)
Male sex	472 (59.6)
Other or unknown	4 (0.6)
Race, n (%)	
American Indian/Alaskan Native	2 (0.3)
Asian	80 (10.1)
Black or African-American	38 (4.8)
Multiple races	14 (1.8)
Native Hawaiian/Other Pacific Islander	8 (1.0)
White	596 (75.3)
Unknown	53 (6.7)
Hispanic/Latino, n (%)	62 (7.8)
Education, n (%)	
High school graduate or less	52 (6.6)
Some college or 2-yr college	167 (21.1)
College graduate or above	566 (71.6)
Unknown	6 (0.7)
Self-reported health, mean (SD) *	3.05 (0.88)
Number of prescription medications, mean (SD), range	5.4 (2.9); 1–15
Health literacy, mean (SD) *	4.3 (0.94)
Reason for apixaban use, n (%)	
Atrial fibrillation	621 (78.5)
Blood clot	180 (22.8)
Stroke	85 (10.8)
After hip/knee surgery	3 (0.4)
Uncertain	5 (0.6)
Other	18 (2.3)
Duration of apixaban use	
1–6 months	36 (4.5)
7–12 months	113 (14.3)
More than 12 months	642 (81.2)
Prior warfarin use	
Yes	275 (34.8)
No	502 (63.5)

Characteristic	
Unsure	13 (1.6)

*Self-reported health and health literacy range from 1–5, with greater numbers indicating better health and greater health literacy