2018

Therapeutic Inertia in Stroke Prevention

Gustavo Saposnik

Therapeutic Decisions in Atrial Fibrillation for Stroke Prevention: The Role of Aversion to Ambiguity and Physicians' Risk Preferences

Luciano A. Sposato, MD,[*,†,‡,§] Devin Stirling,[‖] and Gustavo Saposnik, MD[¶,#,**]

Background: Knowledge-to-action gaps influence therapeutic decisions in atrial fibrillation (AF). Physician-related factors are common, but the least studied. We evaluated the prevalence and determinants of physician-related factors and knowledge-to-action gaps among physicians involved in the management of AF patients. *Design:* In this cross-sectional study, participants from 6 South American countries recruited during an educational program answered questions regarding 16 case scenarios of patients with AF and completed experiments assessing 3 outcome measures: therapeutic inertia, herding, and errors in risk stratification knowledge translated into action (ERSKTA) based on commonly used stratification tools (Congestive heart failure, Hypertension, Age ≥75 years (double), Diabetes mellitus, previous Stroke/transient ischemic attack/thromboembolism (double), Vascular disease, Age 65-74 years, and female gender (score of 0 for males and 1 for female) (CHA_2DS_2-VASc) and Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, and previous Stroke/transient ischemic attack (double) ($CHADS_2$)). Logistic regression analysis was conducted to determine factors associated with the outcomes. *Results:* Overall, 149 physicians were invited to participate, of which 88 (59.1%) completed the online assessment tool. Cardiology was the most frequent specialty (69.3%). Therapeutic inertia was present in 53 participants (60.2%), herding in 66 (75.0%), and ERSKTA in 46 (52.3%). Therapeutic inertia was inversely associated with willingness to take financial risks (odds ratio [OR] .72, 95% confidence interval [CI] .59-.89 per point in the financial risk propensity score), herding was associated with aversion to ambiguity in the medical domain (OR 5.35, 95% CI 1.40-20.46), and ERSKTA was associated with the willingness to take risks (OR

From the *Department of Clinical Neurological Sciences; †Stroke Dementia and Heart Disease Laboratory; ‡Department of Epidemiology and Biostatistics; §Department of Anatomy and Cell Biology; ‖Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada; ¶Division of Neurology, Department of Medicine; #Stroke Outcome Research Center, Division of Neurology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada; and **Laboratory for Social and Neural Systems Research, Department of Economics, University of Zurich, Zurich, Switzerland.

Received January 15, 2018; revision received February 24, 2018; accepted March 9, 2018.

Grant support: This study was partially supported by an unrestricted grant from Boehringer Ingelheim, South American Division. L.A.S. is supported by the Kathleen & Dr Henry Barnett Research Chair in Stroke Research, the Edward and Alma Saraydar Neurosciences Fund, and the Opportunities Fund of the Academic Health Sciences Center Alternative Funding Plan of the Academic Medical Organization of Southwestern Ontario (AMOSO). Dr. Gustavo Saposnik is supported by the Heart and Stroke Foundation of Canada Scientist Award following an open peer-reviewed competition.

Conflict of interest: L.A.S. has received research support from Boehringer Ingelheim, and speaker honoraria from Boehringer Ingelheim and Pfizer. G.S. has received research funds from Boehringer Ingelheim, Roche Pharma (Spain), and HOFFMAN La Roche (Canada), and speaker honoraria from Boehringer Ingelheim.

Address correspondence to Gustavo Saposnik, MD, Stroke Outcomes and Decision Neuroscience Research Unit, Department of Medicine, St. Michael's Hospital, University of Toronto, 55 Queen St E, Suite 931, Toronto, Ontario, M5C 1R6, Canada. E-mail: saposnikg@smh.ca.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.03.005

1.70, 95% CI 1.15-2.50, per point in score). *Conclusions:* Among physicians involved in stroke prevention in AF, individual risk preferences and aversion to ambiguity lead to therapeutic inertia, herding, and errors in risk stratification and subsequent use of oral anticoagulants. Educational interventions, including formal training in risk management and decision-making are needed. **Key Words:** Atrial fibrillation—decision-making—uncertainty—stroke—herding—risk aversion.

Atrial fibrillation (AF) is an extremely common arrhythmia, affecting an estimated 33.5 million people worldwide.[1] It has been long established that patients with AF are exposed to an increased risk of stroke, as well as cardiovascular mortality.[2] Despite substantial evidence showing that anticoagulation based on risk stratification decreases the incident risk of ischemic stroke, AF remains undertreated.[3] Given the rising prevalence of AF with age and the population aging, it is crucial to understand factors influencing the decision-making process.

Several factors related to physicians' individual perceptions can affect medical decision-making. These are common to a wide spectrum of disciplines and medical specialties,[4] and have a substantial impact on diagnostic accuracy, medical management, and outcomes.[5] Therapeutic inertia[6-8] and, to a lower extent, herding,[9] have been the focus of research in recent years and have been found to be prevalent among health-care professionals. Other factors, which are more specific to a given disease, can also influence decision-making. It is well established that risk stratification using available scores is the crucial first step when deciding on oral anticoagulation.[10] Risk stratification scores are regarded as highly valuable heuristic tools to facilitate medical decisions. However, they are commonly underused. In a cohort of Canadian family physicians responsible for prescribing oral anticoagulants (OACs), a stratification risk score was applied among only 43% of the patients.[11] Another challenge resulting from the use of risk stratification scores is translating the results into action, a phenomenon known as "knowledge-to-action gap." Specifically, in the case of stroke prevention in AF (SPAF), the risk stratification knowledge subsequently translated into action encompasses the knowledge about which score strata warrant the use of OACs (e.g., OACs are indicated in male patients with a Congestive heart failure, Hypertension, Age ≥75 years (double), Diabetes mellitus, previous Stroke/transient ischemic attack/thromboembolism (double), Vascular disease, Age 65-74 years, and female gender (score of 0 for males and 1 for female) (CHA_2DS_2-VASc) score >1)[12] and the ensuing action of prescribing the drug.

We aimed to estimate the prevalence of therapeutic inertia, herding, and errors in risk stratification knowledge translated into action (ERSKTA) among regular prescribers of OAC for SPAF, and to identify their associated factors.

Methods

Study Population

The study population comprised physicians from 6 South American countries attending an anticoagulation educational program in Chile. Participants completed an online survey before the event. Participants were invited by Boehringer Ingelheim, the sponsor of the meeting, based on several factors including being opinion leaders in the region, seeing a high volume of patients with AF, or being recognized specialists in their own countries.

Assessment Tools

The study comprised 3 components,[1] including (1) demographic and practical information regarding participants' clinical practice (e.g., specialty, academic versus nonacademic center, outpatient versus inpatient practice, country, mean number of AF patients seen per month)[2]; (2) 16 case scenarios comprising questions regarding risk assessment; and (3) a survey to assess the propensity to take risks and uncertainty aversion. The case scenarios were developed based on risk stratification using CHA_2DS_2-VASc[12] and $CHADS_2$[13] scores. They were prepared considering that the correct decision to anticoagulate did not change whether participants used CHA_2DS_2-VASc or $CHADS_2$ scores. Participants were provided with clinical data, and they were asked to decide whether anticoagulation was indicated for each case scenario to mimic their standard practice. They were allowed to use any tool as they do in their routine clinical practice. Given that poor knowledge about SPAF could impact on ERSKTA, we included 3 case scenarios to determine the proportion of knowledge-to-action care gaps based on the most updated guidelines on the management of AF.[14] ERSKTA is a proxy measure of medical errors[3]; a validated behavioral battery, as defined in our previous studies, was incorporated to determine participants' willingness to take risks (e.g., driving, financial, sports, work, health, and meeting new people), and aversion to uncertainty.[7,15] In addition, we included 3 additional questions regarding (1) confidence when using direct oral anticoagulants (DOACs), (2) satisfaction with the

available time they had in their clinical practice to discuss with their patients about the benefits and risks of anticoagulation, and (3) satisfaction with available information for prescribing DOACs.

Definitions

Therapeutic inertia is defined as the failure of a health-care practitioner to modify a therapy according to what it is recommended as standard of care (initiation, intensification, or reduction).[15] In the care of patients with AF, the failure of a physician to prescribe an OAC when it is indicated (and in the absence of contraindications) would be considered therapeutic inertia.

Herding is described as the phenomena whereby a physician follows the recommendation of a colleague or group rather than using his or her own judgment, even if scientific evidence suggests the opposite.[9] A family physician continuing an improper stroke prevention regimen because it was previously prescribed by a neurologist who appears to be more qualified would be regarded as herding.

ERSKTA involves a stepwise decision-making process that requires, firstly, correct risk stratification. This is followed by the selection of the best therapeutic approach for that patient based on his or her specific risk stratum. ERSKTA can arise because of either errors in stratification or because of the failure to provide the correct treatment, or both. For instance, health-care providers taking care of patients with AF can have ERKSTA because they fail in the risk stratification process (e.g., not formally using a risk stratification score leading to an erroneous subjective estimation of the risk of stroke). ERKSTA can be also the consequence of the lack of the necessary knowledge about what to do in the case of a given risk (e.g., not knowing that patients with a CHA_2DS_2-VASc score of 2 requires oral anticoagulation). Indeed, ERKSTA can arise from the failure to integrate both components of this decision-making process, also known as knowledge to action gap.

Ambiguity aversion was defined as the preference for choices of known probabilities over choices of unknown probabilities.[16] For assessing ambiguity aversion, participants were asked to choose between a visual option with known 50/50 probability of winning 400 or 0 dollars and an option with unknown probability of the same outcomes (represented by a gray bar; Fig 1). Each participant faced 9 pairs of choices (50/50 option versus the increasing proportion of uncertainty). The degree of uncertainty aversion was defined as the proportion of times participants chose the 50/50 option over the uncertain option involving the same outcomes. Total aversion to ambiguity was defined as participant's selection of the 50/50 option for all 9 choices (Fig 1). Similarly, aversion to risk and ambiguity in the health domains were assessed using the same visual tools.[15] Participants were asked to choose between Treatment A (50% probability of survival) or "Treatment B" (the probability of survival is unknown), with the gray bars quantifying how much is unknown about the probability of survival. A more detailed explanation about this tool is presented in the supplemental online file.

Willingness to take risks was assessed according to the German Socio-Economic Panel study (SOEP).[17] The SOEP is a validated survey that assesses participants' willingness to take risks in different domains (financial matters, own health, driving, own occupation, etc.). We used questions as: "How would you rate your willingness to take risks in the following areas. . .."? Areas included financial matters, driving, occupation, and so on, and responses could range from 0 (not at all) to 10 (very much).

Participants' preferences toward OACs were self-reported using a Likert rating scale (e.g., ranging from 0—not comfortable to 10—very comfortable-).[18] Answers were classified as "confident" or "satisfied" if their value was higher than 6.

Outcome Measures

The main outcome measures were the prevalence of therapeutic inertia, herding, and ERSKTA. There were 3 case scenarios to assess the prevalence of herding, another 3 case scenarios to assess the prevalence of therapeutic inertia, and 5 different cases for ERSKTA. Secondary outcomes included factors associated with therapeutic inertia, herding, and ERSKTA.

Statistical Analysis

We determined the prevalence of each of the main outcome measures. We established that each outcome measure was present when at least 1 of the answers to the respective cases was wrong. To provide a more detailed report of their prevalence, we also stratified the results into the number of wrong answers over the total number of questions for each outcome. We performed univariable analyses to identify variables associated with each of the outcome measures. We used a threshold of alpha of less than .02. We further used forward stepwise logistic regression models to identify variables independently associated with the 3 outcomes. All scores were entered as continuous variables. We included the age[19] of participants and monthly volume of AF patients seen[20] in all the regression models because these variables have been previously shown to influence prescribing decisions.

Results

Overall, 149 physicians attending an anticoagulation and thrombosis educational program were invited to participate, of which 88 (59.1%) completed the online assessment tool (completion rate: 59%). Characteristics of the study participants are summarized in Table 1. The mean age

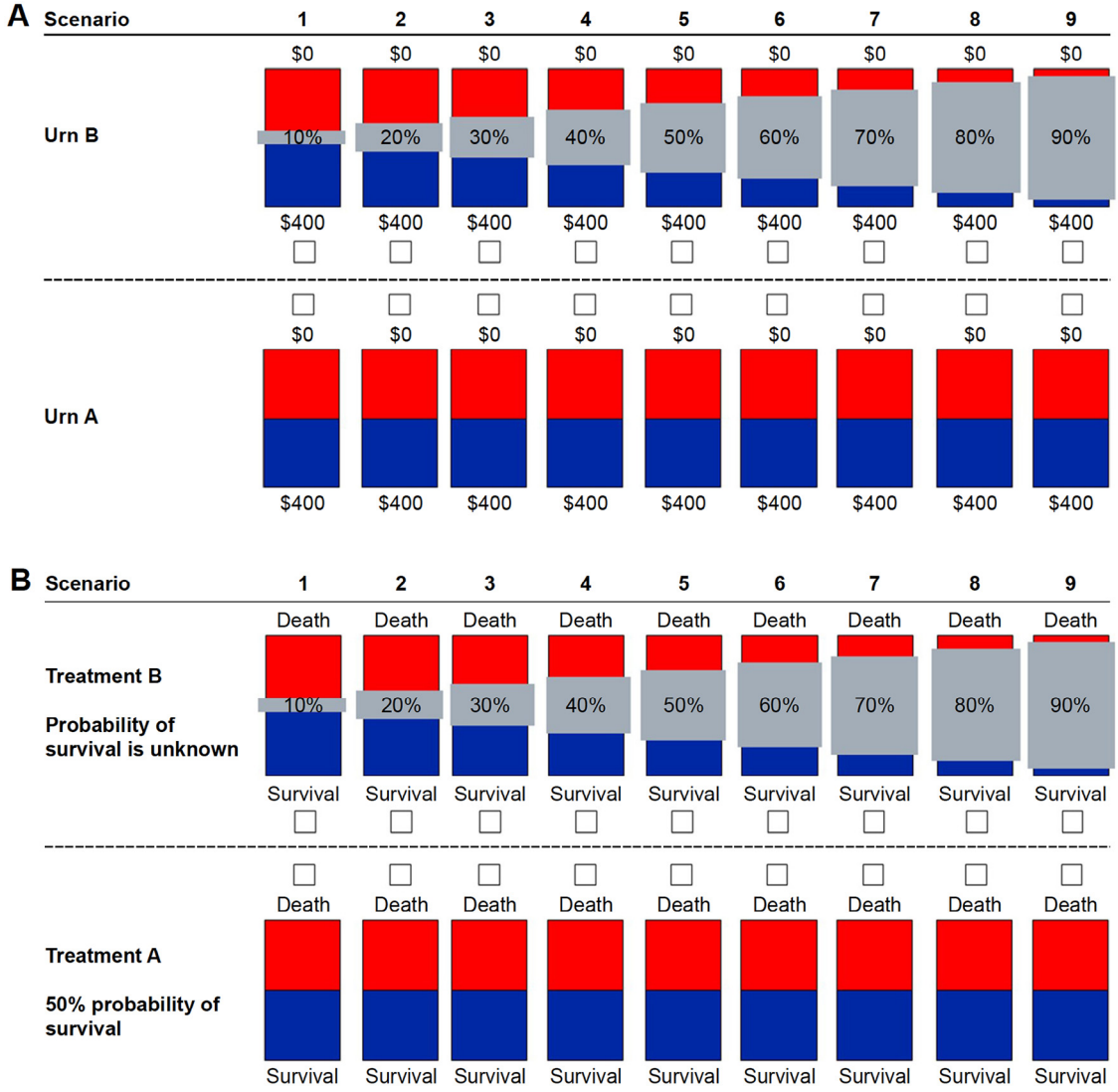

Figure 1. *Assessment of aversion to ambiguity in the Financial and Health domains. (A) Ambiguity aversion in the financial domain. (B) Ambiguity aversion in the health domain. The gray bar represents the degree of uncertainty (unknown probability) ranging from 10% (scenario 1). (Color version of figure is available online.)*

was 47 with a predominance of male physicians (85.2%). Cardiology was the most frequent specialty (69.3%). Most participants worked in both outpatient and inpatient settings (58.0%). Only 37.5% of physicians worked exclusively in nonacademic centers.

Participants' knowledge of SPAF and level of comfort with DOAC use, willingness to take risks, and aversion to medical ambiguity are summarized in Table 2. No participant answered 100% of the SPAF knowledge cases correctly. Overall, 81 physicians (92.0%) expressed that they felt confident about prescribing DOACs.

The prevalence of each outcome and the proportion of incorrect answers for each of the 3 decision-making outcomes are shown in Figure 2. Therapeutic inertia was present in 53 participants (60.2%), whereas negative herding and ERSKTA were observed in 66 (75.0%) and 46 (52.3%) participants, respectively. Table 3 summarizes the regression analyses for the variables independently associated with each of the outcomes. Therapeutic inertia was inversely associated with willingness to take financial risks (odds ratio [OR] .72, 95% confidence interval [CI] .59-.89 per point in the financial risk propensity score). Herding was associated with aversion to ambiguity in the medical domain (OR 5.35, 95% CI 1.40-20.46). ERSKTA was associated with the overall score of willingness to take risks (OR 1.70, 95% CI 1.15-2.50, per point in score).

Discussion

Risk stratification and physicians' individual risk preferences are key factors in the management of AF for stroke prevention. This study evaluated the influence of risk preferences among 88 regular prescribers of OAC for SPAF from South America. Our study showed that 6 of 10 par-

Table 1. *Characteristics of study participants*

Demographics	
Age, mean (SD)	47[10]
Male sex, n (%)	75 (85.2)
Specialty	
Cardiology, n (%)	61 (69.3)
Medicine, n (%)	18 (20.5)
Emergentology, n (%)	5 (5.7)
Other, n (%)	2 (2.3)
Practice setting	
Outpatients, n (%)	24 (27.3)
Inpatients, n (%)	13 (14.8)
Both, n (%)	51 (58.0)
Type of center	
Academic, n (%)	26 (29.5)
Nonacademic, n (%)	33 (37.5)
Both, n (%)	26 (29.5)
Other, n (%)	3 (3.4)
Volume of AF patients seen per month, mean (SD)	22.0 (18.0)

Abbreviations: AF, atrial fibrillation; SD, standard deviation.

Table 2. *SPAF knowledge, OAC use, risk propensity, and aversion to uncertainty*

Variable	Frequency
SPAF knowledge	
All questions correct, n (%)	0 (.0)
1 of 3 questions wrong, n (%)	43 (48.9)
2 of 3 questions wrong, n (%)	38 (43.2)
3 of 3 questions wrong, n (%)	7 (8.0)
Perceptions about DOAC use	
Satisfaction with available data about DOAC, n (%)	65 (73.9)
Satisfaction with available data about DOAC, mean (SD)	7.2 (2.7)
Confident prescribing DOAC, n (%)	81 (92.0)
Confident prescribing DOAC, mean (SD)	8.2 (1.5)
Satisfaction with available time to inform patient about OACs, n (%)	61 (69.3)
Satisfaction with available time to inform patient about OACs, mean (SD)	7.4 (2.1)
Willingness to take risk and aversion to ambiguity	
Risk propensity, n (%)	43 (48.9)
Risk propensity score, mean (SD)	2.5 (1.4)
Financial risk propensity, n (%)	20.0 (22.7)
Financial risk propensity score, mean (SD)	4.6 (2.3)
Financial ambiguity aversion, n (%)	21 (23.9)
Financial ambiguity aversion score, mean (SD)	14.6 (2.6)
Ambiguity averse, n (%)	32 (36.4)
Medical ambiguity aversion score, mean (SD)	15.3 (2.7)

Abbreviations: DOAC, direct oral anticoagulant; OAC, oral anticoagulants; SD, standard deviation; SPAF, stroke prevention in atrial fibrillation.

ticipants exhibited therapeutic inertia. Half of participants were not able to correctly establish whether patients should receive OACs because of errors in the estimation of the associated risk of ischemic stroke and the subsequent translation of the meaning of that risk into the action of using OACs. Finally, 3 out of 4 participants tended to follow improper advice (although perceived more expert), therefore not adhering to the recommended treatment guidelines for stroke prevention. Therapeutic inertia and ERSKTA were independently associated with the participants' willingness to take risks, whereas herding was related to aversion to ambiguity.

The prevalence of therapeutic inertia among South American physicians was surprisingly high (60.2%) compared with Canadian family physicians (23.3%) undertaken in a similar survey for SPAF.[21] Understandably, physicians who are willing to take risks are the ones among whom therapeutic inertia is less prevalent. For instance, in a case of a male subject whose CHA_2DS_2-VASc score changed from 1 to 3 after being diagnosed with systemic hypertension and because of being older, some physicians may wrongly feel reluctant to initiate OACs if that patient had been well and free of vascular events during the last 10 years. Another potential explanation is that physicians may have failed to incorporate the updated information provided in the case scenarios about the patients' statuses to recalculate the risk scores.

The association between herding behavior and aversion to uncertainty supports that, under conditions of greater uncertainty, health-care providers tend to trust the opinion of other colleagues rather than their own judgment.[9] This was earlier proposed by Keynes, who regarded herding as a reaction to uncertainty when one's own ignorance is perceived regarding a specific topic.[22] This association has also been found in the literature on decision-making under uncertainty. Individuals who were more averse to uncertainty showed a greater degree of herding-like behavior, specifically, a preference for known brand names despite their inferior quality, possibly because they felt unfamiliar with the better quality brands, which were newer.[23] It has to be noted that, sometimes, a herding behavior may be appropriate when knowledge about the medical management of a condition is relatively poor as in this cohort. It may be less prevalent when subjects are more certain of the correct course of action. It is not unusual that a more expert physician may have additional knowledge compared with general practitioners, possibly resulting in this deferential type of herding behavior that could be seen as appropriate rather than erroneous.

An alarming number of participants failed to correctly indicate which patients required OACs in at least 1 of the 5 cases assessing ERSKTA, a proxy measure of medical

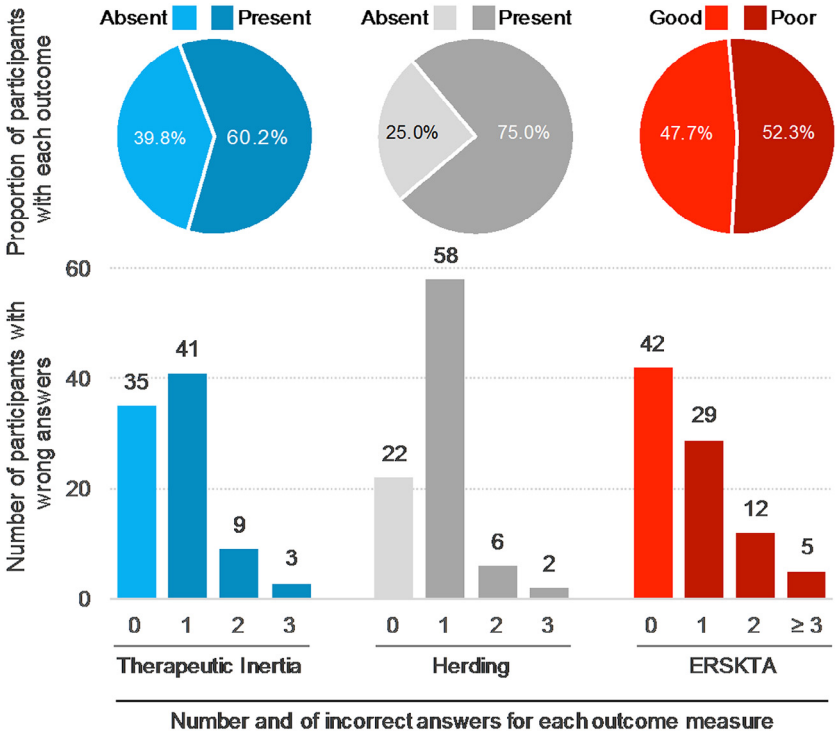

Figure 2. *Prevalence of therapeutic inertia, herding, and poor stratification leading to knowledge-to-action gaps. Abbreviation: ERKSTA, errors in risk stratification knowledge translated into action.*

errors in the management of AF. Furthermore, 20% failed in at least 2 of the 5 case scenarios. Because no participant solved all SPAF knowledge cases properly, we hypothesize that the insufficient knowledge about AF management or the integration of medical information, could have explained, at least partially, the ERSKTA. However, poor SPAF knowledge was not significantly associated with ERSKTA in the multivariable analysis. Rather, ERSKTA was associated with the overall willingness to take risk. This is intuitively reasonable, as physicians who are more

Table 3. *Factors associated with each outcome measure*

Outcome measures	Outcome present	Outcome absent	Unadjusted risk			Adjusted risk		
			OR	95% CI	*P* value	OR	95% CI	*P* value
Therapeutic inertia								
Age, years, mean (SD)	46.3 (9.8)	48.3 (9.3)	.98	.93-1.02	.34	.98	.93-1.02	.35
Monthly number of AF patients, mean (SD)	23.3 (19.7)	20.0 (15.1)	1.01	.99-1.04	.41	1.00	.98-1.04	.56
Willingness to take risk in the financial domain, mean (SD)	3.96 (2.2)	5.51 (2.2)	**.73**	**.59-0.90**	**.003**	**.72**	**.59-0.89**	**.003**
Herding								
Age, years, mean (SD)	47.4 (9.9)	46.1 (8.7)	1.01	.96-1.07	.57	1.00	.94-1.07	.90
Monthly number AF patients, mean (SD)	20.8 (17.2)	25.6 (20.2)	.99	.96-1.01	.28	.98	.95-1.01	.24
Aversion to ambiguity (health domain), n (%)	29/66 (43.9)	3/22 (13.6)	**4.96**	**1.34-18.42**	**.017**	**5.35**	**1.40-20.46**	**.014**
Errors in risk stratification knowledge translated into action (ERSKTA)								
Age, years, mean (SD)	45.4 (9.1)	49.0 (9.9)	.96	.92-1.01	.08	.96	.91-1.01	.11
Monthly number of AF patients, mean (SD)	20.1 (18.8)	24.0 (17.0)	.99	.96-1.01	.30	.98	.95-1.01	.11
Willingness to take risk (overall score), mean (SD)	2.89 (1.5)	2.0 (1.0)	**1.77**	**1.20-2.59**	**.004**	**1.70**	**1.15-2.50**	**.007**

Bold values denote significant differences. Abbreviations: AF, atrial fibrillation; CI, confidence interval; OR, odds ratio; SD, standard deviation.

risk prone may be less interested in using validated tools (CHA_2DS_2-$VASc_2$ and $CHADS_2$,) and to systematically measuring risk. Indeed, the lack of systematic use of risk scores in SPAF results in under- and overestimation of ischemic stroke risk, which can ultimately lead to errors in therapeutic decisions.[11] Yet, this hypothesis conflicts with the results of a prior study in family physicians, whose willingness to take risk in multiple domains was associated with a lower number of errors.[21]

This study has limitations. The results of this study may not be generalizable to other populations because (1) the study cohort was relatively low, (2) the proportion of physicians who accepted to participate was relatively low (59.1%), although similar to prior studies in the field (60.0%), and (3) the cohort comprised participants of a highly selected population of health-care providers (mostly cardiologists) from a specific region of the world (South America).[9] The recruitment of participants was based on selection criteria applied by the sponsor, which could have influenced our findings. However, this phenomenon is likely to underestimate the true magnitude in the "real world," given the expected underperformance of nonopinion leaders or physicians exposed to lower volume of patients with AF compared with the studied population. We cannot rule out the possibility that unmeasured confounders may have affected our results. The application of relevant concepts from decision neuroscience (neuroeconomics) into clinical care is novel and challenging. As a result, it is possible that limitations in the interpretation of these validated tests (Fig 1) may have affected our results. Finally, it is still possible that questions included in our study may have not accurately measured the variables of interest, despite using extensively validated tools.

Despite the aforementioned limitations, this study shows that a large proportion of physicians with expertise in treating patients with AF are prone to errors in their medical decision-making processes, inherent to their individual willingness to take risks, aversion to ambiguity, and their limited ability to translate risk stratification into the decision to anticoagulate. Our findings offer preliminary evidence supporting the need for specific medical education and formal training on medical decision-making processes among health-care professionals treating patients with AF in South America. This training may also need to highlight the most significant principles of oral anticoagulation in SPAF using simple and effective educational tools.[3] Individual perceptions and factors negatively influencing medical decision-making have the potential to change over time, with the latent risk of worsening without proper training.[24] With a better understanding of how they affect the process of decision-making, it may be possible to overcome these sources of medical errors, positively contributing to improving the care of AF patients and to reducing the burden of AF-related cerebrovascular disease. Future directions include the assessment of an educational program or intervention to determine the potential benefits in overcoming herding behavior, therapeutic inertia, and ERSKTA.

Acknowledgments: The authors are grateful for the support of Professors C. Ruff and P. Tobler in the design of the behavioral experiments.

Appendix: Supplementary Material

Supplementary data to this article can be found online at doi:10.1016/j.jstrokecerebrovasdis.2018.03.005.

References

1. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. Circulation 2014;129:837-847.
2. Benjamin EJ, Wolf PA, D'Agostino RB, et al. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation 1998;98:946-952.
3. Cerasuolo JO, Montero-Odasso M, Ibañez A, et al. Decision-making interventions to stop the global atrial fibrillation-related stroke tsunami. Int J Stroke 2017;12:222-228.
4. Blumenthal-Barby JS, Krieger H. Cognitive biases and heuristics in medical decision making: a critical review using a systematic search strategy. Med Decis Making 2015;35:539-557.
5. Saposnik G, Redelmeier D, Ruff CC, et al. Cognitive biases associated with medical decisions: a systematic review. BMC Med Inform Decis Mak 2016;16:138.
6. Seidu S, Than T, Kar D, et al. Therapeutic inertia amongst general practitioners with interest in diabetes. Prim Care Diabetes. 2018;12:87-91.
7. Saposnik G, Sempere AP, Raptis R, et al. Decision making under uncertainty, therapeutic inertia, and physicians' risk preferences in the management of multiple sclerosis (DIScUTIR MS). BMC Neurol 2016;16:58.
8. Nambam B, DuBose SN, Nathan BM, et al. Therapeutic inertia: underdiagnosed and undertreated hypertension in children participating in the T1D Exchange Clinic Registry. Pediatr Diabetes 2016;17:15-20.
9. Saposnik G, Maurino J, Sempere AP, et al. Herding: a new phenomenon affecting medical decision-making in multiple sclerosis care? Lessons learned from DIScUTIR MS. Patient preference and adherence. 2017;11:175-180.
10. Lip GY. The CHA(2)DS(2)-VASc score for stroke risk stratification in patients with atrial fibrillation: a brief history. Eur Heart J 2015;36:2880-2885.
11. Angaran P, Dorian P, Tan MK, et al. The Risk Stratification and Stroke Prevention Therapy Care Gap in Canadian atrial fibrillation patients. Can J Cardiol 2016;32:336-343.
12. Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. Chest 2010;137:263-272.
13. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA 2001;285:2864-2870.
14. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation

developed in collaboration with EACTS. Europace 2016;18:1609-1678.
15. Saposnik G, Maurino J, Sempere AP, et al. Overcoming therapeutic inertia in multiple sclerosis care: a pilot randomized trial applying the traffic light system in medical education. Front Neurol 2017;8:430.
16. Levy I, Snell J, Nelson AJ, et al. Neural representation of subjective value under risk and ambiguity. J Neurophysiol 2010;103:1036-1047.
17. Dohmen T, Falk A, Huffman D, et al. Individual risk attitudes: measurement, determinants, and behavioral consequences. J Eur Econ Assoc 2011;9:522-550.
18. Schoeppe F, Sommer WH, Haack M, et al. Structured reports of videofluoroscopic swallowing studies have the potential to improve overall report quality compared to free text reports. Eur Radiol 2018;28:308-315.
19. Deplanque D, Leys D, Parnetti L, et al. Stroke prevention and atrial fibrillation: reasons leading to an inappropriate management. Main results of the SAFE II study. Br J Clin Pharmacol 2004;57:798-806.
20. Aujoulat I, Jacquemin P, Rietzschel E, et al. Factors associated with clinical inertia: an integrative review. Adv Med Educ Pract 2014;5:141-147.
21. Raptis S, Chen JN, Saposnik F, et al. Aversion to ambiguity and willingness to take risks affect therapeutic decisions in managing atrial fibrillation for stroke prevention: results of a pilot study in family physicians. Patient Prefer Adherence 2017;11:1533-1539.
22. Keynes JM. A Treatise on Money. London: Macmillan, 1930.
23. Muthukrishnan AV, Wathieu L, Xu AJ. Ambiguity aversion and the preference for established brands. Manage Sci 2009;55:1933-1941.
24. Han PK, Schupack D, Daggett S, et al. Temporal changes in tolerance of uncertainty among medical students: insights from an exploratory study. Med Educ Online 2015;20:28285.