OPTIMISING THE USE OF THROMBOPROPHYLAXIS IN ATRIAL FIBRILLATION (AF):

EXPLORING FACTORS AFFECTING DECISION-MAKING

Ekta Pandya

A thesis submitted to the
University of Technology Sydney
in fulfilment of the requirements for the degree of
Master of Pharmacy (Research)
in the
Graduate School of Health - Discipline of Pharmacy

2017

I, Ekta Pandya declare that this thesis, is submitted in fulfilment of the requirements for the award of Master of Pharmacy, in the School of Pharmacy at the University of Technology Sydney.

This thesis is wholly my own work unless otherwise reference or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This document has not been submitted for qualifications at any other academic institution.
[replace this statement with collaborative degree statement if appropriate (see below)] - N/A

[insert Indigenous Cultural and Intellectual Property (ICIP) acknowledgement if appropriate (see below)] -N/A

This research is supported by the Australian Government Research Training Program.

Production Note:
Signature: Signature removed prior to publication.

Date: 22May2020

I. Abstract

The risk of stroke is five-folds higher among patients with atrial fibrillation (AF) in comparison to those without AF. In fact, thromboembolic strokes occurring in AF patients are more disabling and fatal than in patients without AF. This increase in morbidity and mortality due to stroke in patients with atrial fibrillation has become a major global healthcare burden, and for this reason stroke prevention (using antithrombotic agents as the mainstay therapy) has been a critical feature of AF management. Although warfarin (an oral vitamin K antagonist) has been traditionally used for preventing stroke in AF patients, its complex pharmacology (i.e., narrow therapeutic index requiring regular therapeutic monitoring, its interactions with food, alcohol, and other medications), and prescribers' concerns regarding patients' nonadherence to the therapy make the decision-making around the initiation of therapy quite complicated. Consequently, anticoagulants are underutilised in many 'at-risk' patients, exposing them to an increased risk of a preventable stroke. Our research in a hospital-based study that used decision-making support tool i.e., a computerised antithrombotic risk assessment tool (CARAT- a tool developed based on local and international guidelines assists in therapy selection based on patients' individualised risk versus benefit assessment) observed a marginal increase in anticoagulation prescription among eligible patients (57.8% vs 64.7%, P=0.35) in comparison to the baseline prescription. However, many at-risk patients were still not prescribed anticoagulants as recommended by CARAT, and the clinicians' agreement with CARAT recommendation was low. This might have been due to clinicians' perceived fears of risk such as falls,

bleeding, and patients' nonadherence to the therapy. To increase clinicians' acceptance for CARAT tool, studies should further explore its validity in predicting clinical outcomes.

Recently, the direct oral anticoagulants (DOACs) have become available for thromboprophylaxis in patients with AF. These agents have safety and efficacy (in stroke prevention) profiles comparable to warfarin therapy. They also offer some practical advantages over warfarin in terms of not requiring regular therapeutic drug monitoring, plus their interactions with food, alcohol and other medications is limited. However, the DOACs are not completely devoid of risks or challenges to their use. These challenges include: a) the lack of specific drug monitoring tests; b) complicated management of renally-impaired patients; c) limited access to and/or unavailability of antidotes for the management of DOAC-related acute bleeding; d) high 'out-of-pocket' costs for patients in some countries; and e) the potential for patient nonadherence (due to the more frequent dosing required with dabigatran and apixaban). Such conditions present specific challenges for clinicians when prescribing these medications for long-term stroke prophylaxis in patients with AF. In 2014 following the listing of DOACs on the pharmaceutical benefits scheme (PBS) (which subsidises DOACs for stroke prevention in AF), it was important to report their utilisation of anticoagulant prescription in local Australian settings. It was also necessary to updated CARAT 2.0 in assessing whether the prescriptions were based on these revised guidelines. Our study (in a hospital setting in Sydney) found that 52.0% of the people were prescribed anticoagulants. Warfarin was the first-choice anticoagulant prescribed for two-thirds of patients, while the remaining one-third were on DOCAs. However, most of the patients eligible for anticoagulants were not prescribed it but were either prescribed antiplatelets or kept on nil therapy.

In this thesis a structured literature review explored factors influencing patients' preference and adherence for warfarin versus DOACs. This is because research suggests that patients have an important role in the decision-making process for antithrombotic therapy selection in AF. This review discussed patients' perspectives on medications. Here the findings were synthesised to present a framework depicting the five interacting dimensions of adherence: 1) therapy-related factors; 2) patient-related factors; 3) condition-related factors; 4) social–economic factors; and 5) health system factors. From this study, it was clear that patients' views about treatment must be incorporated into the decision-making process to facilitate a) treatment; b) adherence; and c) achieve good clinical outcomes. In line with this study, another study then evaluated the information within web-based resources designed to educate patients on thromboprophylaxis in AF. The content and thematic analysis were conducted on these resources. It was found that the information provided in these resources were varied. It was found that implied bias of some resources towards specific anticoagulant therapies and their imbalanced information on the importance of anticoagulation in AF might misinform or confuse patients. Therefore, patients' engagement in shared decision-making and adherence to medicines might be undermined by the suboptimal quality of information provided in these resources.

II. Acknowledgements

I am grateful to the Graduate School of Health at the University of Technology Sydney for offering me a position in this prestigious institute.

I thank my supervisor A/Prof. Beata V. Bajorek for her guidance. I sincerely thank Elizabeth Anderson, Prof. Clara Chow, Margaret Piper, and Health Information and Services Department for their generous support and guidance during the conduct of the clinical study at Westmead Hospital.

I am indebted to my lovely husband, Dr. Yadunandan Das for his tremendous love and support in this undertaking. I would thank my grandparents and parents, Vaman Das, Vashist Pandya, Krishna Panchal, Neha Bailwal, Asha Bailwal and my extended family for checking on me when I was stressed and feeling low in Australia. I thank my colleagues and friends (Shamsher Singh Khaira, Yishen Wang, Riana Rahmawati, Daniel Sabater, Sabna Krishnan, and Sharon Wong), and friends (Mrs. Karamveer Kaur Khaira, Parthiben Sekar and Sripati Rao) for supporting me and motivating me throughout this process.

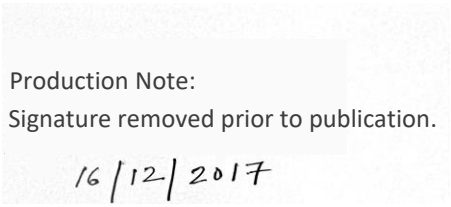
Lastly and most importantly, I would thank Lord Krishna for being so merciful, and giving me the strength and ability to understand, self-reflect and learn from this early research experience.

III. Declaration

This is to certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree, except as fully acknowledged within the text.

I also certify that the research presented in this thesis is genuine, and the outcome of my efforts. Any help that I have received for this research has been acknowledged. In addition, I certify that all information sources and literature used to undertake this research have been acknowledged properly in this thesis.

In accordance with the university-endorsed national guidelines, copy-editing and proofreading services were provided by Dr Leigh Findlay (TrueNature Writing & Editing) and Rosemary Osborne (The Writing Shed).



Signature of Student Date

Ekta Pandya

IV. Abbreviations

ACC	American College of Cardiology
AF	Atrial Fibrillation
AHA	American Heart Association
CARAT	Computerised Antithrombotic Risk Assessment Tool
CCF	Congestive Cardiac Failure
CI	Confidence Interval/s
DOACs	Direct Oral Anticoagulants
DST	Decision Support Tool/s
ESC	European Society of Cardiology
FDA	Food and Drug Administration
HRS	Heart Rhythm Society
Hx	History
NICE	National Institute for Health and Care Excellence
NOACs	Novel/ New Oral Anticoagulants **OR** Non-Vitamin K Antagonist Oral Anticoagulants *Word NOACs was used only in journal articles*
DOACs	Direct Oral Anticoagulants

	Word DOACs is used throughout the thesis expected in some articles
NSAIDs	Non-steroidal anti-inflammatory drugs
NVAF	Non-valvular atrial fibrillation
NSW	New South Wales
QoL	Quality of Life
OR	Odds Ratio
PBS	Pharmaceutical Benefits Scheme
SDM	Shared Decision-Making
SPSS	Statistical Software for Social Sciences
TAG	Therapeutic Advisory Group
TIA	Transient Ischemic Attack
TM	Trademark
Tx	Therapy/ Treatment
WATAG	Western Australian Therapeutic Advisory Group

V. List of published articles

CHAPTER 2:

Title: Impact of a Computerized Antithrombotic Risk Assessment Tool (CARAT) on the prescription of thromboprophylaxis in atrial fibrillation: hospital setting.

Authors: Ekta Pandya, Noman Masood, Yishen Wang, Ines Krass, Beata Bajorek

Publication status: Published Online in Clinical and Applied Thrombosis/ Hemostasis

DOI: 10.1177/1076029616670031

CHAPTER 3:

Title: Contemporary utilisation of antithrombotic therapy for stroke prevention in atrial fibrillation: an audit in an Australian hospital setting

Authors: Ekta Pandya, Elizabeth Anderson, Clara Chow, Yishen Wang, Beata Bajorek

Publication status: Published Online in Therapeutic Advances in Drug Safety

DOI: 10.1177/2042098617744926

CHAPTER 4:

Title: Factors affecting patients' perception on, and adherence to, anticoagulant therapy: anticipating the role of direct oral anticoagulants (DOACs)

Authors: Ekta Pandya, Beata Bajorek

Publication status: Published in The Patient- Patient Centered Outcomes

Volume: 10

Issue: 2

Page number: 163 - 185

DOI: 10.1007/s40271-016-0180-1

CHAPTER 5:

Title: Assessment of web-based education resources informing patients about stroke prevention in atrial fibrillation (AF).

Authors: Ekta Pandya, Beata Bajorek

Publication status: Published in Journal of Clinical Pharmacy and Therapeutics

Volume: 41

Issue: 6

Page number: 667 - 676

DOI: 10.1111/jcpt.12446

VI. Table of contents

VII. Table of figures