SCREENING FOR ATRIAL FIBRILLATION IN CANADIAN PHARMACIES IS A COST-EFFECTIVE STRATEGY

Jean-Eric Tarride MA PhD^{1,2}, Lisa Dolovich PharmD MSc^{3,4}, Gordon Blackhouse MSc, MBA^{1,2}, Jason Robert Guertin MSc PhD^{5,6}, Natasha Burke MSc^{1,2}, Veena Manja MD MSc^{7,8}, Alex Grinvalds BSc⁹, Ting Lim MSc⁹, Jeff S. Healey MD MSc⁹, Roopinder K. Sandhu MD MPH¹⁰

Author Affiliations:

- ¹ Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada
- ² Programs for Assessment of Technology in Health (PATH), Research Institute of St. Joseph's Hamilton, Hamilton, ON, Canada
- ³ Department of Family Medicine, McMaster University, Hamilton, ON, Canada
- ⁴ Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada
- ⁵ Department of Social and Preventive Medicine, Université Laval, Quebec City, QC, Canada
- ⁶ Centre de recherche du CHU de Québec Université Laval, Axe Santé des Populations et Pratiques Optimales en Santé, Hôpital du St-Sacrement, Québec City, QC, Canada
- ⁷ Department of Internal Medicine, State University of New York at Buffalo, Buffalo, NY, USA
- ⁸ VA Western New York Health Care System at Buffalo, Buffalo, NY, USA
- ⁹ Population Health Research Institute, McMaster University, Hamilton, ON, Canada
- ¹⁰ Division of Cardiology, University of Alberta, Edmonton, AB, Canada

Correspondence:

Jean-Eric Tarride, PhD Associate Professor, McMaster University 43 Charlton Ave E, 2nd Floor, Hamilton, ON L8N 1Y3

Tel: (905) 522-1155 ext 37021 Email: tarride@mcmaster.ca

Source of Funding: The PIAAF-Pharmacy study was supported by the Canadian Stroke Prevention Intervention Network, Boehringer Ingelheim and in-kind support from CardioComm

Declaration of Competing Interests:

JET, LD, GB, JRG, NB, VM, AG, TL, and RKS have no competing interests to declare. JSH has research grants from Boehringer Ingelheim and Bristo-Myers Squibb; and has received speaking fees from Servier.

ABSTRACT

Background

Screening for undiagnosed atrial fibrillation (AF) may lead to treatment with oral anticoagulation therapy which can decrease the risk of ischemic stroke. We conducted an economic evaluation of the Program for the Identification of 'Actionable' Atrial Fibrillation: in the Pharmacy Setting (PIAAF-Pharmacy) which screened participants 65 years or older at 30 community pharmacies in Ontario and Alberta between October 2014 and April 2015. AF screening was performed using a 30-second single lead ECG device (HeartCheck, CardioComm). A total of 1145 participants were screened and the prevalence of 'actionable' AF was 2.5% (95% CI, 1.7-3.6), of these, 93% were newly diagnosed AF. To better inform decision-makers, we conducted an economic evaluation of this program.

Methods

A two-part decision model was used to evaluate the short and long-term costs and quality-adjusted life years (QALYs) of a pharmacy screening program for AF compared to no screening. Data from the PIAAF-Pharmacy study was used for the short-term model whereas literature data were used to extrapolate the benefits of the PIAAF-Pharmacy study in the long-term model. Costs and QALYs were calculated from a payer perspective over a lifetime horizon and were discounted at 5%/year.

Results

Screening for AF in pharmacies was associated with higher costs (\$2) and higher QALYs (0.0042) compared to no screening, yielding an incremental cost per QALY gained of \$375. Univariate and probabilistic sensitivity analyses confirmed that screening AF in a pharmacy setting was a cost-effective strategy.

Interpretation

Our economic results support screening for AF in Canadian pharmacies.



INTRODUCTION

Atrial Fibrillation (AF) is the most common abnormal rhythm disorder¹ and the leading cause of stroke.² AF-related stroke is preventable with oral anticoagulation therapy (OAC)^{3,4} however AF is often unrecognized or known but sub-optimally treated (hereafter referred to as 'actionable' AF).⁵ There are sparse data to suggest AF screening strategies are cost-effective.^{6,7} The Program for the Identification of 'Actionable' Atrial Fibrillation in the Pharmacy Setting (PIAAF-Pharmacy) was the first community AF screening program for individuals 65 years of older attending pharmacies in Alberta and Ontario using a handheld single lead ECG device (HeartCheck, CardioComm)⁸. Amongst the 1145 study participants, 2.4% were newly diagnosed with AF. PIAFF-Pharmacy was modelled after the Cardiovascular Health Awareness Program.^{9,10} This analysis presents the economic evaluation of the PIAAF-Pharmacy study to better inform decision makers about the value of screening for AF in Canadian pharmacies.

METHODS

Study overview

A decision analytical model was used to estimate the short-term and long-term costs and effects of the PIAAF-Pharmacy screening program compared to no screening. The model was comprised of two parts. The first part of the model captured the short-term costs and outcomes of the screening program itself based on data from the PIAAF-Pharmacy study⁸. Based on relevant literature, the second part of the model captured the long-term costs and benefits associated with stroke prevention resulting from the diagnosis of previously unrecognized AF. In the absence of dominance (e.g. one

strategy is more effective and less costly than the other)¹¹, an incremental cost per quality-adjusted life years (QALYs) gained was calculated to compare the two strategies (AF screening in pharmacy versus no screening). A lifetime horizon was used in the analysis, with costs and outcomes occurring in the future being discounted at an annual rate of 5%.¹¹ The analysis was taken from a third-party public payer perspective. Univariate and probabilistic sensitivity analyses were conducted to deal with uncertainty in model inputs.

Model structure

Figure 1a provides a graphical representation of the short-term decision model. In the screening arm, individuals with AF are identified based on the positive findings of the single lead ECG and its predictive positive value (PPV) to identify AF. A proportion of these newly diagnosed individuals will receive oral anticoagulants (OACs) for the prevention of stroke. For the "no screening" arm, individuals with undiagnosed AF are assumed to remain undiagnosed and therefore do not receive OAC therapy. Based on the short-term model outcomes, individuals enter the long-term model in one of three health states (Figure 1b): 1) no AF; 2) AF receiving OACs; and 3) AF not receiving OACs. Individuals with AF are at risk of ischemic stroke, intracranial hemorrhage (ICH), and non-ICH major bleeding. ICH is further divided into hemorrhagic stroke and non-hemorrhagic stroke. Individuals with AF who are on OACs are assumed to be at lower risk of ischemic stroke but at higher risk of ICH and non-ICH major bleeds compared to those not receiving OACs. Transitions between health states can occur every 3 months.

Short-term model parameters

Based on the PIAAF-Pharmacy study results⁸, it was assumed that 2.4% of individuals in the screening group would test positive for AF for the first time. The PPV (65.4%) of the single lead ECG used in the study was based on unpublished data from a similar AF screening study conducted in physician offices (as opposed to pharmacies) in which all single lead ECG positive AF were followed up with a 12 lead ECG and a Holter monitor if negative on the 12 lead ECG¹². The PPV was applied to this percentage to calculate the percentage of screened individuals that have AF and are newly diagnosed (2.4% x 65.4%= 1.6%). It was assumed that 71% of newly diagnosed AF individuals will receive OAC treatment for the prevention of stroke based on the fact that 5 out of the 7 individuals in PIAAF-Pharmacy diagnosed with AF saw a GP within 6 weeks of the screening date and received an OAC prescription by the end of the 3 month study follow-up. Cost data from the PIAAF-Pharmacy study were used to calculate the cost per AF screen by dividing the total cost of the screening sessions conducted in PIAAF-Pharmacy study by the number of individuals screened within the study. The total cost of the screening sessions was estimated by summing three cost categories: 1) training of personnel conducting the screening sessions; 2) in-pharmacy screening sessions including transmission of results to family physicians; and 3) costs of ECGs used within screening sessions. Individuals in the "no screening" group were assumed to remain undiagnosed for the remainder of their lives.

Long-term model assumptions

The following presents the key assumptions for the long-term model in terms of stroke and bleeding risk, mortality, cost of events, and utilities. A summary of the long-term

model variables is also provided in Appendix 1 along with other model inputs used in the short- and long-term models (e.g. cost and utility data).

Stroke and bleeding risk

The average CHA₂DS₂-VASc score for individuals diagnosed with AF in the PIAAF-Pharmacy study was used in the model (i.e., 3.3). The annual risk of stroke in the absence of OAC therapy and the risk of ICH and non-ICH major bleeding for AF individuals were based on findings from a Swedish cohort study involving 182,000 individuals diagnosed with AF¹³. This study was also used to assign the model cohort the average HAS-BLED score (2.18) since the HAS-BLED scores were not captured in the PIAAF-Pharmacy study.

For individuals with AF that received an OAC therapy, the relative risk of ischemic stroke and major bleeding compared to those not receiving an OAC therapy was applied separately for individuals that were treated with warfarin and for those on direct oral anticoagulants (DOACs). For individuals taking warfarin, the relative risk of ischemic stroke and major bleeding was based on a meta-analysis by Lip *et al.* ¹⁴. For the individuals receiving DOACs, data from Ruff *et al.* ⁴'s meta-analysis of ischemic stroke and major bleeding relative to warfarin were used. The relative risk of events for DOACs compared to no treatment was estimated indirectly by multiplying the relative risk of events for DOACs versus warfarin by the relative risk of events for warfarin compared to no treatment.

Mortality

For individuals without AF or for individuals with AF who do not develop an event (e.g. stroke), age- and gender-specific mortality rates were applied based on Canadian life tables^{15, 16}. The one-year mortality rate after ischemic stroke (37.3%) was based on findings from McGrath *et al.*¹⁷. The one-year mortality rate post ICH (35.2%) was based on in-hospital mortality reported in Alonso *et al.*¹⁸ extrapolated to 1 year post-ICH mortality by applying the ratio of 30 day mortality to 1 year as observed for ischemic stroke in McGrath *et al.*¹⁷. Mortality after 1 year post stroke (ischemic or hemorrhagic) was assumed to be 2.3 times higher than for the general population based on data from Hardie *et al.*¹⁹. Non-ICH major bleeding was associated with a 7.4% mortality rate²⁰.

Costs

Based on Canadian registry data, it was assumed that 52% of individuals receiving OACs would receive warfarin while 48% would receive a DOAC ²¹. The cost of warfarin was based on a regimen of 5 mg per day. Individuals receiving warfarin were also assigned monitoring costs based on estimates used in a Canadian economic evaluation of AF treatments by Coyle *et al.*²². Unit costs of OAC therapy were based on 2016 reimbursement prices from the Ontario Drug Benefit formulary²³. Individuals suffering an ischemic stroke or an ICH were assigned separate costs for the first year and subsequent years post event based on Canadian data ²⁴⁻²⁷. All costs were expressed in \$CAN 2016. When necessary, the health care component of the Canadian consumer price index was used to adjust to \$CAN 2016²⁸.

Utilities

Individuals in the model with or without AF but with no events were assigned age- and gender-specific general population EQ-5D utility values²⁹. Individuals suffering an ischemic stroke or ICH (hemorrhagic stroke and non-hemorrhagic stroke) were assigned a utility weight of 0.60 to reflect the decreased long-term quality of life after these events. This utility weight was estimated by combining the average utility for stroke according to modified Rankin score (mRS 0-2, mRS 3-5) reported by Rivero-Arias³⁰ with the proportion of individuals in these mRS categories, as derived from data from the Active A trial³¹. The stroke utility weight was multiplied by the age- and gender-specific population utility value for the cohort of patients that suffer a stroke.

Analysis of Uncertainty

The uncertainty around the base case cost-effectiveness results was first evaluated using probabilistic sensitivity analyses (PSA). In the PSA, the model results were simulated 1000 times with values from model input variables being drawn from distributions specific to each model parameter (Appendix 1) using Monte Carlo techniques.³² Parameter uncertainty around the base case results were expressed using a cost-effectiveness acceptability curve (CEAC) which shows the probability that AF screening is cost-effective across different willingness-to-pay thresholds.

In addition to the PSA, deterministic sensitivity analyses were conducted in which costeffectiveness results were evaluated while changing the value of a single model
parameter at a time (cost per AF screen, proportion of AF receiving OAC, PPV,
proportion of undiagnosed AF becoming diagnosed annually, time horizon, stroke costs

22, proportion of OAC that are DOACs,).

RESULTS

With a cost per patient screened of \$65 (Appendix 2), the model estimated that, compared to no screening, the PIAAF-Pharmacy screening intervention would result in higher expected costs (\$2), more life years (0.0039) and more QALYs (0.0045) over a lifelong time horizon, yielding an incremental cost per QALY gained of \$375 as shown in Table 1. The increased per-patient costs associated with the screening strategy (\$65) and OAC management (\$49) are partially offset by the decreased costs of ischemic stroke (-\$144) as shown in Table 2.

The results of the PSA, incorporating the uncertainty in the parameter values, indicate that the probability that AF screening is cost-effective is 93% and 95% if the willingness to pay for a QALY gained is \$50,000 or \$100,000, respectively (Figure 2). The results of various deterministic sensitivity analyses, given in Table 3, indicate that the AF screening strategy is dominant or less than \$50,000 per QALY in all sensitivity analyses except where: 1) the proportion of individuals with confirmed AF that receive an OAC is 10% or less (compared to 71% in the base case analysis); 2) the PPV of the single lead ECG is 0.10 or lower (compared to 0.654 in our base case analysis); or 3) the proportion of individuals with AF in the "no screening" arm that get diagnosed symptomatically is 20% or higher annually (compared to 0% in the base case analyses).

INTERPRETATION

The results of the economic evaluation of the PIAAF-Pharmacy study indicates that screening individuals 65 years of age or older for AF in Canadian pharmacies is highly cost-effective compared to no screening, yielding an incremental cost/QALY gained of

\$375. The upfront costs associated with the screening were mostly offset by reductions in ischemic stroke-related costs due to the initiation of OAC treatment after identification of AF. Except in unlikely situations (e.g. 10% of newly diagnosed AF individuals would be prescribed an OAC when diagnosed with AF), the screening strategy was the dominant or a cost-effective strategy in all sensitivity analyses, thus improving our confidence in the results.

These findings are fairly consistent with those of a cost-effectiveness analysis of an Australian pharmacy AF screening program of individuals 65 years or older which vielded an incremental cost per QALY gained of AUD\$5,988 (CAN\$5,928 33). This study assumed an underlying prevalence of undiagnosed AF of 1.4%, and a sensitivity and specificity of the AF screening test of 98.5% and 91.5%. The cost per screen was \$AUD20 (CAN\$20). In Sweden, the long-term cost-effectiveness of a non-pharmacy mass AF screening program ⁶ was estimated to be €4,313/QALY gained (CAN\$6,341/QALY 33). In this study the cost per screen was assumed to be €106 (CAN\$ 156) and the percentage of screened individuals diagnosed with AF was assumed to be 3%. It was further assumed that 93% of patients identified with AF would receive an OAC. In comparison to these two studies, our model assumed in the base case analyses that 2.4% of seniors will test positive for AF for the first time at a cost of \$65 per screened individual. Furthermore, we used a PPV of 65.4% to calculate the proportion of screened AF patients that are true positive (1.6%) and assumed that 71% of true positive patients will receive OAC treatment.

There are a number of limitations to this economic evaluation. First, cost-effectiveness results were driven by predictions of ischemic stroke and other AF treatment events

which were not observed but predicted based on short-term screening results. Another limitation was related to the assumption around the percentage of individuals diagnosed with AF through screening that would end up being prescribed an OAC (71%). This percentage was based on data from the PIAAF-Pharmacy study in which 5 out of the 7 individuals who had seen their physician by six weeks were prescribed an OAC. To deal with the uncertainty associated with some assumptions and associated parameter values, sensitivity analyses were conducted and indicated that the results were robust except for extreme and unlikely situations (Table 3). Third, our economic evaluation only focused on AF and we did not integrate additional benefits associated with the PIAAF-Pharmacy study such as the detection of other modifiable stroke risk factors during the screening (e.g. high blood pressure or risk of diabetes) that have already been shown to be clinically and economically advantageous. 9, 10 Inclusion of those additional factors would result in additional benefits with the program and would most likely result in overall cost-savings. As per the study design, the intervention was conducted by study coordinators and volunteers during scheduled screening sessions. As a result, some of their time in the pharmacy was spent waiting for eligible participants. It is reasonable to consider that an AF screening program could be better integrated into pharmacy workflows in collaboration with other pharmacy programs such as vaccinations thus cutting down waiting time and therefore the cost per screened patient.

The results of this study have several policy implications. The PIAAF-Pharmacy study indicated that screening AF and other modifiable risk factors in the pharmacy setting is feasible and is the dominant or cost-effective strategy compared to no screening, even at a cost of \$65 per screen. Given this, efforts should be made by provincial

governments and pharmacies to implement such programs in Canada. Adding AF screening in pharmacies should be considered along with other evidence-informed screening for metabolic disorders to identify high risk patients. ^{10, 34}



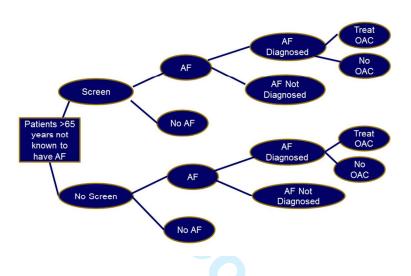
REFERENCES

- 1. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation*. 2006;114(2):119-25.
- 2. Marini C, De Santis F, Sacco S, Russo T, Olivieri L, Totaro R, et al. Contribution of atrial fibrillation to incidence and outcome of ischemic stroke: results from a population-based study. *Stroke*. 2005;36(6):1115-9.
- 3. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. *Ann Intern Med*. 2007;146(12):857-67.
- 4. Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet*. 2014;383(9921):955-62.
- 5. Gladstone DJ, Bui E, Fang J, Laupacis A, Lindsay MP, Tu JV, et al. Potentially preventable strokes in high-risk patients with atrial fibrillation who are not adequately anticoagulated. *Stroke*. 2009;40(1):235-40.
- 6. Aronsson M, Svennberg E, Rosenqvist M, Engdahl J, Al-Khalili F, Friberg L, et al. Costeffectiveness of mass screening for untreated atrial fibrillation using intermittent ECG recording. *Europace*. 2015;17(7):1023-9.
- 7. Lowres N, Neubeck L, Salkeld G, Krass I, McLachlan AJ, Redfern J, et al. Feasibility and costeffectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study. *Thromb Haemost*. 2014;111(6):1167-76.
- 8. Sandu RK, Dolovich L, Deif B, Barake W, Agarwal G, Grinvalds A, et al. High Prevalence of Modifiable Stroke Risk Factors Identified in a Pharmacy-based Screening Program. *Open Heart*. 2016;3:e000515. doi: 10.1136/openhrt-2016-000515
- 9. Goeree R, von Keyserlingk C, Burke N, He J, Kaczorowski J, Chambers L, et al. Economic appraisal of a community-wide cardiovascular health awareness program. *Value Health*. 2013;16(1):39-45
- 10. Kaczorowski J, Chambers LW, Dolovich L, Paterson JM, Karwalajtys T, Gierman T, et al. Improving cardiovascular health at population level: 39 community cluster randomised trial of Cardiovascular Health Awareness Program (CHAP). *BMJ*. 2011;342:d442.
- 11. Guidelines for the economic evaluation of health technologies: Canada. [3rd edition]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2006.
- 12. Dr. Russell Quinn. Libin Cardiovascular Institute of Alberta, University of Calgary, Calgary, Alberta: personal communication. 2016.
- 13. Friberg U, Stewart AD, Rice WR. X- and Y-chromosome linked paternal effects on a life-history trait. *Biology Letters*. 2012;8(1):71-3.
- 14. Lip GY, Edwards SJ. Stroke prevention with aspirin, warfarin and ximelagatran in patients with non-valvular atrial fibrillation: a systematic review and meta-analysis. *Thrombosis Research*. 2006;118(3):321-33.
- 15. Statistics Canada. *Table 1a. Complete life table, males, Canada, 2009 to 2011.* Ottawa: Statistics Canada; 2015.
- 16. Statistics Canada. *Table 1b. Complete life table, females, Canada, 2009 to 2011.* Ottawa: Statistics Canada; 2015.
- 17. McGrath ER, Kapral MK, Fang J, Eikelboom JW, Conghaile Ao, O'Conghaile A, et al. Association of atrial fibrillation with mortality and disability after ischemic stroke. *Neurology*. 2013;81(9):825-32.

- 18. Alonso A, Bengtson LGS, MacLehose RF, Lutsey PL, Chen LY, Lakshminarayan K. Intracranial hemorrhage mortality in atrial fibrillation patients treated with dabigatran or warfarin. *Stroke*. 2014;45(8):2286-91.
- 19. Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-year survival after first-ever stroke in the perth community stroke study. *Stroke*. 2003;34(8):1842-6.
- 20. Straube S, Tramer MR, Moore RA, Derry S, McQuay HJ. Mortality with upper gastrointestinal bleeding and perforation: effects of time and NSAID use. *BMC Gastroenterol*. 2009;9:41.
- 21. Ha ACT, Singh N, Cox JL, Mancini GBJ, Dorian P, Fournier C, et al. Oral Anticoagulation for Stroke Prevention in Canadian Practice: Stroke Prevention and Rhythm Interventions in Atrial Fibrillation (SPRINT-AF) Registry. *Can J Cardiol*. 2016;32(2):204-10.
- 22. Coyle D, Coyle K, Cameron C, Lee K, Kelly S, Steiner S, et al. Cost-effectiveness of new oral anticoagulants compared with warfarin in preventing stroke and other cardiovascular events in patients with atrial fibrillation. *Value Health*. 2013;16(4):498-506.
- 23. Ontario Ministry of Health and Long Term Care. Drugs funded by Ontario Drug Benefit (ODB) Program: e-formulary [Internet]. Toronto: Queen's Printer for Ontario; 2010 [updated 13/04/2009, version 2.0]. Available from: https://www.formulary.health.gov.on.ca/formulary/.
- 24. Blackhouse G, Assasi N, Xie F, Gaebel K, Campbell K, Healey JS, et al. Cost-effectiveness of catheter ablation for rhythm control of atrial fibrillation. *Int J Vasc Med*. 2013;2013:262809.
- 25. Goeree R BG, Petrovic R, Salama S. Cost of stroke in Canada: a one-year prospective study. *J Med Econ.* 2005;8:20.
- 26. Mittmann N, Seung SJ, Hill MD, Phillips SJ, Hachinski V, Cote R, et al. Impact of disability status on ischemic stroke costs in Canada in the first year. *Can J Neurol Sci.* 2012;39(6):793-800.
- 27. Pateint Cost Estimator [Internet]. Canadian Institute for Health Information (CIHI); c1996-2017. [cited 2016 October 26]. Available from: www.cihi.ca/en/spending-and-health-workforce/spending/patient-cost-estimator.
- 28. Statistics Canada. Statistics Canada. Consumer Price Index, health and personal care, by province (Canada). Ottawa: Statistics Canada; 2016 2016.
- 29. Kind P, Hardman G, Macran S. *UK population norms for EQ-5D*. Discussion Paper 172 York, United Kingdom: Centre for Health Economics, The University of York; 1999 1999.
- 30. Rivero-Arias O, Ouellet M, Gray A, Wolstenholme J, Rothwell PM, Luengo-Fernandez R. Mapping the modified Rankin scale (mRS) measurement into the generic EuroQol (EQ-5D) health outcome. *Med Decis Making*. 2010;30(3):341-54.
- Investigators A, Connolly SJ, Pogue J, Hart RG, Hohnloser SH, Pfeffer M, et al. Effect of clopidogrel added to aspirin in patients with atrial fibrillation. *N Engl J Med*. 2009;360(20):2066-78.
- 32. Briggs A SM, Claxton K. *Decision Modelling for Health Economic Evaluation*. Oxford University Press; 2006.
- 33. Daily Currency Converter [Internet]. 2016 [cited 2016 October 26]. Available from: www.bankofcanada.ca/rates/exchange/daily-converter.
- 34. Tsuyuki RT, Johnson JA, Teo KK, Simpson SH, Ackman ML, Biggs RS, et al. A randomized trial of the effect of community pharmacist intervention on cholesterol risk management: the Study of Cardiovascular Risk Intervention by Pharmacists (SCRIP). *Arch Intern Med.* 2002;162(10):1149-55.

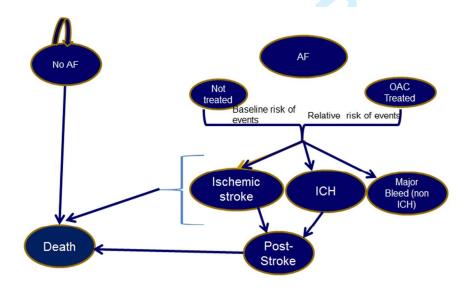
Figure 1: Atrial Fibrillation Screening Model Structure

1a: Graphical representation of the short-term AF screening model



1b: Graphical representation of the long-term AF screening model

Individuals start the long term model in one of three health states: 1) No AF; 2) AF not treated with an OAC; or 3) AF treated with an OAC



Abbreviations: AF-atrial fibrillation, ICH-intracranial hemorrhage, OAC-oral anticoagulants

Figure 2: Cost-effectiveness acceptability curve

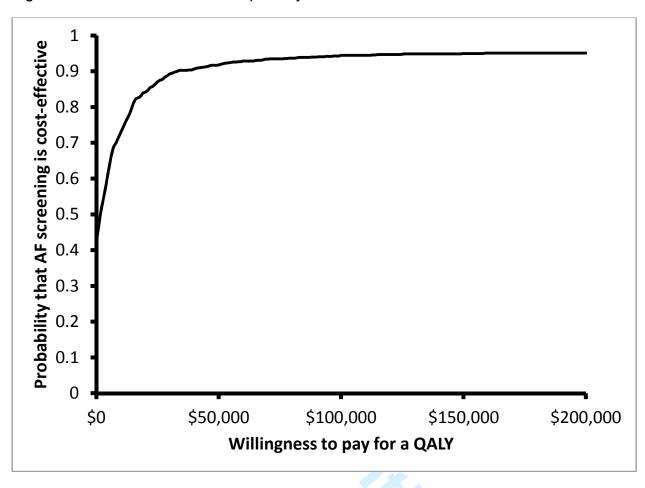


Table 1: Base-case cost-effectiveness results

Intervention	Costs	LYs	QALYs	Incremental \$/LY gained	Incremental \$/QALY gained
PIAAF-Pharmac	;y				
Screening	\$356	7.496	5.714		
No Screen	\$355	7.493	5.710		
Incremental	\$2	0.0039	0.0045	\$428	\$375

Abbreviations: PIAAF-Pharmacy = Program for the Identification of 'Actionable' Atrial Fibrillation: in the Pharmacy Setting, Lys = Life Years, QALYs = Quality Adjusted Life Years



Table 2: Breakdown of expected costs by category

			Ischemic		Major	
	Intervention	OAC	stroke	ICH	bleeds	Total
PIAAF-Pharmacy						
Screening	\$65	\$49	\$168	\$53	\$21	\$356
No Screen	\$0	\$0	\$312	\$33	\$10	\$355
Incremental	\$65	\$49	-\$144	\$20	\$11	\$2

Abbreviations: PIAAF-Pharmacy = Program for the Identification of 'Actionable' Atrial Fibrillation: in the Pharmacy Setting, OAC = oral anticoagulants, ICH = intracranial hemorrhage



Table 3: One way sensitivity analyses: PIAAF-Pharmacy Screening versus no screening (base case: incremental cost per QALY gained; \$1,175/QALY gained)

	Incremental costs	Incremental QALYS	Incremental cost/ QALY gained	
Cost of screen (ba		QALIS	QALI gailleu	
\$100	\$37	0.0045	\$8,229	
\$90	\$27	0.0045	\$5,984	
\$80	\$17	0.0045	\$3,740	
\$70	\$7	0.0045	\$1,495	
\$60	-\$3	0.0045	dominates	
\$50	-\$13	0.0045	dominates	
\$40	-\$23	0.0045	dominates	
\$30	-\$33	0.0045	dominates	
_				
•	ly diagnosed A	F individuals tl	nat receive an OAC	
(base case=0.71)		2		
1	-\$24	0.0062	dominates	
0.9	-\$15	0.0056	dominates	
0.8	-\$6	0.0050	dominates	
0.7	\$3	0.0044	\$673	
0.6	\$12	0.0037	\$3,154	
0.5	\$21	0.0031	\$6,629	
0.4	\$30	0.0025	\$11,841	
0.3	\$38	0.0019	\$20,527	
0.2	\$47	0.0012	\$37,900	
0.1	\$56	0.0006	\$90,018	
Positive predictive	e value of single	e lead ECG (ba	se case=0.62)	
1	-\$32	0.0068	dominates	
0.9	-\$22	0.0061	dominates	
8.0	-\$12	0.0054	dominates	
0.7	-\$3	0.0048	dominates	
0.6	\$7	0.0041	\$1,688	
0.5	\$17	0.0034	\$4,870	
0.4	\$26	0.0027	\$9,641	
0.3	\$36	0.0020	\$17,595	
0.2	\$46	0.0014	\$33,501	
0.1	\$55	0.0007	\$81,221	
Proportion of undiagnosed AF individuals that become diagnosed				

each year (base ca	se=0.0)		
0	\$2	0.0045	\$375
0.05	\$32	0.0024	\$12,983
0.1	\$42	0.0017	\$25,674
0.2	\$51	0.0010	\$50,939
0.3	\$54	0.0007	\$75,887
0.4	\$56	0.0006	\$100,476
0.5	\$58	0.0005	\$124,700
Time horizon, year	's (base case=l	ifetime)	
5	\$32	0.0010	\$31,430
10	\$11	0.0026	\$4,314
15	\$5	0.0037	\$1,455
20	\$5	0.0041	\$1,185
25	\$5	0.0042	\$1,175
Alternative			
stroke costs	\$41	0.0045	\$9,231
Monforin			
Warfarin represents			
100% OACs*	-\$14	0.0036	dominates
10070 07100	Ψιι	0.000	dominates
DOACs			
represent 100%			
of OACs*	\$19	0.0054	\$3,478

^{*}base case, warfarin and DOAC's represents 52% and 48% of OAC use respectively

Abbreviations: QALYs = Quality Adjusted Life Years, OAC = oral anticoagulants, ECG = electrocardiogram, AF = Atrial Fibrillation

Appendix 1: Model parameters, distributions used in probabilistic analyses and data sources

	Model		
Variable	value	Distribution	Reference
SHORT-TERM MODEL VARIABI	LES		
Proportion of screened individuals testing positive for AF on single lead ECG	0.024	beta (α=27 , β=1118)	1
Positive predictive value of single lead ECG	0.654	beta (α=50 , β=27)	12
Proportion of confirmed AF that receive an OAC	0.71	beta (α =5 , β =2)	1
LONG-TERM MODEL VARIABLI	ES		
Annual risk of event in absence			
Ischemic stroke (CHA_2DS_2 -VASc = 3.2)	0.048	beta (α=85 , β=1683)	2
ICH without OAC (HAS-BLED = 2.18)	0.006	beta (α=201 , β=33285)	2
Major bleed (non-ICH) (HAS- BLED = 2.18)	0.023	beta (α=770 , β=32715)	2
Relative risk of events: warfarir	n vs. no OAC		
RR ischemic stroke	0.33	lognormal (µ=-1.1 o=0.24)	3
RR major bleeding	2.2	lognormal (µ=0.80, o= 0.47)	3
Relative risk of events: DOAC v	s. warfarin		
RR ischemic stroke	0.92	lognormal (μ=-0.08, σ=0.05)	4
RR hemorrhagic stroke	0.49	lognormal (μ=0.71, σ=0.13)	4
RR ICH (non-hemorrhagic stroke)	0.46	lognormal (µ=-0.79, o= 0.16)	4
RR major bleed (non-ICH)	0.97	lognormal (μ=-0.03, σ= 0.04)	4
Proportion of OACs prescribed that are DOACs	0.48	beta (α=366 , β=416)	5
Relative risk of events: DOAC v			
RR ischemic stroke	0.3	Determined by other variables	Indirect: 4, 3
RR hemorrhagic stroke	1.09	Determined by other variables	Indirect: 4, 3
RR ICH (non-hemorrhagic stroke)	1.01	Determined by other variables	Indirect: 4, 3
RR major bleed (non-ICH)	2.15	Determined by other variables	Indirect: 4, 3
Annual OAC costs			

DOAC (average of dabigatran, rivaroxaban, apixaban)	\$1,271.65	Fixed	6
Warfarin	\$24.63	Fixed	6
INR testing with warfarin	\$247.76	gamma (α=25,β=9.91)	7
Annual event costs			
Ischemic stroke 1st year	\$57,024	gamma (α=25,β= 2281)	8
Ischemic stroke 2nd+ years	\$7,085	gamma (α=25,β=283)	9
ICH 1st year	\$67,386	gamma (α=25,β= 2695)	10
ICH 2nd+ years	\$6,087	gamma (α= 25,β= 244)	9
Major bleed (non-ICH)	\$4,870	gamma (α=25,β=195)	11
Utility variables			
General population males aged 75+	0.75	beta (α =193 , β =64)	12
General population females aged 75+	0.71	beta (α =412 , β = 168)	12
Proportion stroke with mRS 3-5	0.45	beta (α=208, β= 259)	13
Utility weight mRS 0-2	0.81	beta (α=1128, β=256)	14
Utility weight mRS 3-5	0.34	beta (α=45, β= 86)	14
Utility weight stroke	0.6	Determined by other variables	Indirect: 13, 14
Mortality			
Annual general population	varies by age and gender	Fixed	15, 16
1 year following ischemic stroke	0.37	beta (α=1027 , β=1726)	17
1 year following ICH	0.35	beta (α =806 , β =1484)	18
RR of death vs. general population 2+ year's post stroke	2.3	lognormal (μ =-0.83, σ = 0.16)	19
Major bleed (non-ICH)	0.074	beta (α=4870 , β=60940)	20

Abbreviations: AF = Atrial Fibrillation, ECG = electrocardiogram, OAC = oral anticoagulants, ICH = intracranial hemorrhage, RR = relative risk, DOAC = direct oral anticoagulants, INR = international normalised ratio, mRS = modified Rankin Scale

Appendix 2: Breakdown of costs associated with the PIAAF-Pharmacy Screening Program for AF, number of individuals screened, and average cost per screen

Costs associated with developing the training module and training the session coordinators and volunteers	
Development of a training module	\$1,564.40
Management of session coordinators and volunteers, wage	\$1,701.29
Costs associated with AF screening in participating pharmacies	
Session coordinators, wage	\$42,504.46
Site-specific hosting fees	\$13,200.00
Costs associated with electrocardiograms used during the screening sessions	
Electrocardiogram devices	\$7,560.00
Electrodes	\$341.10
Upload and reading of electrocardiograms	\$4,548.00
Electrocardiogram data storage	\$2,500.00
Total screening costs associated with the PIAAF-Pharmacy Study	\$73,919.25
Total number of individuals screened	1,137
Average cost per screen	\$65.01