Primary Care Atrial Fibrillation Service: Outcomes from Consultant-led anticoagulation assessment clinics in the Primary Care setting

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Primary Care Atrial Fibrillation Service: Outcomes from Consultant-led anticoagulation assessment clinics in the Primary Care setting

Short title: Primary Care Atrial Fibrillation Service

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ABSTRACT

Objective:

Stroke-risk in atrial fibrillation (AF) can be significantly reduced by appropriate thromboembolic prophylaxis. However NICE estimates suggest that up to half of eligible AF patients are not anticoagulated, with severe consequences for stroke prevention. We aimed to determine the effect of an innovative Primary Care AF (PCAF) service on anticoagulation uptake in a cohort of high-risk AF patients.

Methods:

The PCAF service is a novel cooperative pathway providing specialist resources within GP practices. It utilises a 4-phase protocol to identify high-risk AF patients (CHA_{2}DS_{2}-VASC≥1) who are sub-optimally anticoagulated, and delivers Consultant-led anticoagulation assessment within the local GP practice. We assessed rates of anticoagulation in high-risk patients before and after PCAF service intervention, and determined compliance with newly-initiated anticoagulation at follow-up.

Results:

The PCAF service was delivered in 56 GP practices (population 386,624; AF prevalence 2.1%) between June 2012 and June 2014. 1579 high-risk AF patients with sub-optimal anticoagulation (either not taking any anticoagulation or taking warfarin but with a low time-in-therapeutic-range) were invited for review, with 86% attending. Of 1063 eligible patients on no anticoagulation, 1020 (96%) agreed to commence warfarin (459 (43%)) or a non-vitamin K antagonist oral anticoagulant (NOAC, 561 (53%)). The overall proportion of eligible patients receiving anticoagulation improved from 77% to 95% (P<0.0001). Additionally, 111/121 (92%) patients sub-optimally treated with warfarin agreed to switch to a NOAC. Audit of eight practices after 195 [185-606] days showed that 90% of patients commenced on a new anticoagulant therapy had continued treatment. Based on data extrapolated from previous studies, around 30-35 strokes per year may have been prevented in these previously under-treated high-risk patients.
Conclusions:

Systematic identification of AF patients with high stroke-risk and consultation in PCAF Consultant-led clinics effectively delivers oral anticoagulation to high-risk AF patients in the community.

Article summary:

Strengths and limitations of this study

- This study directly assessed the impact of a novel approach of delivering Consultant-led anticoagulation assessment clinics in GP practices.
- The outcomes of this study of an innovative cross-boundary model are therefore not just relevant to anticoagulation, but also to preventative management in other spheres of medicine.
- The study was not performed as a controlled trial.
- Only a random sample of the patients was assessed to ascertain adherence to anticoagulation therapy.
- Our estimates on stroke prevention through the intervention are based on estimates of the effect of anticoagulation derived from other studies.
INTRODUCTION:

Atrial fibrillation (AF) is the cause of one in four strokes,[1-4] and approximately 5% of unselected patients admitted for acute stroke have previously undiagnosed AF.[5] Optimal prevention of AF-related strokes is of obvious interest to patients with AF, as well as avoiding the cost of stroke management to health care systems.[6] Oral anticoagulation (OAC) using vitamin K antagonists (most commonly warfarin) or non-vitamin K antagonist oral anticoagulant (NOAC) drugs can prevent approximately two-thirds of AF-related strokes.[7, 8] NOAC therapy can be delivered with a simpler infrastructure in a cost-effective way,[9-11] and with a lower risk for bleeding, especially for intracranial haemorrhage.[8, 12] Despite the clear benefits in high-risk AF patients, OAC is underused in AF patients: the National Institute for Health and Clinical Excellence (NICE) estimates that 42% of patients that should be anticoagulated are not,[13] and similar observations have been made in other countries. The reasons for this are likely to be multifactorial, including concerns from GPs and patients regarding bleeding risk, the need for regular INR monitoring on vitamin K antagonists, unsystematic identification and management of AF patients in need of OAC, and lack of awareness of this need.

There are some data that hospital clinicians with specialist training in the management of AF will achieve higher anticoagulation rates in AF patients than general practitioners or internists.[14] However, most AF patients are not under specialist care in the NHS. The recently-released atrial fibrillation management guideline from NICE focuses on the need for improved rates of anticoagulation in AF patients at elevated risk of stroke,[15] and a related NICE document “How to Change Practice” promotes the concept of better integration between primary and secondary care.[16]

Foreseeing this healthcare priority, we instituted an innovative Primary Care Atrial Fibrillation (PCAF) Service in GP practices in Merseyside in June 2012. The PCAF service provides a hospital Consultant-led service offering specialist expertise in the management of AF patients at high stroke-risk within
GP practices, and has now expanded to involve GP practices across England and Wales. We aimed to determine the outcomes and effect of this service over the two years since its inception.

METHODS:

The PCAF service

Practice enrolment:

GP practices were informed of the availability of the service through direct systematic marketing or by approaching CCG Commissioning Managers and/or Medicines Management teams. As the service expanded, interest was expressed from GP practices based on recommendations from previously-enrolled practices.

Pathway:

In each enrolled GP practice, the PCAF service was delivered via four phases, with an additional practice education programme (Figure 1):

Phase 1:

The PRIMIS+ AF Query Case Finder Set was used to search all patient records (excluding those who were on the AF register) to ensure no high-risk patients were missed by virtue of not currently being listed on the AF register, and identified those patients with a possible or probable diagnosis of AF. A trained member of the PCAF team provided a comprehensive case note review of all identified patients, with the outcome being one of:

- AF confirmed,
- patient does not have AF, or
- patient referred for further investigation to ascertain a diagnosis of AF.

If required, specialist support was provided by a PCAF Consultant Physician.

Phase 2:
The GRASP-AF tool was used to audit all patients on the AF register, including those added following Phase 1, to identify those at high-risk of stroke in whom anticoagulation is recommended or should be considered (CHA$_2$DS$_2$-VASc score $\geq$1, excluding females with no additional risk factors) who were not currently receiving anticoagulation therapy.[17] A PCAF professional provided a comprehensive case note review of all identified patients, with the outcome being one of:

- AF confirmed and patient eligible for a PCAF face-to-face review,
- AF confirmed but only eligible for a ‘virtual notes review’ (applicable to patients who were either housebound or were resident in a nursing home and were unable to attend the clinic), or
- Patient not eligible for a PCAF review. This was applicable to patients in whom AF had resolved (for example, a single episode following a surgical procedure), anticoagulation was contra-indicated (defined as previous major bleeding or severe risk of bleeding) or there was no evidence of AF in their past medical history.

Phase 2 allowed another opportunity for patients to be categorised as not suffering from AF (and were therefore taken off the AF register), or to be referred to diagnostics or secondary care for further review. In addition, all patients who were currently receiving warfarin had their time-in-therapeutic-range (TTR) over the prior six-month period calculated using an electronic TTR calculator; those who had a sub-optimal TTR (defined as $<65\%$) were also deemed to be at high risk and therefore eligible for review to assess the optimal anticoagulation strategy.[15]

Phase 3:

A PCAF administrator sent out a letter of invitation with a pre-booked appointment to all eligible patients two weeks in advance of the PCAF clinic. Literature detailing the reason for the clinic review and the risks and benefits of anticoagulation was also included with the invitation letter. Patients were then contacted by telephone one week prior to their appointment to explain the service and
answer any queries, and again one day prior in order to minimise non-attendance ("call and recall"
approach).

Phase 4:

A Consultant Cardiologist or Consultant Stroke Physician delivered PCAF anticoagulation assessment
clinics within the patient’s GP practice. The patient’s current treatment was reviewed and, where
appropriate, anticoagulation was prescribed in accordance with NICE guidelines and/or the local
medicines management formulary. Other aspects of medical treatment for AF, such a rate or
rhythm control therapies, were also reviewed where appropriate.

Education:

GPs, nurse clinicians, practice nurses and practice pharmacists were invited to take part in the
Consultant-led PCAF anticoagulation clinics, allowing opportunities for shared learning and
discussion of individual cases. Additionally, staff members from enrolled practices had access to a
Consultant-led Continuous Professional Development education programme.

Assessment of outcomes:

The eventual outcome for each identified high-risk AF patient in the PCAF pathway was recorded in
the individual practices’ network drive as well as on a central database. We assessed the uptake of
anticoagulation in appropriate patients after intervention of the PCAF service compared to before.

To assess on-going compliance with the prescribed treatment, case notes for patients who were
prescribed a new or alternative anticoagulant agent were reviewed in a subset of GP practices in
which the PCAF pathway had been completed at least 6 months prior.

Statistical analysis:

Continuous variables that are normally distributed are expressed as mean±standard deviation, and
variables that are not normally distributed are expressed as a median [interquartile range].

Proportions were compared using the Chi square test. All tests were two-sided and $P<0.05$ was
considered statistically significant.
RESULTS:

To date, the PCAF pathway has been implemented in 56 GP practices serving a population of 386,624 registered patients. Outcomes from the 4 phases of the PCAF pathway are detailed below.

Patients not on anticoagulation (Figure 2):

Phase 1:
For the 56 practices, clarification of the AF register resulted in a total population with AF of 7945 patients (prevalence 2.1%).

Phase 2:
7487 (94%) of these patients had a CHA$_2$DS$_2$-VASc score of ≥1, of whom 4178 (56%; per-practice range 29-78%) were already on anticoagulation. Case notes were then reviewed for 2914 patients not on anticoagulation, with 1335 (46%) patients judged not to be eligible for anticoagulation. This was due to either: anticoagulation not indicated (female gender the only risk factor), a contraindication to anticoagulation, an incorrect Read code for AF (commonly due to the application of an AF Read code at the time of investigation but not removed when AF not found), or resolution of AF. This left 1579 patients who were eligible for, but not on, anticoagulation.

Phase 3:
These 1579 patients were invited to PCAF anticoagulation clinics using the “call and recall” approach, of whom 1358 (86%) attended for review within two weeks of invitation, with only 14% of patients failing to attend.

Phase 4:
Following review in clinic of the 1358 patients who attended, 1063 (78%) were confirmed to be eligible for anticoagulation. Of these patients, 84% had a CHA$_2$DS$_2$-VASc score of 2 or more, with the remaining 16% patients having a score of 1. Eighty-five percent of these patients were also eligible
using the criterion of a CHADS2 score ≥1, with 52% having a CHADS2 score ≥2. Antiplatelet therapy was being taken by 71% of patients at the time of review. Eleven percent (n=117) of the 1063 patients not on anticoagulation had previously suffered a stroke or transient ischemic attack (TIA).

Following the consultation, 1020 (96%) patients agreed to commence anticoagulation (warfarin in 43% and a NOAC in 53%). With regard to the 561 patients commenced on a NOAC, 12% of patients had previously tried but not tolerated warfarin, 21% had previously declined warfarin and 67% preferred a NOAC over warfarin. NOAC prescription was distributed amongst the three agents as follows: apixaban - 17%, dabigatran - 49%, and rivaroxaban - 34%.

Of the 43 (4%) patients that did not agree to commence anticoagulation therapy at the time of their consultation, only 16 patients declined treatment, with the remaining 27 preferring to defer their decision pending further discussion with their GP.

Overall, taking into account all exclusions (patients deemed not to have AF and those ineligible for anticoagulation), the total number of patients eligible for anticoagulation registered to these 56 GP practices was 5471. With the intervention of the PCAF service, the proportion receiving anticoagulation improved from 77% (4187/5471) to 95% (5207/5471) (P<0.0001).

Patients with a sub-optimal TTR (Figure 3):

4178 patients in the 56 GP practices were already anticoagulated with warfarin. Case notes and INR records were reviewed for 3295 of these patients. 387 (12%) patients with a sub-optimal TTR (<65%) were identified and invited for review, of whom 83% attended. After clinical review, the majority of patients (62%) were advised to continue on warfarin. Reasons for this decision included: an improved TTR over recent readings, a clear reason for previous INR variability (such as previous courses of antibiotics), significant renal dysfunction contraindicating use of a NOAC, compliance issues that could be addressed at the clinic visit, or concerns over non-compliance, in which case warfarin was felt more appropriate to a NOAC as compliance could continue to be assessed through
INR monitoring. 121 (38%) patients were offered a NOAC, with 111 (92%) agreeing to change therapy.

**Follow-up data:**

Eight random GP practices that had hosted the PCAF service at least 6 months previously were audited. A total of 87 patients initiated on a new anticoagulant agent were identified (median follow-up 195[185-606] days). The characteristics of these patients (age 75±9 years, 60% male, median CHADS2 score 2[1-3], median CHA2DS2-VASc score 3[2-4]) were similar to those of the 1063 patients invited to PCAF clinics (age 74±10 years, 53% male, CHADS2 score 2[1-3], CHA2DS2-VASc score 4[2-6]). Twenty-five patients had been commenced on warfarin, 51 patients had been initiated on a NOAC as a first-line agent, and 11 patients had been switched from warfarin to a NOAC.

Of the 25 patients commenced on warfarin, 19 (76%) remained on this treatment at the time of the audit. One further patient had suffered recurrent deep vein thromboses on warfarin and had been switched by a Consultant Haematologist to a low-molecular-weight heparin, and therefore remained anticoagulated. Two patients had died during the follow-up period. In both cases, warfarin had been continued at the time of death and the deaths were unrelated to bleeding or stroke. Only three of the 25 patients requested to stop warfarin, resulting in an overall compliance rate of 88%.

For the 62 patients initiated on a NOAC, 50 (81%) remained on a NOAC. Three patients (all of whom had previously not been on any anticoagulation) had requested to switch to warfarin and remained anticoagulated. Three patients had died during follow-up; they had each remained on NOAC therapy up to the time of death and neither bleeding nor stroke were related to the cause of death. In one case, a new diagnosis of significant renal dysfunction was made (eGFR 35 ml/min) and NOAC therapy was stopped by the patient’s GP. Five patients requested to stop anticoagulation, with three of these switching to an antiplatelet agent. Overall, the compliance rate with NOAC treatment was 85% (53/62), and with any anticoagulation therapy was 90% (56/62).
Taking both the warfarin and NOAC groups into account, 78 of 87 (90%) patients had continued anticoagulation following PCAF intervention, either the initial agent or an alternative.

**DISCUSSION:**

During the implementation of PCAF, we made several observations that can inform the future management of AF patients: 1) there is a significant proportion of patients with AF at high risk of stroke in primary care that are not treated with OAC (23%), with a further group of patients inadequately anticoagulated with warfarin, and 2) a consultant-led anticoagulation service in the community will get the majority of these patients anticoagulated, including the facility for individual, patient-oriented anticoagulation decisions. Importantly, the PCAF intervention led to high compliance with newly-initiated anticoagulation. Taken together, PCAF has the potential to improve the utilisation of OAC, and to prevent strokes in high-risk AF patients.

Evidence generated in the last decade underpins the use of OAC in the vast majority of patients with AF, i.e. those with stroke risk factors (at least one, and certainly two of the CHA\textsubscript{2}DS\textsubscript{2}-VASc risk factors).\[18, 19\] This was reflected in previous NICE guidance on atrial fibrillation, published in June 2006, that listed all but female gender of the CHA\textsubscript{2}DS\textsubscript{2}-VASc risk factors for use in stroke-risk stratification.\[20\] Hence, guidance applicable in the Merseyside region has effectively advocated anticoagulation use since 2006 in most patients who would now accrue a score of 1 or more under the CHA\textsubscript{2}DS\textsubscript{2}-VASc scoring system, though this has been substantially clarified in the latest guidance.\[15\] Despite this guidance, the PCAF program identified 1063 high-risk patients without OAC, of whom 892 (84%) had a CHA\textsubscript{2}DS\textsubscript{2}-VASc score ≥2 and 171 (16%) had a CHA\textsubscript{2}DS\textsubscript{2}-VASc score of 1.\[18, 19\]

Clinician-initiated health improvement reviews in primary care are known to commonly suffer from low attendance rates. However, the PCAF service was able to achieve an overall attendance rate of 85%. This is likely to be in part due to the “call and recall” approach employed, with a letter invitation followed by phone call reminders one week and again one day prior to the appointment.
Hence, this study corroborates prior studies showing that attendance rates can be improved with telephone reminders.[21, 22] In addition, it is possible that improved attendance may also have been related to the opportunity to see a specialist in the setting of their GP surgery.

Finally, the PCAF service has demonstrated a marked increase in the uptake of anticoagulation in high-risk AF patients, including those who had previously been offered but refused anticoagulation. In some cases, the option of NOAC agents that do not require monitoring will have facilitated this decision, but past research has also shown that rates of uptake are dependent on patient perceptions of the value of anticoagulation.[23] We believe that the increased experience with managing anticoagulation in AF patients, particularly with regard to NOACs, possessed by secondary care physicians in the fields of cardiology and stroke medicine helps to alter patients’ perceptions in many cases towards acceptance and continuation of anticoagulation.

Prevention of strokes by the PCAF service:

The PCAF service predominantly identifies the at-risk primary prevention population, though a small proportion (11%) had suffered a previous stroke or TIA. In primary prevention patients, approximately 35 patients need to be treated with warfarin for a year to prevent one stroke, whereas, in patients with a prior stroke, the number needed to treat (NNT) is around 12.[7, 24] Equivalent data are not available for the three available NOACs, but all have shown equivalent or superior efficacy compared to warfarin,[25-27] and modelling data have suggested a lower NNT compared to warfarin for each agent.[28] In this study, 1020 patients were newly anticoagulated due to the PCAF intervention, of whom 111 were secondary prevention patients. Compliance with therapy at follow-up was 90%, or approximately 918 patients. Furthermore, there were 111 patients who were previously on warfarin with a sub-optimal TTR who have now commenced a NOAC. Based on the estimated efficacy, the intervention of the PCAF service may have prevented around 30 to 35 strokes per year in these 56 GP practices.

The PCAF service as a model of care:
In the traditional model of care, only a small proportion of patients typically gain access to specialist hospital-based resources. Within the field of AF, these are usually patients requiring input regarding rhythm management. At the same time, however, it is extremely difficult for primary care clinicians to not only be aware of developments in all areas of medicine, but also to have the knowledge and confidence to implement them. With specific regard to anticoagulation in patients with AF in primary care, familiarity with the CHA\textsubscript{2}-DS\textsubscript{2}-VASc scoring system may not be universal, particularly as the CHADS\textsubscript{2} score is still utilised for the Quality and Outcomes Framework (QOF). Additionally, primary care clinicians may have little or no experience with the NOAC agents, in part due to their relatively recent release and approval, and in part due to the limited number of conditions for which they are indicated.

The PCAF service took an innovative approach by bridging this boundary between primary and secondary care, providing specialist resources within the primary care setting. This strategy has two distinct advantages. Firstly, patients currently managed solely within primary care are reviewed and, where appropriate, their anticoagulation treatment is optimised. Secondly, the educational legacy left within the GP practice following completion of the PCAF pathway enables such optimal treatment to be carried forward for future patients.

**Limitations:**

The PCAF intervention was not performed as a controlled trial, and our estimates on stroke prevention through the intervention are based on estimates of the effect of OAC derived from other studies. Furthermore, we only had resources to audit a random sample of the patients (8 GP practices) to ascertain adherence to anticoagulation therapy, and did not directly assess anticoagulation in all patients entered into PCAF.

**CONCLUSIONS:**

The PCAF service is an innovative care pathway bridging the boundary between primary and secondary care. Systematic identification of AF patients with high stroke-risk and consultation in
Consultant-led clinics through this service effectively delivers OAC to high-risk AF patients in the community, with evidence of excellent continued compliance with treatment.

**Funding:**

The PCAF service was initially seed-funded through support from three pharmaceutical companies: Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. These companies make the three NOAC agents. This funding support was used for set-up costs of the service, staff salaries and reimbursement of physicians. None of the industry funding was paid directly to the physicians involved in the service, and the support was not contingent on the prescription of NOACs through the service. Following expansion of the service, with demonstration of effective outcomes, the service is now funded primarily through commissioning by Clinical Commissioning Groups. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

**Competing Interest statement:**

All authors have completed the ICMJE uniform disclosure at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; Inspira Health Solutions Ltd., of which LP is a director and RMT/NC are employees, has received funding from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. to support the set-up of the PCAF service; MD has received physician fees from Inspira Health Solutions Ltd. for delivering PCAF clinics; JDM has received speaker fees from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. and has received physician fees from Inspira Health Solutions Ltd. for delivering PCAF clinics; PK has received consulting fees and honoraria from 3M Medica, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi-Sankyo, Johnson & Johnson, Medtronic, Merck, MSD, Pfizer, Sanofi, Servier, and Takeda, and research grants from 3M Medica/MEDA Pharma, Bristol-Myers Squibb, Pfizer, Cardiovascular Therapeutics, Daiichi Sankyo, Sanofi Aventis, and St. Jude Medical; DG has received speaker fees from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. and has received physician fees from
Inspira Health Solutions Ltd. for delivering PCAF clinics; no other relationships or activities that could appear to have influenced the submitted work.

Author contributions:

Moloy Das: Study design, data analysis and interpretation, drafting of the manuscript, final approval and is accountable for all aspects of the work.

Lee Panter: Study conception, drafting of the manuscript, final approval and is accountable for all aspects of the work.

Gareth J Wynn: Data interpretation, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Rob M Taylor: Data acquisition and analysis, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Neil Connor: Study conception, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Joseph D Mills: Study conception, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Paulus Kirchhof: Study design, drafting and critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Dhiraj Gupta: Study conception and design, drafting and critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Contributorship/Guarantor:

There are no contributors in addition to the named authors. Dr. Dhiraj Gupta is the guarantor for the study.

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Ethics approval:

Ethics approval was not required for this study.

Transparency declaration:

The manuscript’s guarantor affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
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Figures legends:

Figure 1: Graphic showing the four phases of the PCAF service pathway

Figure 2: CONSORT flowchart showing outcomes for patients not on anticoagulation identified through the PCAF service. AF = atrial fibrillation, OAC = oral anticoagulation.

Figure 3: CONSORT flowchart showing outcomes for patients on warfarin with a sub-optimal TTR identified through the PCAF service. INR = International Normalised Ratio; TTR = time-in-therapeutic range; NOAC = non-vitamin K antagonist oral anticoagulant.
Figure 1: Graphic showing the four phases of the PCAF service pathway
80x51mm (300 x 300 DPI)
Figure 2: CONSORT flowchart showing outcomes for patients not on anticoagulation identified through the PCAF service. AF= atrial fibrillation, OAC = oral anticoagulation.

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103x75mm (300 x 300 DPI)
STROBE Statement—checklist of items that should be included in reports of observational studies

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# Primary Care Atrial Fibrillation Service: Outcomes from Consultant-led anticoagulation assessment clinics in the Primary Care setting in the United Kingdom

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Primary Care Atrial Fibrillation Service: Outcomes from Consultant-led anticoagulation assessment clinics in the Primary Care setting in the United Kingdom

Short title: Primary Care Atrial Fibrillation Service

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Key words: Atrial fibrillation; anticoagulation; neurologic events; health care delivery

Word count: 3311
ABSTRACT

Objective:

Stroke-risk in atrial fibrillation (AF) can be significantly reduced by appropriate thromboembolic prophylaxis. However NICE estimates suggest that up to half of eligible AF patients are not anticoagulated, with severe consequences for stroke prevention. We aimed to determine the outcome of an innovative Primary Care AF (PCAF) service on anticoagulation uptake in a cohort of high-risk AF patients in the United Kingdom.

Methods:

The PCAF service is a novel cooperative pathway providing specialist resources within GP practices. It utilises a 4-phase protocol to identify high-risk AF patients (CHA\textsubscript{2}DS\textsubscript{2}-VASc\geq1) who are sub-optimally anticoagulated, and delivers Consultant-led anticoagulation assessment within the local GP practice. We assessed rates of anticoagulation in high-risk patients before and after PCAF service intervention, and determined compliance with newly-initiated anticoagulation at follow-up.

Results:

The PCAF service was delivered in 56 GP practices (population 386,624; AF prevalence 2.1%) between June 2012 and June 2014. 1579 high-risk AF patients with sub-optimal anticoagulation (either not taking any anticoagulation or taking warfarin but with a low time-in-therapeutic-range) were invited for review, with 86% attending. Of 1063 eligible patients on no anticoagulation, 1020 (96%) agreed to commence warfarin (459 (43%)) or a non-vitamin K antagonist oral anticoagulant (NOAC, 561 (53%)). The overall proportion of eligible patients receiving anticoagulation improved from 77% to 95% (P<0.0001). Additionally, 111/121 (92%) patients sub-optimally treated with warfarin agreed to switch to a NOAC. Audit of eight practices after 195 [185-606] days showed that 90% of patients commenced on a new anticoagulant therapy had continued treatment. Based on data extrapolated from previous studies, around 30-35 strokes per year may have been prevented in these previously under-treated high-risk patients.
Conclusions:

Systematic identification of AF patients with high stroke-risk and consultation in PCAF Consultant-led clinics effectively delivers oral anticoagulation to high-risk AF patients in the community.

Article summary:

Strengths and limitations of this study

- This study directly assessed the outcome of a novel approach of delivering Consultant-led anticoagulation assessment clinics in GP practices.
- The study was not performed as a controlled trial.
- Only a random sample of the patients was assessed to ascertain adherence to anticoagulation therapy.
- Our estimates on stroke prevention through the intervention are based on estimates of the effect of anticoagulation derived from other studies.
INTRODUCTION:

Atrial fibrillation (AF) is the cause of one in four strokes,[1-4] and approximately 5% of unselected patients admitted for acute stroke have previously undiagnosed AF.[5] Optimal prevention of AF-related strokes is of obvious interest to patients with AF, as well as avoiding the cost of stroke management to health care systems.[6] Oral anticoagulation (OAC) using vitamin K antagonists (most commonly warfarin) or non-vitamin K antagonist oral anticoagulant (NOAC) drugs can prevent approximately two-thirds of AF-related strokes.[7, 8] NOAC therapy can be delivered with a simpler infrastructure in a cost-effective way,[9-11] and with a lower risk for bleeding, especially for intracranial haemorrhage.[8, 12] Despite the clear benefits in high-risk AF patients, OAC is underused in AF patients: the National Institute for Health and Clinical Excellence (NICE) estimates that 42% of patients that should be anticoagulated are not,[13] and similar observations have been made in other countries.[14, 15] The reasons for this are likely to be multifactorial, including concerns from GPs and patients regarding bleeding risk, the need for regular INR monitoring on vitamin K antagonists, unsystematic identification and management of AF patients in need of OAC, and lack of awareness of this need.

There are some data that hospital clinicians with specialist training in the management of AF will achieve higher anticoagulation rates in AF patients than general practitioners or internists.[16] However, most AF patients are not under specialist care in the NHS. The recently-released atrial fibrillation management guideline from NICE focuses on the need for improved rates of anticoagulation in AF patients at elevated risk of stroke,[17] and a related NICE document “How to Change Practice” promotes the concept of better integration between primary and secondary care.[18]

Foreseeing this healthcare priority, we instituted an innovative Primary Care Atrial Fibrillation (PCAF) Service in GP practices in Merseyside in the United Kingdom in June 2012. The PCAF service provides a hospital Consultant-led service offering specialist expertise in the management of AF patients at
high stroke-risk within GP practices, and has now expanded to involve GP practices across England
and Wales. We aimed to determine the outcomes of this service over the two years since its
inception.

METHODS:
The PCAF service

PCAF service staff:
The PCAF service involved three groups of staff:

1) Trained healthcare professionals with a nursing or allied health professional background
   (termed “PCAF professionals”)
2) Consultant Cardiologists or Consultant Stroke Physicians from local hospitals
3) Office administrative staff

Practice enrolment:
GP practices were informed of the availability of the service through direct systematic marketing or
by approaching CCG Commissioning Managers and/or Medicines Management teams. As the service
expanded, interest was expressed from GP practices based on recommendations from previously-
enrolled practices.

Pathway:
In each enrolled GP practice, the PCAF service was delivered via four phases, with an additional
practice education programme (Figure 1):

Phase 1:
The PRIMIS+ AF Query Case Finder Set is an automated electronic tool used widely in primary care in
the United Kingdom. It is used to search electronic patient records to identify entries in the medical
history that may potentially indicate a diagnosis of AF (for example, “irregular pulse” or “digoxin
therapy”). In Phase 1 of the PCAF service, this tool was used to search the records of all patients not
currently listed on the practice’s AF register in order to identify any further patients with a possible
or probable diagnosis of AF. This was to ensure that no high-risk patients were missed by virtue of
not currently being listed on the AF register. A PCAF professional then performed a comprehensive
case note review of all identified patients, with the outcome being one of:

- AF confirmed,
- patient does not have AF, or
- patient referred for further investigation to ascertain a diagnosis of AF.

If required, specialist support was provided by a PCAF Consultant Physician.

**Phase 2:**

The GRASP-AF tool was then applied. This is an audit tool created in partnership with NHS Improving
Quality that is used to risk-stratify patients and determine their current anticoagulation therapy.[19]

This tool was used to audit all patients on the AF register, including those added following Phase 1,
to identify those at high-risk of stroke in whom anticoagulation is recommended or should be
considered (CHA\textsubscript{2}DS\textsubscript{2}-VASc score ≥1, excluding females with no additional risk factors) but who were
not currently receiving anticoagulation therapy.[20] The PCAF professional performed a
comprehensive case note review of all identified patients, with the outcome being one of:

- AF confirmed and patient eligible for a PCAF face-to-face review,
- AF confirmed but only eligible for a ‘virtual notes review’ (applicable to patients who were
either housebound or were resident in a nursing home and were unable to attend the clinic),
or
- Patient not eligible to be invited for review in a PCAF clinic as anticoagulation therapy would
not be indicated. This was applicable to the following groups of patients:

1) patients who had previously suffered an episode of AF but this had subsequently
resolved (for example, a single episode of AF following a surgical procedure or AF
related to thyrotoxicosis which had since been successfully treated)
2) patients with a current contra-indication to anticoagulation (defined as on-going or recent untreated major bleeding, previous intracranial bleeding, or a severe risk of bleeding)

3) patients in whom, after a thorough review of their clinical records, it was found that there was no evidence that they had ever had AF.

In addition, all patients who were currently receiving warfarin had their time-in-therapeutic-range (TTR) over the prior six-month period calculated using an electronic TTR calculator; those who had a sub-optimal TTR (defined as <65%) were also deemed to be at high risk and therefore eligible for review to assess the optimal anticoagulation strategy.[17]

Phase 3:
An office administrator sent out a letter of invitation with a pre-booked appointment to all eligible patients two weeks in advance of the PCAF clinic. Literature detailing the reason for the clinic review and the risks and benefits of anticoagulation was also included with the invitation letter. Patients were then contacted by telephone one week prior to their appointment to explain the service and answer any queries, and again one day prior in order to minimise non-attendance (“call and recall” approach).

Phase 4:
A Consultant Cardiologist or Consultant Stroke Physician delivered PCAF anticoagulation assessment clinics within the patient’s GP practice. The patient’s current treatment was reviewed and, where appropriate, anticoagulation was prescribed in accordance with NICE guidelines and/or the local medicines management formulary. Other aspects of medical treatment for AF, such a rate or rhythm control therapies, were also reviewed where appropriate.

Education:
GPs, nurse clinicians, practice nurses and practice pharmacists were invited to take part in the Consultant-led PCAF anticoagulation clinics, allowing opportunities for shared learning and
discussion of individual cases. Additionally, staff members from enrolled practices had access to a Consultant-led Continuous Professional Development education programme.

**Assessment of outcomes:**

The eventual outcome for each identified high-risk AF patient in the PCAF pathway was recorded in the individual practices’ network drive as well as on a central database. We assessed the uptake of anticoagulation in appropriate patients after intervention of the PCAF service compared to before. To assess on-going compliance with the prescribed treatment, case notes for patients who were prescribed a new or alternative anticoagulant agent were reviewed in a subset of GP practices in which the PCAF pathway had been completed at least 6 months prior. As per the definitions listed by the NHS Health Research Authority, this study was classified as a service evaluation rather than research and therefore did not require ethical review by a Research Ethics Committee.

**Statistical analysis:**

Continuous variables that are normally distributed are expressed as mean ± standard deviation, and variables that are not normally distributed are expressed as a median [interquartile range (IQR)]. Proportions were compared using the Chi square test. All tests were two-sided and *P*<0.05 was considered statistically significant.

**RESULTS:**

To date, the PCAF pathway has been implemented in 56 GP practices serving a population of 386,624 registered patients. For an average practice of 6000-7000 patients, it took approximately 12 hours for a PCAF professional to utilise the search tools and perform a review of patient case notes, around 3 hours for administrative staff to send invitation letters and contact patients by phone, and approximately 4 hours for a physician (supported by a PCAF professional) to deliver the anticoagulation assessment clinic.
Outcomes from the 4 phases of the PCAF pathway are detailed below.

**Patients not on anticoagulation (Figure 2):**

**Phase 1:**
For the 56 practices, clarification of the AF register resulted in a total population with AF of 7945 patients (prevalence 2.1%).

**Phase 2:**
7487 (94%) of these patients had a CHA\textsuperscript{2}DS\textsubscript{2}-VASc score of ≥1, of whom 4178 (56%; per-practice range 29-78%) were already on anticoagulation. Case notes were then reviewed for 2914 patients not on anticoagulation, with 1335 (46%) patients judged not to be eligible for anticoagulation. This was due to either: anticoagulation not indicated (female gender the only risk factor), a contraindication to anticoagulation, an incorrect Read code for AF (commonly due to the application of an AF Read code at the time of investigation but not removed when AF not found), or resolution of AF. This left 1579 patients who were eligible for, but not on, anticoagulation.

**Phase 3:**
These 1579 patients were invited to PCAF anticoagulation clinics using the “call and recall” approach, of whom 1358 (86%) attended for review within two weeks of invitation, with only 14% of patients failing to attend.

**Phase 4:**
Following review in clinic of the 1358 patients who attended, 1063 (78%) were confirmed to be eligible for anticoagulation. Of these patients, 84% had a CHA\textsuperscript{2}DS\textsubscript{2}-VASc score of 2 or more, with the remaining 16% patients having a score of 1. Eighty-five percent of these patients were also eligible using the criterion of a CHADS2 score ≥1, with 52% having a CHADS2 score ≥2. Antiplatelet therapy was being taken by 71% of patients at the time of review. Eleven percent (n=117) of the 1063 patients not on anticoagulation had previously suffered a stroke or transient ischemic attack (TIA).
Following the consultation, 1020 (96%) patients agreed to commence anticoagulation (warfarin in 43% and a NOAC in 53%). With regard to the 561 patients commenced on a NOAC, 12% of patients had previously tried but not tolerated warfarin, 21% had previously declined warfarin and 67% preferred a NOAC over warfarin. NOAC prescription was distributed amongst the three agents as follows: apixaban - 17%, dabigatran - 49%, and rivaroxaban - 34%.

Of the 43 (4%) patients that did not agree to commence anticoagulation therapy at the time of their consultation, only 16 patients declined treatment, with the remaining 27 preferring to defer their decision pending further discussion with their GP.

Overall, taking into account all exclusions (patients deemed not to have AF and those ineligible for anticoagulation), the total number of patients eligible for anticoagulation registered to these 56 GP practices was 5471. With the intervention of the PCAF service, the proportion receiving anticoagulation improved from 77% (4187/5471) to 95% (5207/5471) (P<0.0001).

**Patients with a sub-optimal TTR (Figure 3):**

4178 patients in the 56 GP practices were already anticoagulated with warfarin. Case notes and INR records were reviewed for 3295 of these patients. 387 (12%) patients with a sub-optimal TTR (<65%) were identified and invited for review, of whom 83% attended. After clinical review, the majority of patients (62%) were advised to continue on warfarin. Reasons for this decision included: an improved TTR over recent readings, a clear reason for previous INR variability (such as previous courses of antibiotics), significant renal dysfunction contraindicating use of a NOAC, compliance issues that could be addressed at the clinic visit, or concerns over non-compliance, in which case warfarin was felt more appropriate to a NOAC as compliance could continue to be assessed through INR monitoring. 121 (38%) patients were offered a NOAC, with 111 (92%) agreeing to change therapy.

**Follow-up data:**
Eight random GP practices that had hosted the PCAF service at least 6 months previously were audited. A total of 87 patients initiated on a new anticoagulant agent were identified (median follow-up 195 [IQR 185-606] days). The characteristics of these patients (age 75±9 years, 60% male, median CHADS2 score 2 [1-3], median CHA2DS2-VASc score 3 [2-4]) were similar to those of the 1063 patients invited to PCAF clinics (age 74±10 years, 53% male, CHADS2 score 2 [1-3], CHA2DS2-VASc score 4 [2-6]). Twenty-five patients had been commenced on warfarin, 51 patients had been initiated on a NOAC as a first-line agent, and 11 patients had been switched from warfarin to a NOAC.

Of the 25 patients commenced on warfarin, 19 (76%) remained on this treatment at the time of the audit. One further patient had suffered recurrent deep vein thromboses on warfarin and had been switched by a Consultant Haematologist to a low-molecular-weight heparin, and therefore remained anticoagulated. Two patients had died during the follow-up period. In both cases, warfarin had been continued at the time of death and the deaths were unrelated to bleeding or stroke. Only three of the 25 patients requested to stop warfarin, resulting in an overall compliance rate of 88%.

For the 62 patients initiated on a NOAC, 50 (81%) remained on a NOAC. Three patients (all of whom had previously not been on any anticoagulation) had requested to switch to warfarin and remained anticoagulated. Three patients had died during follow-up; they had each remained on NOAC therapy up to the time of death and neither bleeding nor stroke were related to the cause of death. In one case, a new diagnosis of significant renal dysfunction was made (eGFR 35 ml/min) and NOAC therapy was stopped by the patient’s GP. Five patients requested to stop anticoagulation, with three of these switching to an antiplatelet agent. Overall, the compliance rate with NOAC treatment was 85% (53/62), and with any anticoagulation therapy was 90% (56/62).

Taking both the warfarin and NOAC groups into account, 78 of 87 (90%) patients had continued anticoagulation following PCAF intervention, either the initial agent or an alternative.

DISCUSSION:
During the implementation of PCAF, we made several observations that can inform the future management of AF patients: 1) there is a significant proportion of patients with AF at high risk of stroke in primary care that are not treated with OAC (23%), with a further group of patients inadequately anticoagulated with warfarin, and 2) a consultant-led anticoagulation service in the community will get the majority of these patients anticoagulated, including the facility for individual, patient-oriented anticoagulation decisions. Importantly, the PCAF intervention led to high compliance with newly-initiated anticoagulation. Taken together, PCAF has the potential to improve the utilisation of OAC, and to prevent strokes in high-risk AF patients.

Evidence generated in the last decade underpins the use of OAC in the vast majority of patients with AF, i.e. those with stroke risk factors (at least one, and certainly two of the CHA₂DS₂-VASc risk factors).[21, 22] This was reflected in previous NICE guidance on atrial fibrillation, published in June 2006, that listed all but female gender of the CHA₂DS₂-VASc risk factors for use in stroke-risk stratification.[23] Hence, guidance applicable in the Merseyside region has effectively advocated anticoagulation use since 2006 in most patients who would now accrue a score of 1 or more under the CHA₂DS₂-VASc scoring system, though this has been substantially clarified in the latest guidance.[17] Despite this guidance, the PCAF program identified 1063 high-risk patients without OAC, of whom 892 (84%) had a CHA₂DS₂-VASc score ≥2 and 171 (16%) had a CHA₂DS₂-VASc score of 1.[21, 22]

Clinician-initiated health improvement reviews in primary care are known to commonly suffer from low attendance rates. However, the PCAF service was able to achieve an overall attendance rate of 85%. This is likely to be in part due to the “call and recall” approach employed, with a letter invitation followed by phone call reminders one week and again one day prior to the appointment. Hence, this study corroborates prior studies showing that attendance rates can be improved with telephone reminders.[24, 25] In addition, it is possible that improved attendance may also have been related to the opportunity to see a specialist in the setting of their GP surgery.
Finally, the PCAF service has demonstrated a marked increase in the uptake of anticoagulation in high-risk AF patients, including those who had previously been offered but refused anticoagulation. In some cases, the option of NOAC agents that do not require monitoring will have facilitated this decision, but past research has also shown that rates of uptake are dependent on patient perceptions of the value of anticoagulation.[26] We believe that the increased experience with managing anticoagulation in AF patients, particularly with regard to NOACs, possessed by secondary care physicians in the fields of cardiology and stroke medicine helps to alter patients’ perceptions in many cases towards acceptance and continuation of anticoagulation.

**Prevention of strokes by the PCAF service:**

The PCAF service predominantly identifies the at-risk primary prevention population, though a small proportion (11%) had suffered a previous stroke or TIA. In primary prevention patients, approximately 35 patients need to be treated with warfarin for a year to prevent one stroke, whereas, in patients with a prior stroke, the number needed to treat (NNT) is around 12.[7, 27] Equivalent data are not available for the three available NOACs, but all have shown equivalent or superior efficacy compared to warfarin,[28-30] and modelling data have suggested a lower NNT compared to warfarin for each agent.[31] In this study, 1020 patients were newly anticoagulated due to the PCAF intervention, of whom 111 were secondary prevention patients. Compliance with therapy at follow-up was 90%, or approximately 918 patients. Furthermore, there were 111 patients who were previously on warfarin with a sub-optimal TTR who have now commenced a NOAC. Based on the estimated efficacy, the intervention of the PCAF service may have prevented around 30 to 35 strokes per year in these 56 GP practices.

**The PCAF service as a model of care:**

In the traditional model of care, only a small proportion of patients typically gain access to specialist hospital-based resources. Within the field of AF, these are usually patients requiring input regarding rhythm management. At the same time, however, it is extremely difficult for primary care clinicians
to not only be aware of developments in all areas of medicine, but also to have the knowledge and confidence to implement them. With specific regard to anticoagulation in patients with AF in primary care, familiarity with the CHA\textsubscript{2}DS\textsubscript{2}-VASc scoring system may not be universal, particularly as the CHADS2 score is still utilised for the Quality and Outcomes Framework (QOF). Additionally, primary care clinicians may have little or no experience with the NOAC agents, in part due to their relatively recent release and approval, and in part due to the limited number of conditions for which they are indicated.

The PCAF service took an innovative approach by bridging this boundary between primary and secondary care, providing specialist resources within the primary care setting. This strategy has two distinct advantages. Firstly, patients currently managed solely within primary care are reviewed and, where appropriate, their anticoagulation treatment is optimised. Secondly, the educational legacy left within the GP practice following completion of the PCAF pathway enables such optimal treatment to be carried forward for future patients.

Limitations:

The PCAF intervention was not performed as a controlled trial, and our estimates on stroke prevention through the intervention are based on estimates of the effect of OAC derived from other studies. Furthermore, we only had resources to audit a random sample of the patients (8 GP practices) to ascertain adherence to anticoagulation therapy, and did not directly assess anticoagulation in all patients entered into PCAF.

CONCLUSIONS:

The PCAF service is an innovative care pathway bridging the boundary between primary and secondary care. Systematic identification of AF patients with high stroke-risk and consultation in Consultant-led clinics through this service effectively delivers OAC to high-risk AF patients in the community, with evidence of excellent continued compliance with treatment.
Funding:

The PCAF service was initially seed-funded through support from three pharmaceutical companies: Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. These companies make the three NOAC agents. This funding support was used for set-up costs of the service, staff salaries and reimbursement of physicians. None of the industry funding was paid directly to the physicians involved in the service, and the support was not contingent on the prescription of NOACs through the service. Following expansion of the service, with demonstration of effective outcomes, the service is now funded primarily through commissioning by Clinical Commissioning Groups. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing Interest statement:

All authors have completed the ICMJE uniform disclosure at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; Inspira Health Solutions Ltd., of which LP is a director and RMT/NC are employees, has received funding from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. to support the set-up of the PCAF service; MD has received physician fees from Inspira Health Solutions Ltd. for delivering PCAF clinics; JDM has received speaker fees from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. and has received physician fees from Inspira Health Solutions Ltd. for delivering PCAF clinics; PK has received consulting fees and honoraria from 3M Medica, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi-Sankyo, Johnson & Johnson, Medtronic, Merck, MSD, Pfizer, Sanofi, Servier, and Takeda, and research grants from 3M Medica/MEDA Pharma, Bristol-Myers Squibb, Pfizer, Cardiovascular Therapeutics, Daiichi Sankyo, Sanofi Aventis, and St. Jude Medical; DG has received speaker fees from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. and has received physician fees from Inspira Health Solutions Ltd. for delivering PCAF clinics; no other relationships or activities that could appear to have influenced the submitted work.

Author contributions:
Moloy Das: Study design, data analysis and interpretation, drafting of the manuscript, final approval and is accountable for all aspects of the work.

Lee Panter: Study conception, drafting of the manuscript, final approval and is accountable for all aspects of the work.

Gareth J Wynn: Data interpretation, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Rob M Taylor: Data acquisition and analysis, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Neil Connor: Study conception, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Joseph D Mills: Study conception, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Paulus Kirchhof: Study design, drafting and critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Dhiraj Gupta: Study conception and design, drafting and critical revision of the manuscript, final approval and is accountable for all aspects of the work.

Contributorship/Guarantor:

There are no contributors in addition to the named authors. Dr. Dhiraj Gupta is the guarantor for the study.

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Ethics approval:

Ethics approval was not required for this study.

Data sharing:

There are no additional unpublished data from the study.

Transparency declaration:

The manuscript’s guarantor affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
REFERENCES:


National Institute for Health and Care Excellence.


Figures legends:

Figure 1: Graphic showing the four phases of the PCAF service pathway

Figure 2: CONSORT flowchart showing outcomes for patients not on anticoagulation identified through the PCAF service. AF = atrial fibrillation, OAC = oral anticoagulation.

Figure 3: CONSORT flowchart showing outcomes for patients on warfarin with a sub-optimal TTR identified through the PCAF service. INR = International Normalised Ratio; TTR = time-in-therapeutic range; NOAC = non-vitamin K antagonist oral anticoagulant.
Figure 1: Graphic showing the four phases of the PCAF service pathway
199x127mm (300 x 300 DPI)
Figure 2: CONSORT flowchart showing outcomes for patients not on anticoagulation identified through the PCAF service. AF= atrial fibrillation, OAC = oral anticoagulation.

AF population: 7945

Untreated high risk patients: 1579 (19.9%)

Attended review: 1358 (17.1%)

AF confirmed: 1195 (15.0%)

Eligible for anticoagulation: 1063 (13.4%)

Agreed to anticoagulation: 1020 (12.8%)

- Already taking OAC
- Incorrect AF Read code
- AF resolved
- Contraindication to OAC

Did not attend: 221 (2.8%)

No AF - removed from register: 163 (2.1%)

Ineligible for anticoagulation: 132 (1.7%)

Declined/deferred OAC: 43 (0.5%)
Figure 3: CONSORT flowchart showing outcomes for patients on warfarin with a sub-optimal TTR identified through the PCAF service. INR = International Normalised Ratio; TTR = time-in-therapeutic range; NOAC = non-vitamin K antagonist oral anticoagulant.

Patients on warfarin: 4178

Case notes/INR records RVd 3295 (78.9%)

Sub-optimal TTR – invited: 387 (9.3%)

Did not attend: 66 (1.6%)

Attended review: 321 (7.7%)

Advised to remain on warfarin: 200 (4.8%)

Offered NOAC: 121 (2.9%)

Declined NOAC: 10 (0.2%)

Agreed to NOAC: 111 (2.7%)
STROBE Statement—checklist of items that should be included in reports of observational studies

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<tr>
<th>Item No</th>
<th>Recommendation</th>
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<tr>
<td><strong>Title and abstract</strong></td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract</td>
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<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
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<td><strong>Introduction</strong></td>
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<td>Background/rationale</td>
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<td>Explain the scientific background and rationale for the investigation being reported</td>
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<td>Objectives</td>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
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<td><strong>Methods</strong></td>
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<td>Study design</td>
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<td>Present key elements of study design early in the paper</td>
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<td>Setting</td>
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<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
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<td>Participants</td>
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<td>(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</td>
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<td>Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants</td>
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<td>(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed</td>
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<td>Case-control study—For matched studies, give matching criteria and the number of controls per case</td>
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<td>Variables</td>
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<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
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<td>Data sources/measurement</td>
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<td>Bias</td>
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<td>Describe any efforts to address potential sources of bias</td>
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<td>Study size</td>
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<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</td>
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<td>Statistical methods</td>
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<td>(a) Describe all statistical methods, including those used to control for confounding</td>
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<td>(b) Describe any methods used to examine subgroups and interactions</td>
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<td>(c) Explain how missing data were addressed</td>
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<td>(e) Describe any sensitivity analyses</td>
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Results

Participants

(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed

(b) Give reasons for non-participation at each stage

(c) Consider use of a flow diagram

Descriptive data

(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders

(b) Indicate number of participants with missing data for each variable of interest

(c) Cohort study—Summarise follow-up time (e.g., average and total amount)

Outcome data

Cohort study—Report numbers of outcome events or summary measures over time

Case-control study—Report numbers in each exposure category, or summary measures of exposure

Cross-sectional study—Report numbers of outcome events or summary measures

Main results

(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included

(b) Report category boundaries when continuous variables were categorized

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses

Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results

Summarise key results with reference to study objectives

Limitations

Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias

Interpretation

Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence

Generalisability

Discuss the generalisability (external validity) of the study results

Other information

Funding

Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Primary Care Atrial Fibrillation Service: Outcomes from Consultant-led anticoagulation assessment clinics in the Primary Care setting in the United Kingdom

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Primary Care Atrial Fibrillation Service: Outcomes from Consultant-led anticoagulation assessment clinics in the Primary Care setting in the United Kingdom

Short title: Primary Care Atrial Fibrillation Service

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Key words: Atrial fibrillation; anticoagulation; neurologic events; health care delivery

Word count: 3311
ABSTRACT

Objective:

Stroke-risk in atrial fibrillation (AF) can be significantly reduced by appropriate thromboembolic prophylaxis. However NICE estimates suggest that up to half of eligible AF patients are not anticoagulated, with severe consequences for stroke prevention. We aimed to determine the outcome of an innovative Primary Care AF (PCAF) service on anticoagulation uptake in a cohort of high-risk AF patients in the United Kingdom.

Methods:

The PCAF service is a novel cooperative pathway providing specialist resources within GP practices. It utilises a 4-phase protocol to identify high-risk AF patients (CHA2DS2-VASc≥1) who are sub-optimally anticoagulated, and delivers Consultant-led anticoagulation assessment within the local GP practice. We assessed rates of anticoagulation in high-risk patients before and after PCAF service intervention, and determined compliance with newly-initiated anticoagulation at follow-up.

Results:

The PCAF service was delivered in 56 GP practices (population 386,624; AF prevalence 2.1%) between June 2012 and June 2014. 1579 high-risk AF patients with sub-optimal anticoagulation (either not taking any anticoagulation or taking warfarin but with a low time-in-therapeutic-range) were invited for review, with 86% attending. Of 1063 eligible patients on no anticoagulation, 1020 (96%) agreed to commence warfarin (459 (43%)) or a non-vitamin K antagonist oral anticoagulant (NOAC, 561 (53%)). The overall proportion of eligible patients receiving anticoagulation improved from 77% to 95% (P<0.0001). Additionally, 111/121 (92%) patients sub-optimally treated with warfarin agreed to switch to a NOAC. Audit of eight practices after 195 [185-606] days showed that 90% of patients commenced on a new anticoagulant therapy had continued treatment. Based on data extrapolated from previous studies, around 30-35 strokes per year may have been prevented in these previously under-treated high-risk patients.
Conclusions:
Systematic identification of AF patients with high stroke-risk and consultation in PCAF Consultant-led clinics effectively delivers oral anticoagulation to high-risk AF patients in the community.

Article summary:
Strengths and limitations of this study

- This study directly assessed the outcome of a novel approach of delivering Consultant-led anticoagulation assessment clinics in GP practices.
- The study was not performed as a controlled trial.
- Only a random sample of the patients was assessed to ascertain adherence to anticoagulation therapy.
- Our estimates on stroke prevention through the intervention are based on estimates of the effect of anticoagulation derived from other studies.
INTRODUCTION:

Atrial fibrillation (AF) is the cause of one in four strokes,[1-4] and approximately 5% of unselected patients admitted for acute stroke have previously undiagnosed AF.[5] Optimal prevention of AF-related strokes is of obvious interest to patients with AF, as well as avoiding the cost of stroke management to health care systems.[6] Oral anticoagulation (OAC) using vitamin K antagonists (most commonly warfarin) or non-vitamin K antagonist oral anticoagulant (NOAC) drugs can prevent approximately two-thirds of AF-related strokes.[7, 8] NOAC therapy can be delivered with a simpler infrastructure in a cost-effective way,[9-11] and with a lower risk for bleeding, especially for intracranial haemorrhage.[8, 12] Despite the clear benefits in high-risk AF patients, OAC is underused in AF patients: the National Institute for Health and Clinical Excellence (NICE) estimates that 42% of patients that should be anticoagulated are not,[13] and similar observations have been made in other countries.[14, 15] The reasons for this are likely to be multifactorial, including concerns from GPs and patients regarding bleeding risk, the need for regular INR monitoring on vitamin K antagonists, unsystematic identification and management of AF patients in need of OAC, and lack of awareness of this need.

There are some data that hospital clinicians with specialist training in the management of AF will achieve higher anticoagulation rates in AF patients than general practitioners or internists.[16] However, most AF patients are not under specialist care in the NHS. The recently-released atrial fibrillation management guideline from NICE focuses on the need for improved rates of anticoagulation in AF patients at elevated risk of stroke,[17] and a related NICE document “How to Change Practice” promotes the concept of better integration between primary and secondary care.[18]

Foreseeing this healthcare priority, we instituted an innovative Primary Care Atrial Fibrillation (PCAF) Service in GP practices in Merseyside in the United Kingdom in June 2012. The PCAF service provides a hospital Consultant-led service offering specialist expertise in the management of AF patients at
high stroke-risk within GP practices, and has now expanded to involve GP practices across England and Wales. We aimed to determine the outcomes of this service over the two years since its inception.

METHODS:

The PCAF service

PCAF service staff:

The PCAF service involved three groups of staff:

1) Trained healthcare professionals with a nursing or allied health professional background (termed “PCAF professionals”)

2) Consultant Cardiologists or Consultant Stroke Physicians from local hospitals

3) Office administrative staff

Practice enrolment:

GP practices were informed of the availability of the service through direct systematic marketing or by approaching CCG Commissioning Managers and/or Medicines Management teams. As the service expanded, interest was expressed from GP practices based on recommendations from previously-enrolled practices.

Pathway:

In each enrolled GP practice, the PCAF service was delivered via four phases, with an additional practice education programme (Figure 1):

Phase 1:

The PRIMIS+ AF Query Case Finder Set is an automated electronic tool used widely in primary care in the United Kingdom. It is used to search electronic patient records to identify entries in the medical history that may potentially indicate a diagnosis of AF (for example, “irregular pulse” or “digoxin therapy”). In Phase 1 of the PCAF service, this tool was used to search the records of all patients not
currently listed on the practice’s AF register in order to identify any further patients with a possible or probable diagnosis of AF. This was to ensure that no high-risk patients were missed by virtue of not currently being listed on the AF register. A PCAF professional then performed a comprehensive case note review of all identified patients, with the outcome being one of:

• AF confirmed,

• patient does not have AF, or

• patient referred for further investigation to ascertain a diagnosis of AF.

If required, specialist support was provided by a PCAF Consultant Physician.

Phase 2:
The GRASP-AF tool was then applied. This is an audit tool created in partnership with NHS Improving Quality that is used to risk-stratify patients and determine their current anticoagulation therapy.[19] This tool was used to audit all patients on the AF register, including those added following Phase 1, to identify those at high-risk of stroke in whom anticoagulation is recommended or should be considered (CHA\textsubscript{2}-DS\textsubscript{2}-VASc score ≥1, excluding females with no additional risk factors) but who were not currently receiving anticoagulation therapy.[20] The PCAF professional performed a comprehensive case note review of all identified patients, with the outcome being one of:

• AF confirmed and patient eligible for a PCAF face-to-face review,

• AF confirmed but only eligible for a ‘virtual notes review’ (applicable to patients who were either housebound or were resident in a nursing home and were unable to attend the clinic), or

• Patient not eligible to be invited for review in a PCAF clinic as anticoagulation therapy would not be indicated. This was applicable to the following groups of patients:

1) patients who had previously suffered an episode of AF but this had subsequently resolved (for example, a single episode of AF following a surgical procedure or AF related to thyrotoxicosis which had since been successfully treated)
2) patients with a current contra-indication to anticoagulation (defined as on-going or recent untreated major bleeding, previous intracranial bleeding, or a severe risk of bleeding)

3) patients in whom, after a thorough review of their clinical records, it was found that there was no evidence that they had ever had AF.

In addition, all patients who were currently receiving warfarin had their time-in-therapeutic-range (TTR) over the prior six-month period calculated using an electronic TTR calculator; those who had a sub-optimal TTR (defined as <65%) were also deemed to be at high risk and therefore eligible for review to assess the optimal anticoagulation strategy.[17]

Phase 3:

Two weeks before the scheduled PCAF clinic, an office administrator sent a letter to patients eligible for clinic review inviting them to attend a PCAF appointment. Literature detailing the reason for the clinic review and the risks and benefits of anticoagulation was also included with the invitation letter. Patients were then contacted by telephone one week prior to their appointment to explain the service and answer any queries, and again one day prior in order to minimise non-attendance ("call and recall" approach).

Phase 4:

A Consultant Cardiologist or Consultant Stroke Physician delivered PCAF anticoagulation assessment clinics within the patient’s GP practice. The patient’s current treatment was reviewed and, where appropriate, anticoagulation was prescribed in accordance with NICE guidelines and/or the local medicines management formulary. Other aspects of medical treatment for AF, such as a rate or rhythm control therapies, were also reviewed where appropriate.

Education:

GPs, nurse clinicians, practice nurses and practice pharmacists were invited to take part in the Consultant-led PCAF anticoagulation clinics, allowing opportunities for shared learning and
discussion of individual cases. Additionally, staff members from enrolled practices had access to a Consultant-led education programme. Practice staff attending this programme could count this towards their Continuing Professional Development/Continuing Medical Education targets for their annual appraisal but no other incentives for attendance were offered.

Assessment of outcomes:

The eventual outcome for each identified high-risk AF patient in the PCAF pathway was recorded in the individual practices’ network drive as well as on a central database. We assessed the uptake of anticoagulation in appropriate patients after intervention of the PCAF service compared to before. To assess on-going compliance with the prescribed treatment, case notes for patients who were prescribed a new or alternative anticoagulant agent were reviewed in a subset of GP practices in which the PCAF pathway had been completed at least 6 months prior. As per the definitions listed by the NHS Health Research Authority, this study was classified as a service evaluation rather than research and therefore did not require ethical review by a Research Ethics Committee.

Statistical analysis:

Continuous variables that are normally distributed are expressed as mean ± standard deviation, and variables that are not normally distributed are expressed as a median [interquartile range (IQR)]. Proportions were compared using the Chi square test. All tests were two-sided and P<0.05 was considered statistically significant.

RESULTS:

To date, the PCAF pathway has been implemented in 56 GP practices serving a population of 386,624 registered patients. For an average practice of 6000-7000 patients, it took approximately 12 hours for a PCAF professional to utilise the search tools and perform a review of patient case notes, around 3 hours for administrative staff to send invitation letters and contact patients by phone, and
approximately 4 hours for a physician (supported by a PCAF professional) to deliver the anticoagulation assessment clinic.

Outcomes from the 4 phases of the PCAF pathway are detailed below.

**Patients not on anticoagulation (Figure 2):**

**Phase 1:**
For the 56 practices, clarification of the AF register resulted in a total population with AF of 7945 patients (prevalence 2.1%).

**Phase 2:**
7487 (94%) of these patients had a CHA$_2$DS$_2$-VASc score of ≥1, of whom 4178 (56%; per-practice range 29-78%) were already on anticoagulation. Case notes were then reviewed for 2914 patients not on anticoagulation, with 1335 (46%) patients judged not to be eligible for anticoagulation. This was due to either: anticoagulation not indicated (female gender the only risk factor), a contraindication to anticoagulation, an incorrect Read code for AF (commonly due to the application of an AF Read code at the time of investigation but not removed when AF not found), or resolution of AF. This left 1579 patients who were eligible for, but not on, anticoagulation.

**Phase 3:**
These 1579 patients were invited to PCAF anticoagulation clinics using the “call and recall” approach, of whom 1358 (86%) attended for review within two weeks of invitation. Only 221 (14%) patients did not attend for review, with 13 (1%) declining the invitation and 208 (13%) failing to attend.

**Phase 4:**
Following review in clinic of the 1358 patients who attended, 1063 (78%) were confirmed to be eligible for anticoagulation. Of these patients, 84% had a CHA$_2$DS$_2$-VASc score of 2 or more, with the remaining 16% patients having a score of 1. Eighty-five percent of these patients were also eligible using the criterion of a CHADS2 score ≥1, with 52% having a CHADS2 score ≥2. Antiplatelet therapy
was being taken by 71% of patients at the time of review. Eleven percent (n=117) of the 1063 patients not on anticoagulation had previously suffered a stroke or transient ischemic attack (TIA).

Following the consultation, 1020 (96%) patients agreed to commence anticoagulation (warfarin in 43% and a NOAC in 53%). With regard to the 561 patients commenced on a NOAC, 12% of patients had previously tried but not tolerated warfarin, 21% had previously declined warfarin and 67% preferred a NOAC over warfarin. NOAC prescription was distributed amongst the three agents as follows: apixaban - 17%, dabigatran - 49%, and rivaroxaban - 34%.

Of the 43 (4%) patients that did not agree to commence anticoagulation therapy at the time of their consultation, only 16 patients declined treatment, with the remaining 27 preferring to defer their decision pending further discussion with their GP.

Overall, taking into account all exclusions (patients deemed not to have AF and those ineligible for anticoagulation), the total number of patients eligible for anticoagulation registered to these 56 GP practices was 5471. With the intervention of the PCAF service, the proportion receiving anticoagulation improved from 77% (4187/5471) to 95% (5207/5471) (P<0.0001).

**Patients with a sub-optimal TTR (Figure 3):**

4178 patients in the 56 GP practices were already anticoagulated with warfarin. Case notes and INR records were reviewed for 3295 of these patients. 387 (12%) patients with a sub-optimal TTR (<65%) were identified and invited for review, of whom 83% attended. After clinical review, the majority of patients (62%) were advised to continue on warfarin. Reasons for this decision included: an improved TTR over recent readings, a clear reason for previous INR variability (such as previous courses of antibiotics), significant renal dysfunction contraindicating use of a NOAC, compliance issues that could be addressed at the clinic visit, or concerns over non-compliance, in which case warfarin was felt more appropriate to a NOAC as compliance could continue to be assessed through
INR monitoring. 121 (38%) patients were offered a NOAC, with 111 (92%) agreeing to change therapy.

**Follow-up data:**

Eight random GP practices that had hosted the PCAF service at least 6 months previously were audited. A total of 87 patients initiated on a new anticoagulant agent were identified (median follow-up 195[IQR 185-606] days). The characteristics of these patients (age 75±9 years, 60% male, median CHADS2 score 2[1-3], median CHA₂DS₂-VASc score 3[2-4]) were similar to those of the 1063 patients invited to PCAF clinics (age 74±10 years, 53% male, CHADS2 score 2[1-3], CHA₂DS₂-VASc score 4[2-6]). Twenty-five patients had been commenced on warfarin, 51 patients had been initiated on a NOAC as a first-line agent, and 11 patients had been switched from warfarin to a NOAC.

Of the 25 patients commenced on warfarin, 19 (76%) remained on this treatment at the time of the audit. One further patient had suffered recurrent deep vein thromboses on warfarin and had been switched by a Consultant Haematologist to a low-molecular-weight heparin, and therefore remained anticoagulated. Two patients had died during the follow-up period. In both cases, warfarin had been continued at the time of death and the deaths were unrelated to bleeding or stroke. Only three of the 25 patients requested to stop warfarin, resulting in an overall compliance rate of 88%.

For the 62 patients initiated on a NOAC, 50 (81%) remained on a NOAC. Three patients (all of whom had previously not been on any anticoagulation) had requested to switch to warfarin and remained anticoagulated. Three patients had died during follow-up; they had each remained on NOAC therapy up to the time of death and neither bleeding nor stroke were related to the cause of death. In one case, a new diagnosis of significant renal dysfunction was made (eGFR 35 ml/min) and NOAC therapy was stopped by the patient’s GP. Five patients requested to stop anticoagulation, with three of these switching to an antiplatelet agent. Overall, the compliance rate with NOAC treatment was 85% (53/62), and with any anticoagulation therapy was 90% (56/62).
Taking both the warfarin and NOAC groups into account, 78 of 87 (90%) patients had continued anticoagulation following PCAF intervention, either the initial agent or an alternative.

DISCUSSION:

During the implementation of PCAF, we made several observations that can inform the future management of AF patients: 1) there is a significant proportion of patients with AF at high risk of stroke in primary care that are not treated with OAC (23%), with a further group of patients inadequately anticoagulated with warfarin, and 2) a consultant-led anticoagulation service in the community will get the majority of these patients anticoagulated, including the facility for individual, patient-oriented anticoagulation decisions. Importantly, the PCAF intervention led to high compliance with newly-initiated anticoagulation. Taken together, PCAF has the potential to improve the utilisation of OAC, and to prevent strokes in high-risk AF patients.

Evidence generated in the last decade underpins the use of OAC in the vast majority of patients with AF, i.e. those with stroke risk factors (at least one, and certainly two of the CHA$_2$DS$_2$-VASc risk factors).[21, 22] This was reflected in previous NICE guidance on atrial fibrillation, published in June 2006, that listed all but female gender of the CHA$_2$DS$_2$-VASc risk factors for use in stroke-risk stratification.[23] Hence, guidance applicable in the Merseyside region has effectively advocated anticoagulation use since 2006 in most patients who would now accrue a score of 1 or more under the CHA$_2$DS$_2$-VASc scoring system, though this has been substantially clarified in the latest guidance.[17] Despite this guidance, the PCAF program identified 1063 high-risk patients without OAC, of whom 892 (84%) had a CHA$_2$DS$_2$-VASc score ≥2 and 171 (16%) had a CHA$_2$DS$_2$-VASc score of 1.[21, 22]

Clinician-initiated health improvement reviews in primary care are known to commonly suffer from low attendance rates. However, the PCAF service was able to achieve an overall attendance rate of 85%. This is likely to be in part due to the “call and recall” approach employed, with a letter invitation followed by phone call reminders one week and again one day prior to the appointment.
Hence, this study corroborates prior studies showing that attendance rates can be improved with telephone reminders.\[24, 25\] In addition, it is possible that improved attendance may also have been related to the opportunity to see a specialist in the setting of their GP surgery.

Finally, the PCAF service has demonstrated a marked increase in the uptake of anticoagulation in high-risk AF patients, including those who had previously been offered but refused anticoagulation. In some cases, the option of NOAC agents that do not require monitoring will have facilitated this decision, but past research has also shown that rates of uptake are dependent on patient perceptions of the value of anticoagulation.\[26\] We believe that the increased experience with managing anticoagulation in AF patients, particularly with regard to NOACs, possessed by secondary care physicians in the fields of cardiology and stroke medicine helps to alter patients’ perceptions in many cases towards acceptance and continuation of anticoagulation.

**Prevention of strokes by the PCAF service:**

The PCAF service predominantly identifies the at-risk primary prevention population, though a small proportion (11\%) had suffered a previous stroke or TIA. In primary prevention patients, approximately 35 patients need to be treated with warfarin for a year to prevent one stroke, whereas, in patients with a prior stroke, the number needed to treat (NNT) is around 12.\[7, 27\]

Equivalent data are not available for the three available NOACs, but all have shown equivalent or superior efficacy compared to warfarin,\[28-30\] and modelling data have suggested a lower NNT compared to warfarin for each agent.\[31\] In this study, 1020 patients were newly anticoagulated due to the PCAF intervention, of whom 111 were secondary prevention patients. Compliance with therapy at follow-up was 90\%, or approximately 918 patients. Furthermore, there were 111 patients who were previously on warfarin with a sub-optimal TTR who have now commenced a NOAC. Based on the estimated efficacy, the intervention of the PCAF service may have prevented around 30 to 35 strokes per year in these 56 GP practices.

**The PCAF service as a model of care:**


In the traditional model of care, only a small proportion of patients typically gain access to specialist hospital-based resources. Within the field of AF, these are usually patients requiring input regarding rhythm management. At the same time, however, it is extremely difficult for primary care clinicians to not only be aware of developments in all areas of medicine, but also to have the knowledge and confidence to implement them. With specific regard to anticoagulation in patients with AF in primary care, familiarity with the CHA₂DS₂-VASc scoring system may not be universal, particularly as the CHADS² score is still utilised for the Quality and Outcomes Framework (QOF). Additionally, primary care clinicians may have little or no experience with the NOAC agents, in part due to their relatively recent release and approval, and in part due to the limited number of conditions for which they are indicated.

The PCAF service took an innovative approach by bridging this boundary between primary and secondary care, providing specialist resources within the primary care setting. This strategy has two distinct advantages. Firstly, patients currently managed solely within primary care are reviewed and, where appropriate, their anticoagulation treatment is optimised. Secondly, the educational legacy left within the GP practice following completion of the PCAF pathway enables such optimal treatment to be carried forward for future patients.

**Limitations:**

The PCAF intervention was not performed as a controlled trial, and our estimates on stroke prevention through the intervention are based on estimates of the effect of OAC derived from other studies. Furthermore, we only had resources to audit a random sample of the patients (8 GP practices) to ascertain adherence to anticoagulation therapy, and did not directly assess anticoagulation in all patients entered into PCAF.

**CONCLUSIONS:**

The PCAF service is an innovative care pathway bridging the boundary between primary and secondary care. Systematic identification of AF patients with high stroke-risk and consultation in
Consultant-led clinics through this service effectively delivers OAC to high-risk AF patients in the community, with evidence of excellent continued compliance with treatment.

**Funding:**

The PCAF service was initially seed-funded through support from three pharmaceutical companies: Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. These companies make the three NOAC agents. This funding support was used for set-up costs of the service, staff salaries and reimbursement of physicians. None of the industry funding was paid directly to the physicians involved in the service, and the support was not contingent on the prescription of NOACs through the service. Following expansion of the service, with demonstration of effective outcomes, the service is now funded primarily through commissioning by Clinical Commissioning Groups. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

**Competing Interest statement:**

All authors have completed the ICMJE uniform disclosure at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; Inspira Health Solutions Ltd., of which LP is a director and RMT/NC are employees, has received funding from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. to support the set-up of the PCAF service; MD has received physician fees from Inspira Health Solutions Ltd. for delivering PCAF clinics; JDM has received speaker fees from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. and has received physician fees from Inspira Health Solutions Ltd. for delivering PCAF clinics; PK has received consulting fees and honoraria from 3M Medica, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi-Sankyo, Johnson & Johnson, Medtronic, Merck, MSD, Pfizer, Sanofi, Servier, and Takeda, and research grants from 3M Medica/MEDA Pharma, Bristol-Myers Squibb, Pfizer, Cardiovascular Therapeutics, Daiichi Sankyo, Sanofi Aventis, and St. Jude Medical; DG has received speaker fees from Bayer Ltd., Boehringer Ingelheim Ltd. and Pfizer Ltd. and has received physician fees from
Insperia Health Solutions Ltd. for delivering PCAF clinics; no other relationships or activities that could appear to have influenced the submitted work.

**Author contributions:**

**Moloy Das:** Study design, data analysis and interpretation, drafting of the manuscript, final approval and is accountable for all aspects of the work.

**Lee Panter:** Study conception, drafting of the manuscript, final approval and is accountable for all aspects of the work.

**Gareth J Wynn:** Data interpretation, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

**Rob M Taylor:** Data acquisition and analysis, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

**Neil Connor:** Study conception, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

**Joseph D Mills:** Study conception, critical revision of the manuscript, final approval and is accountable for all aspects of the work.

**Paulus Kirchhof:** Study design, drafting and critical revision of the manuscript, final approval and is accountable for all aspects of the work.

**Dhiraj Gupta:** Study conception and design, drafting and critical revision of the manuscript, final approval and is accountable for all aspects of the work.

**Contributorship/Guarantor:**

There are no contributors in addition to the named authors. Dr. Dhiraj Gupta is the guarantor for the study.

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**Data sharing:**

There are no additional unpublished data from this study.

**Ethics approval:**

Ethics approval was not required for this study.

**Transparency declaration:**

The manuscript’s guarantor affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
REFERENCES:


Figures legends:

Figure 1: Graphic showing the four phases of the PCAF service pathway

Figure 2: CONSORT flowchart showing outcomes for patients not on anticoagulation identified through the PCAF service. AF = atrial fibrillation, OAC = oral anticoagulation.

Figure 3: CONSORT flowchart showing outcomes for patients on warfarin with a sub-optimal TTR identified through the PCAF service. INR = International Normalised Ratio; TTR = time-in-therapeutic range; NOAC = non-vitamin K antagonist oral anticoagulant.
Figure 1: Graphic showing the four phases of the PCAF service pathway
199x127mm (300 x 300 DPI)
Figure 2: CONSORT flowchart showing outcomes for patients not on anticoagulation identified through the PCAF service. AF = atrial fibrillation, OAC = oral anticoagulation.

AF population: 7945
- Already taking OAC
- Incorrect AF Read code
- AF resolved
- Contraindication to OAC

Untreated high risk patients: 1579 (19.9%)

Attended review: 1358 (17.1%)

AF confirmed: 1195 (15.0%)

Eligible for anticoagulation: 1063 (13.4%)

Agreed to anticoagulation: 1020 (12.8%)

Did not attend: 221 (2.8%)

No AF - removed from register: 163 (2.1%)

Ineligible for anticoagulation: 132 (1.7%)

Declined/deferred OAC: 43 (0.5%)
Figure 3: CONSORT flowchart showing outcomes for patients on warfarin with a sub-optimal TTR identified through the PCAF service. INR = International Normalised Ratio; TTR = time-in-therapeutic range; NOAC = non-vitamin K antagonist oral anticoagulant.

Patients on warfarin: 4178
Case notes/INR records RVd 3295 (78.9%)
Sub-optimal TTR – invited: 387 (9.3%)
Attended review: 321 (7.7%)
Offered NOAC: 121 (2.9%)
Agreed to NOAC: 111 (2.7%)

Did not attend: 66 (1.6%)
Advised to remain on warfarin: 200 (4.8%)
Declined NOAC: 10 (0.2%)

189x138mm (300 x 300 DPI)
STROBE Statement—checklist of items that should be included in reports of observational studies

<table>
<thead>
<tr>
<th>Item No</th>
<th>Recommendation</th>
<th>Page number</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>(a) Indicate the study’s design with a commonly used term in the title or the abstract</td>
<td>2</td>
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<tr>
<td></td>
<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
<td>2</td>
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<tr>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
<td>4</td>
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<tr>
<td>3</td>
<td>State specific objectives, including any prespecified hypotheses</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>Present key elements of study design early in the paper</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
<td>5-6</td>
</tr>
<tr>
<td>6</td>
<td>(a) Cohort study—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</td>
<td>5-6</td>
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<td></td>
<td>Case-control study—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</td>
<td>N/A</td>
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<tr>
<td></td>
<td>Cross-sectional study—Give the eligibility criteria, and the sources and methods of selection of participants</td>
<td>N/A</td>
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<td></td>
<td>(b) Cohort study—For matched studies, give matching criteria and number of exposed and unexposed</td>
<td>N/A</td>
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<td>Case-control study—For matched studies, give matching criteria and the number of controls per case</td>
<td>N/A</td>
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<tr>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
<td>7</td>
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<tr>
<td>8</td>
<td>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group</td>
<td>7</td>
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<tr>
<td>9</td>
<td>Describe any efforts to address potential sources of bias</td>
<td>N/A</td>
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<tr>
<td>10</td>
<td>Explain how the study size was arrived at</td>
<td>8</td>
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<tr>
<td>11</td>
<td>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why</td>
<td>N/A</td>
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<tr>
<td>12</td>
<td>(a) Describe all statistical methods, including those used to control for confounding</td>
<td>7</td>
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<tr>
<td></td>
<td>(b) Describe any methods used to examine subgroups and interactions</td>
<td>N/A</td>
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<tr>
<td></td>
<td>(c) Explain how missing data were addressed</td>
<td>N/A</td>
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<tr>
<td></td>
<td>(d) Cohort study—If applicable, explain how loss to follow-up was addressed</td>
<td>N/A</td>
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<td>Case-control study—If applicable, explain how matching of cases and controls was addressed</td>
<td>N/A</td>
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<td></td>
<td>Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy</td>
<td>N/A</td>
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<td>(e) Describe any sensitivity analyses</td>
<td>N/A</td>
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### Results

<table>
<thead>
<tr>
<th>Participants</th>
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<tbody>
<tr>
<td>13*</td>
<td>8-10</td>
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<tr>
<td>(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</td>
<td></td>
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<tr>
<td>(b) Give reasons for non-participation at each stage N/A</td>
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<td>(c) Consider use of a flow diagram Figs 2&amp;3</td>
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<th>Descriptive data</th>
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<tr>
<td>14*</td>
<td>10</td>
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<tr>
<td>(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders</td>
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<tr>
<td>(b) Indicate number of participants with missing data for each variable of interest N/A</td>
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<td>(c) Cohort study—Summarise follow-up time (eg, average and total amount) N/A</td>
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<tr>
<th>Outcome data</th>
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<tr>
<td>15*</td>
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<tr>
<td>Cohort study—Report numbers of outcome events or summary measures over time</td>
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<td>Case-control study—Report numbers in each exposure category, or summary measures of exposure N/A</td>
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<tr>
<td>Cross-sectional study—Report numbers of outcome events or summary measures N/A</td>
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<th>Main results</th>
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<tr>
<td>16</td>
<td>N/A</td>
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<tr>
<td>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included</td>
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<td>(b) Report category boundaries when continuous variables were categorized N/A</td>
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<td>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period N/A</td>
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<tr>
<th>Other analyses</th>
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<tr>
<td>17</td>
<td>N/A</td>
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<tr>
<td>Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses</td>
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### Discussion

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<th>Key results</th>
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<tr>
<td>18</td>
<td>11</td>
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<tr>
<td>Summarise key results with reference to study objectives</td>
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<tr>
<th>Limitations</th>
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<tr>
<td>19</td>
<td>12</td>
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<tr>
<td>Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias</td>
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<tr>
<th>Interpretation</th>
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<tr>
<td>20</td>
<td>11-12</td>
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<tr>
<td>Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence</td>
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<th>Generalisability</th>
<th>Page number</th>
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<tr>
<td>21</td>
<td>12</td>
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<tr>
<td>Discuss the generalisability (external validity) of the study results</td>
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### Other information

<table>
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<tr>
<th>Funding</th>
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<tr>
<td>22</td>
<td>14</td>
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<tr>
<td>Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based</td>
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
Primary Care Atrial Fibrillation Service: outcomes from consultant-led anticoagulation assessment clinics in the primary care setting in the UK

Moloy Das, Lee Panter, Gareth J Wynn, Rob M Taylor, Neil Connor, Joseph D Mills, Paulus Kirchhof and Dhiraj Gupta

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