OPTIMIZING THE USE OF ORAL ANTICOAGULANT THERAPY FOR ATRIAL FIBRILLATION IN PRIMARY CARE: A PHARMACIST-LED INTERVENTION

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Background: Updated evidence-based guidelines for the management of atrial fibrillation (AF) necessitate patient review, particularly with respect to oral anticoagulants, to ensure maximum health gain around stroke prophylaxis.

Objective: To quantify the level of anticoagulation utilisation in patients with a CHA2DS2-VASc ≥1/≥2 (male/female) according to evidence-based guidelines and to assess the impact of a pharmacist-led intervention to optimise therapy.

Setting: Fifteen general medical practices in Liverpool, North-West England with a practice population of 99,129.

Method: GRASP-AF software was employed to interrogate patient electronic medical records to identify and risk stratify AF patients (using CHA2DS2-VASc). A pharmacist then reviewed the medical records of those of patients not anticoagulated and with a CHA2DS2-VASc ≥1/≥2 (male/female). Recommendations were discussed with a general practitioner (GP) and those patients in whom the need for anticoagulation was agreed were invited for a

consultation with either the pharmacist or GP and therapy optimised where appropriate. The GPs were responsible for managing those patients referred for diagnosis confirmation or further specialist opinion.

Main outcome measures: Proportion of patients eligible/not eligible for anticoagulation; proportions in whom anticoagulants initiated, refused, antiplatelets discontinued.

Results: Five hundred and twenty-three patients (31% of patients identified with AF and a CHA2DS2-VASc ≥1/≥2 (male/female)) were not receiving an anticoagulant (26 subsequently died or left the practice leaving 497). Three hundred and eighty-two (77%) pharmacist recommendations to a GP were agreed without modification. Following outcomes of diagnostic investigations and specialist referrals, 202 (41%) patients were candidates for anticoagulation, 251 (51%) were not eligible for anticoagulation, 103 (21%) were anticoagulated (56 warfarin, 47 DOAC).

Conclusion: A pharmacist-led intervention re-aligned oral anticoagulant therapy to the latest evidence based guidelines for stroke prophylaxis, whilst simultaneously correcting the over-utilisation of antiplatelet therapy.

Key words: Atrial fibrillation, pharmacist, stroke, anticoagulant

Implication for practice

- Pharmacists can have a major impact on increasing the uptake of oral anticoagulants in those with AF.
- While patient consultations should embrace a shared decision making approach, a sizeable proportion of patients may still refuse oral anticoagulant treatment.
- Practice models should be reviewed to ensure that patients are prescribed the evidence-based treatment from the point of diagnosis.

Introduction Atrial fibrillation (AF) is the most commonly diagnosed arrhythmia, with a systematic review of 184 population-based studies providing an estimate of the global prevalence at around 33.5 million [1]. The burden of AF is great, being associated with a five-fold increase in the risk of stroke in those with non-valvular AF and a 17-fold increase in those with valvular-AF [2]. The prevalence of AF is predicted to rise significantly due to several factors including an aging population [3], and greater prevalence of hypertension, obesity and diabetes [4], leading to AF being labelled a 'global epidemic' [5,6]. While the risk of stroke can be managed effectively with oral anticoagulants, bleeding is a major drawback hence careful consideration of risks and benefits is required [7]. Stroke and bleeding risk are not homogenous in the population and must be calculated on an individual patient basis by using CHA_2DS_2-VASc (congestive heart failure/left ventricular dysfunction, hypertension, age ≥75 years [doubled], diabetes, stroke [doubled] - vascular disease, age 65-74 years,

sex category [female]) and HASBLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INRs, elderly (age >65 years), drugs/alcohol concomitantly) classifications which stratify risk based on the presence of co-morbidities [7].

In recent years, three major developments have resulted in the necessity to update evidence-based guidance for the management of AF. Direct oral anticoagulants (DOACs) that are non-inferior to warfarin for AF stroke prophylaxis have been introduced to clinical practice [8-11]. Furthermore, the role of aspirin in AF related stroke prophylaxis is now in doubt with the emergence of evidence that oral anticoagulation is more effective [12-14]. Aspirin has also been shown to be ineffective compared to placebo or no therapy [15] with no overall net clinical benefit [16]. Recent evidence also suggests that anticoagulation should be considered at lower stroke risk levels than advised by previous guidance [17,18]. Such developments have led to the update of guidelines in 2010 from The European Society of Cardiology (ESC) and in 2014 from The National Institute of Clinical Excellence (NICE) in England and Wales which now state that anticoagulation with warfarin or DOAC should be considered for patients with a CHA_2DS_2-VASc ≥1/≥2 (male/female) [7,19]. The current American Heart Association guidelines also advocate consideration of anticoagulation at a CHA_2DS_2-VASc ≥1 but do not distinguish between gender.

Despite this plethora of evidence, it has been shown consistently that patient management in terms of the use of anticoagulants is suboptimal [20-23]. There is, however, a paucity of published literature describing approaches that have

been adopted to address this shortfall. The Anticoagulant Programme East London, United Kingdom (UK) (APEL) was an improvement program conducted in three Clinical Commissioning Groups (CCGs, bodies which serve a specific geographical location with responsibility for commissioning healthcare services) [24]. Education, dedicated software and support were provided to medical practices to implement change, resulting in an increase in the proportion of patients being anticoagulated. The Primary Care Atrial Fibrillation (PCAF) service employed consultants to review AF patients in 56 UK medical practices (population 386,624) and initiate anticoagulation [25]. While several pharmacist led interventions aiming to improve management of AF have been described, these were all based in secondary care with small sample sizes [26-28]. To date, no published work describes a pharmacist led intervention in primary care in the UK.

NHS England has embarked on an investment program that will see 1,970 pharmacists practising clinically within medical practices by 2020 [29]. The General Practice Forward View report from NHS England states that "pharmacists remain one of the most underutilised professional resources in the system and we must bring their considerable skills in to play more fully" [29].

Aims of the study

The aims of the study were to quantify the level of anticoagulation utilisation in patients in primary care with a CHA_2DS_2-VASc ≥1/≥2 (male/female) according to NICE guidelines [19], and to assess the impact of a pharmacist-led intervention to optimise therapy.

Ethical approval

Ethical approval was obtained from the Research Ethics Panel of the School of Pharmacy and Life Sciences, Robert Gordon University, Scotland. Advice obtained from an NHS ethics committee indicated that approval was not required. Management approval to conduct the study was obtained from Liverpool Community Health (LCH) and Liverpool CCG.

Method

Design

A clinical audit of practice against NICE guidelines [19], followed by pharmacist intervention to optimise anticoagulant prescribing.

Setting

The study was conducted in Liverpool, a major city in the North-West of England, which has a stroke mortality rate 20% greater in those less than 75 years compared to patients in similar CCGs in England [30]. Sixty-one primary care medical practices participated in the study, which took place over a period of one year from February 2015. Prior to study commencement, an educational session covering the study aim and processes was delivered by the project lead to each medical practice.

Inclusion and exclusion criteria

Patients included had a history of any form of AF, a CHA_2DS_2-VASc ≥1/≥2 (male/female) and were not prescribed an oral anticoagulant at the time of the study. There were no exclusions.

Patient identification

The GRASP-AF (Guidance on Risk Assessment and Stroke Prevention for Atrial Fibrillation) software, developed in partnership with NHS Improving Quality, was utilised to identify patients. The software scanned medical practice electronic

records producing a list of patients with a documented diagnosis of AF and risk stratified patients according to CHA_2DS_2-VASc scores. Those with a CHA_2DS_2-VASc ≥1/≥2 (male/female) not currently prescribed an oral anticoagulant were identified for further review.

Patient review

A team of medicines management staff were involved at various stages of the patient reviews, with training provided by the overall study lead to promote a consistent approach. Three pharmacists conducted the reviews independently, according to a standard operating procedure developed by the project lead, with support from the lead anticoagulant pharmacist, lead cardiovascular disease pharmacist and by the joint head of medicines management at LCH.

The medical records of each patient were reviewed by a pharmacist to determine eligibility for anticoagulation. This included: determination of the validity of the AF diagnosis (confirmed by ECG); clinical course of AF since diagnosis; previous AF related therapy decisions, particularly exposure to anticoagulants (with reasons for any discontinuation) and patient refusal of anticoagulation (with reasons); relevant medical and social history; and presence of any contraindication or cautions to the use of anticoagulants. A HASBLED score was calculated to quantify bleeding risk, based on which a recommendation was made by the pharmacist to the GP in terms of: possible candidate for anticoagulation; not suitable for anticoagulation; GP or specialist decision/investigation required; and diagnosis confirmation required. In addition,

for patients prescribed antiplatelet therapy for lone AF (i.e. no other valid indication), the recommendation was made for them to attend their GP for an antiplatelet risk/benefit discussion.

Patient reviews (including the CHA_2DS_2-VASc and HASBLED scores) and recommendations were documented on standard templates and presented to the GPs, either by email or paper-based, depending on the individual GP and medical practice preferences. Those recommendations which the GPs agreed were recorded in the patients' electronic medical records using a standard template. A face-to-face discussion between GP and pharmacist was arranged to reach consensus on any non-agreed recommendations.

Patient consultations

Those patients in whom the decision to commence anticoagulation was agreed were invited by letter to make an appointment at the medical practice for a consultation with either the pharmacist or GP (depending on GP and medical practice preference). Domiciliary visits were arranged for housebound patients. The consultation focused on: individual stroke and bleeding risks (with or without anticoagulation); the poor risk/benefit of antiplatelets for stroke prevention (if relevant) [12-16]; and information on the available anticoagulant options to reduce stroke risk (including benefits and weaknesses). The NICE AF patient decision aid was a key tool utilised by pharmacists to ensure a shared decision making approach was employed [31]. Relevant scientific information was provided in a patient oriented manner (e.g. pictorial representations of

stroke and bleeding risk) whilst also taking into account patient values and preferences [32]. A record of the outcome of the consultation (patient agreement or not with the recommendation) was recorded in the electronic medical record.

Those patients opting for warfarin were referred directly to the anticoagulant service for counselling and initiation. Patients electing a DOAC were referred for baseline blood tests (urea and electrolytes, liver functions tests and full blood count), following which they were invited back for counselling and initiation (blood results permitting). The GPs were responsible for the management of those patients requiring investigations (e.g. ECGs) or specialist input. Medical practices were revisited by a member of the research team after four and six months to ensure that recommendations (e.g. specialist advice sought) had been actioned.

The study flowchart is provided in Figure 1.

Data analysis

Data were analysed using descriptive statistics.

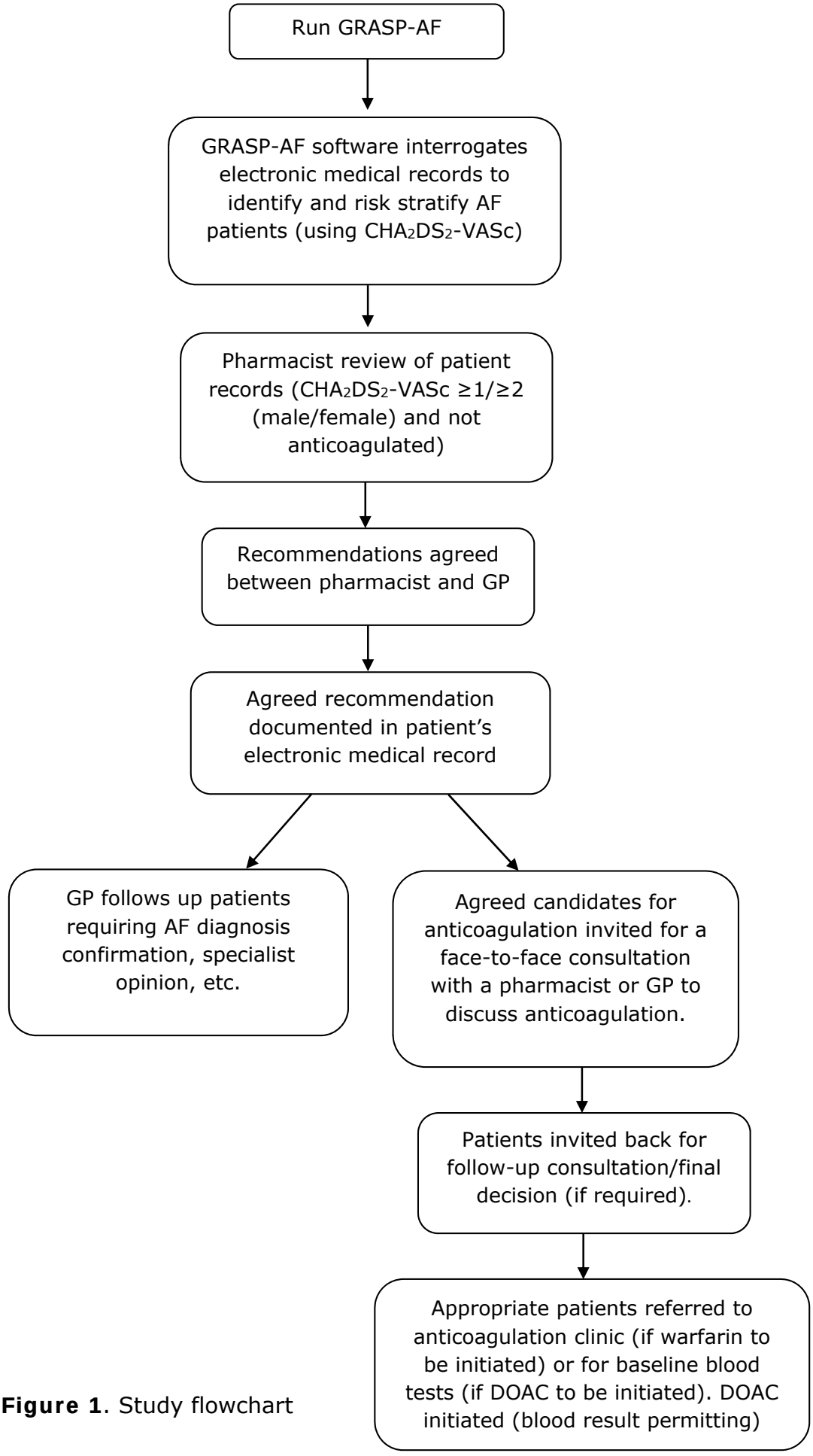

Figure 1. Study flowchart

Results

From a combined practice population of 99,129, a study population of 497 was derived, as illustrated in Figure 2.

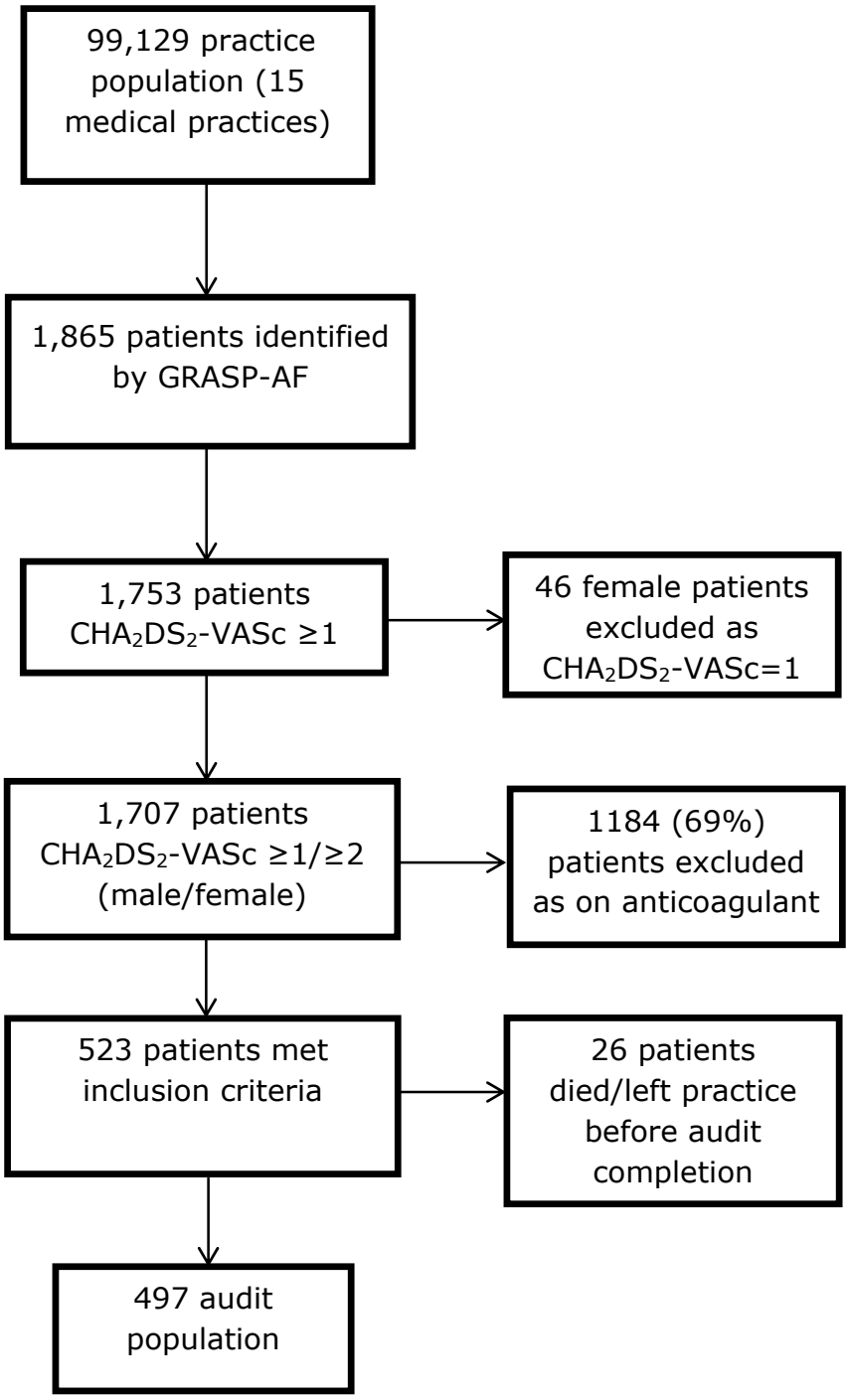

Figure 2. Derivation of study population

The mean age of the study population was 75.5 (standard deviation, SD 11.9) years with 291 (58.6%) male. The mean CHA_2DS_2-VASc score was 3.32 (SD 1.6) with almost one quarter (23.9%) at score 3 and one fifth (20.1%) at score 4. One hundred and seventy (34.2%) patients had previously been on an anticoagulant and 61 (12.2%) patients had previously declined an anticoagulant. Three hundred and sixty-six patients were prescribed an antiplatelet agent.

Pharmacist recommendations

Following pharmacist review of the medical notes, patients were categorised into five groups (Figure 3).

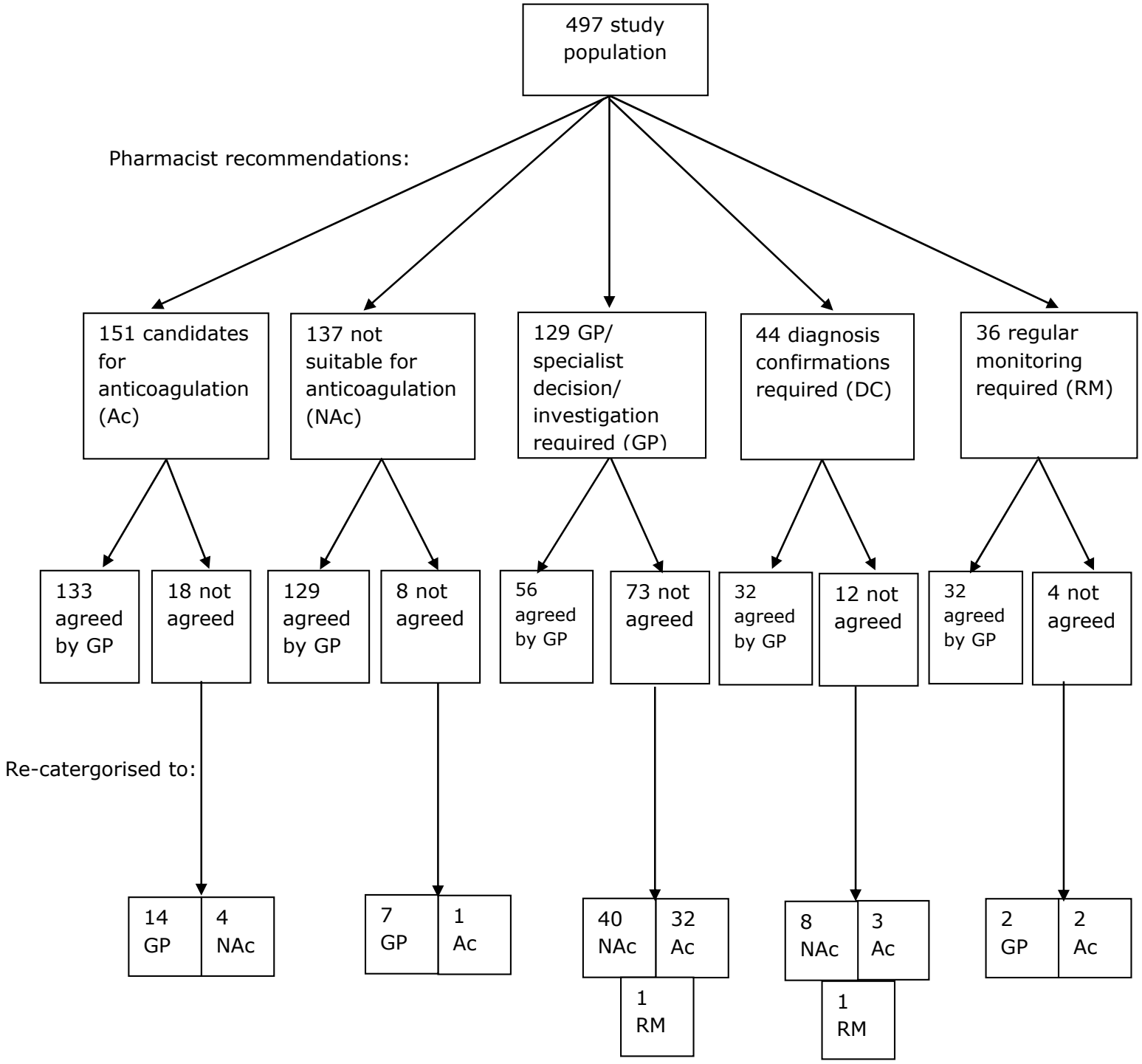

Figure 3. Fate of patients following pharmacist review of medical notes

The GPs agreed with 382 (76.9%) of recommendations without modification, with the major area of disagreement being in relation to those patients referred by the pharmacist to the GP for their opinion, further investigation or specialist input. Following pharmacist and GP input, 171 (34.4%) patients were identified as candidates for anticoagulation, 181 (36.4%) were not suitable for anticoagulation (142 contraindicated, 39 not indicated), 79 (15.9%) required further investigation or specialist input, 32 (6.4%) required confirmation of diagnosis and 34 (6.8%) required regular monitoring of pulse and AF symptoms. One hundred and eleven patients were investigated further (e.g. ECGs, referral to specialists), following which 31 patients were deemed suitable for anticoagulation giving a total of 202 (40.6%) patients for anticoagulation.

Patients deemed suitable for anticoagulation

Average patient age was 75.8 (SD 10.9) years, with 115 (56.9%) male and a mean CHA_2DS_2-VASc of 3.4 (SD 1.5). Of these 202 patients, 103 (51.0%) commenced an anticoagulant (59 at GP consultation and 44 at pharmacist consultation); 85 (83.3%) were switched from antiplatelet to anticoagulant. Fifty-six patients (54.4%) commencing an anticoagulant opted for warfarin and the others DOAC treatment. A further 76 (37.6%) refused anticoagulation (45 GP consultation, 31 pharmacist consultation), 16 (7.9%) failed to attend and 7 (3.5%) commenced an anticoagulant in secondary care.

Of 49 candidates for anticoagulation who had previously declined anticoagulation, 23 (46.9%) agreed to commence treatment, with the remainder refusing.

Patients not suitable for anticoagulation

One hundred and sixty-five patients were deemed unsuitable for anticoagulation (see Table 1), with the majority of patients (135, 81.8%) having multiple contraindications.

Table 1: Contraindications to anticoagulant therapy (n=165)

Contraindication	**Number of patients**	**%**
Poor prognosis - e.g. palliative, advanced malignancy.	19	11.5
Significant renal or hepatic disease.	15	9.1
History of serious bleed - e.g. subarachnoid haemorrhage, Haemorrhagic stroke, GI bleed/haemorrhage.	38	23.0
Gastrointestinal (GI) disease - e.g. inflammatory bowel disease, GI ulceration, varices.	39	23.6
Haematological abnormalities - e.g. anaemia, coagulopathies, myelodysplasia.	25	15.2
Central nervous system disease - e.g. dementia, epilepsy, paranoid psychosis.	47	28.5
As advised by secondary care	23	13.9
Miscellaneous contraindications e.g. injurious falls, poor compliance, alcohol dependence.	67	40.6

Discussion

This study demonstrated that oral anticoagulation for the management of AF could be optimised as a direct result of a pharmacist-led intervention in primary care. There was a high level of GP agreement with the pharmacist recommendations and indeed the GPs viewed that even more patients should be anticoagulated when referred by the pharmacists for further investigation. Many patients could not receive anticoagulants due to one or more contraindication and a number were reluctant to commence an anticoagulant. Of all patients with CHA_2DS_2-VASc ≥1/≥2 (male/female), this study resulted a 6% increase in anticoagulant prescribing.

There is overwhelming evidence that optimising the management of AF through anticoagulant prescribing will lead to a marked decrease in stroke prevalence. While estimations in the literature are derived from studies of warfarin, DOACs are non-inferior to warfarin [8-11] and modelling data suggests a lower number needed to treat for DOACs [33,25]. Using study findings and warfarin based figures, the interventions implemented in this study are estimated to have averted 3.78 stokes/year and 29.1 strokes over a lifetime (0.039 strokes/year and 0.30 over a lifetime averted/person anticoagulated) [34]. These estimates must be interpreted with caution as they assume patient adherence, although the shared decision making approach employed should have had a positive impact on patient adherence [35].

Patient anticoagulation refusal rates were similar (approximately 40%) for both pharmacists and GPs, despite the implementation of a shared decision making approach. While these refusals rates are similar to other studies employing the same approach [37,38,39], this is still worrying given the evidence of benefit which these patients are not deriving. One limitation of this study is that no data were collected on reasons for refusal. However, qualitative studies provide the following explanations: patient perception of increased bleeding risk; individual patient preferences; personally held beliefs [37,38,40]; feeling unable to make a judgement; reluctance to change therapy [40]; and aversions to taking medication [41]. There is also limited evidence that shared decision making may lead to more conservative decision making [42], with some patients expressing a desire to leave the final decision to the practitioner [43]. Refusal rates may have been influenced by perceptions of warfarin and it being labelled as a 'rat poison'. In a randomised trial of AF thromboprophylaxis, 36% of patients changed their original decision to be treated with a blinded drug once the name had been unblinded as warfarin [44]. While some claim that optimal patient care will be achieved when evidence based medicine and shared decision making are combined [45], others suggest that performance measures should focus on the proportion of eligible patients participating in shared decision making rather than on the uptake of medication [46].

Our study adds to the evidence base around beneficial effects of pharmacists working in general medical practices care, complementing other studies demonstrating: identification of high risk patients and improved disease management [47]; and increased evidence based prescribing [48]. In a

systematic review of 38 studies examining the effectiveness of clinical pharmacists in a primary care, pharmacist input was shown to be favourable in chronic disease management and quality use of medicines [49]. This evidence base helps provide justification for the investment into primary care pharmacists by NHS England.

While this study optimised anticoagulation retrospectively, practice should also be remodelled to ensure that patients receive the most appropriate evidence-based therapy at the time of diagnosis rather than having to be corrected at a later stage.

To our knowledge, this is the first study which reports a primary care pharmacist led intervention in the management of patients with AF in the UK. There are, however, limitations hence the study should be interpreted with caution. The study was conducted in 15 medical practices in one city of the UK hence the results may not be generalisable to other practices in the UK and beyond, particularly those settings with major differences in healthcare structures and processes. There was limited follow-up of patients to determine persistence and adherence with oral anticoagulants and no measures of impact on health outcomes. Furthermore, no economic evaluation was included in the study.

Future research could extend this study to include pharmacist independent prescribers who could change and commence therapy without the need for further GP input [50,51]. There is need to explore patient perceptions and

experiences of the pharmacist service. An economic evaluation is also warranted.

Conclusion

A pharmacist-led intervention realigned oral anticoagulant therapy to the latest evidence based guidelines for stroke prophylaxis, whilst simultaneously correcting the over-utilisation of antiplatelet therapy. There, however, remains a need to consider those patients in whom anticoagulants are contraindicated and to research those patients refusing anticoagulants.

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