the incidence of HIV/AIDS in adults (15–49 years) is between 6.4% and 11.9% [5]. Africa, like Europe, has an ageing population but with a biphasic age distribution, the old and the young. The strong and economically active have been removed in large numbers by HIV/AIDS. The elderly are thus economically and socially important in these societies and yet treatments for the neurodegenerative diseases they are inevitably going to suffer are out of reach economically.

Dotchin and co-workers’ paper, however, does remind us of the opportunities that exist in Africa for our understanding of Parkinson’s disease. Some of the rural communities are stable over long periods of time and in Tanzania 62.5% of the population live in rural areas [6]; there are fewer pollutants and potentially less compounding variables in terms of understanding the epidemiology of Parkinson’s disease. We have learnt much about the nature and causation of the disease by examining populations in which disease prevalence is very different from the western world, and there is an urgent need to study Parkinson’s disease and other degenerative disorders in these populations. A more urgent need however is to address the humanitarian aspects of an untreated but treatable disease, which is often forgotten in the context of overwhelming numbers of infectious disorders. The effects of medical migration that have resulted in many African doctors emigrating to wealthier countries such as the United Kingdom [7], results in the grossly inadequate number of neurologists and the virtual absence of geriatricians. This issue affects specialists [8] from many countries, and needs to be urgently addressed by the western world.

References

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Warfarin versus aspirin in the elderly in primary prophylaxis for atrial fibrillation

Atrial fibrillation is a common cardiac arrhythmia in adults. A recent European based community study showed an overall prevalence of 5.5%. The prevalence and incidence of AF increases with age, with an incidence of 1.1 per 1,000 for ages 55–59 years rising to 20.7 per 1,000 for ages 80–84 years [1]. AF is an independent risk factor for stroke. The Framingham Study showed 14.7% of strokes are associated with AF. There is a clear relationship between increasing age and incidence of AF associated strokes: 6.7% of strokes are related to AF in patients aged 50–59 years, rising to 36.2% in patients aged 80–89 years [2]. Evidence also shows AF related strokes have a poorer prognosis when compared with non-AF strokes, with larger neurological deficits, increased medical complications and higher in-patient mortality [3].

Primary thromboprophylaxis in AF has been demonstrated in clinical trials to reduce stroke. A meta-analysis looking at primary prevention showed an absolute risk reduction for stroke of 2.7% (number needed to treat for 1 year to prevent one stroke [NNT] was 37) with dose-adjusted warfarin compared with placebo, whilst aspirin conferred an absolute risk reduction of 1.5% (NNT 67). When dose-adjusted warfarin was compared to aspirin, the absolute risk
reduction of stroke was 0.6% in warfarinized patients (NNT 167) [4]. Another recent meta-analysis which included both primary and secondary prevention trials showed warfarin does have a small, but statistically significant increase in the incidence of major bleeding events; this risk is approximately double the haemorrhagic risk, which occurs with treatment with aspirin. However, the overall stroke reduction outweighs the bleeding risk. This absolute risk reduction is greatest in those patients with the highest stroke risk. This demonstrates a need for risk stratification [5]. These clinical trials were conducted in a relatively young population: the mean age at study entry was 69 years in the warfarin-placebo trials, with only approximately 20% of the subjects older than 75 years, similar age ranges were found in the aspirin-placebo and warfarin-aspirin trials [4]. Close monitoring of patients during trials means results are not always reproducible in clinical practice; however, similar stroke prevention and bleeding rates to those found in the trials have been observed in clinical practice [6].

The elderly with AF are at an increased risk of strokes and potentially have the most to gain from anticoagulation. The incidence of polypharmacy, comorbidities, falls, small vessel disease and visual and cognitive impairment rises with age, affecting bleeding risk. Warfarin is frequently under prescribed in this population due to physicians’ belief that age is associated with increased haemorrhagic risk. [7]. Two clinical trials have compared haemorrhagic risk with warfarin in an elderly population (>75 years) and a younger control group. No significant difference was found between the elderly and the control group, but one study showed a trend towards an increase in major haemorrhage with age [8, 9]. Systematic review of the randomised controlled trials of AF, stroke and major haemorrhage demonstrated an absolute risk reduction in stroke, which was substantially higher than the risk of bleeding in patients 75 years and older [5]. A recent trial even suggests the frail elderly benefit from anticoagulation in AF [10]. The therapeutic range of the INR is also important, maintaining an INR of 2.0–3.0 decreased the risk of major bleeding and thrombosis in the >75 years age group [8]. These trials all include a mix of primary and secondary thromboprophylaxis.

In this issue of Age and Ageing Rash et al. present a study comparing primary thromboprophylaxis with dose-adjusted warfarin and aspirin in octogenarians with chronic AF [11]. It is an important trial, which addresses this issue of therapy in the elderly population. Due to underpowering of the trial it did not achieve its primary aim of assessing the benefit of warfarin over aspirin. It showed dose-adjusted warfarin was well tolerated in octogenarians, resulting in no serious bleeding episodes or side effects. Warfarin had fewer adverse events than aspirin, 6% of patients developed adverse events on warfarin compared with 33% in the aspirin arm, a statistically significant result. Almost 20% of the aspirin arm withdrew due to gastrointestinal side effects. However, the study used Aspirin 300 mg once a day, which is at the upper limit of the dose ranges (75–300 mg) recommended in the NICE guidelines [12]. The risk of peptic ulcer bleeding with aspirin is dose related [13]. Tolerability may improve with a lower dose of aspirin. Alternatively patients in the aspirin wing could be coprescribed a proton pump inhibitor (PPI). Prophylactic use of PPIs is common in clinical practice. Further research is required into what dose of aspirin has maximum efficacy and tolerability, and if there is any benefit to co-prescribing a PPI.

The study found that the percentage time that the INR was within range (2.0–3.0) was comparable with previous studies at 69.2%. The trial also included a sub-study looking at compliance. The median percentage of days that the correct warfarin dose was taken was 96.4% and 100% in the aspirin wing. A high compliance rate and good INR control suggests that octogenarians are able to manage the complexities of dose-adjusted warfarin. However, the authors mention a lower than expected mortality rate, which may be explained by the strict inclusion criteria resulting in only healthy patients being recruited. The low major haemorrhage rate and high compliance with therapy may also be due to selection bias.

The recently published NICE guidelines on the management of AF include thromboprophylaxis. Stroke risk stratification is advocated in all patients with AF and thromboprophylaxis recommended unless contraindicated or in lone AF. The suitable thromboprophylactic agent is determined by the individual patient’s absolute risk of stroke and bleeding. Age 65 years or older confers a moderate to high risk of stroke. Dose-adjusted warfarin is recommended in patients with AF and one high or two moderate stroke risk factors, with a target INR of 2.5 (range 2.0–3.0). Aspirin 75–300 mg should be used in patients with a low stroke risk. The relative risk benefit of each patient’s thromboprophylactic treatment should be reviewed regularly and adjusted as necessary. Individual patient’s personal preference should also be considered when choosing an antithrombotic agent. A recent study showed pictorial information could be used to communicate this subject effectively with older patients (median age 81 years) [14].

In conclusion there is little current evidence to guide clinical management of primary thromboprophylaxis in the elderly with AF. Patients over 75 years old are often excluded from trials. However, age is an independent risk factor for stroke in patients with AF and the elderly have the most to gain from anticoagulation. Further research is required comparing the risks and benefits of dose-adjusted standard dose warfarin and aspirin in the elderly. Previous studies have recruited mainly from secondary care, whilst in clinical practice chronic stable AF is a community-managed condition. These questions hope to be answered by the ongoing BAFTA trial, a randomised control trial recruiting from primary care, looking at thromboprophylaxis and AF in the over 75 year olds [15]. Current management should be based on NICE guidelines [12]. Audit should be built into all clinical practice to ensure standards are being met and to improve anticoagulation rates in eligible patients. Further work on INR monitoring is also required, comparing community, hospital or self monitoring to find the safest, most acceptable and cost-effective method. The use of other
thromboprophylactic agents may be relevant in the elderly. The combination of other antiplatelet agents with aspirin may be a useful alternative, particularly in the high-risk patients with recurrent falls or poor medication compliance. In the future Antithrombin inhibitors and Factor Xa inhibitors currently in the clinical trial stages may overcome the need for regular blood monitoring and reduce the drug and food interactions currently seen with warfarin.

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