

## Invited Editorial

*To accompany Hendriks J et al*

### **Integrated care for the management of atrial fibrillation – what are the key components and important outcomes?**

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In this issue of *Europace*, Hendriks and colleagues report the findings of a post-hoc analysis of the effect of a nurse-led integrated AF care package, supported by a bespoke software system based on then current (2010) European Society of Cardiology guidelines, compared to usual care (out-patient cardiologist clinic) on all-cause mortality in 712 patients with AF.(1) Integrated care resulted in fewer all-cause deaths compared to usual care (13 (3.7%) vs. 29 (8.1%); hazard ratio (HR) 0.44; 95% confidence intervals (CI) 0.23-0.85; p=0.014). Of note, all deaths were adjudicated by an independent panel of experts who were blinded to treatment allocation.

Investigation of the impact of integrated AF care on mortality is important given that 7 out of every 10 deaths in AF patients are attributable to cardiovascular causes.(2) Death is finite and although other outcomes, such as stroke reduction and quality of life are important, interventions that impact on mortality are imperative and identifying what components of these interventions reduce mortality (and other outcomes) is vital. As the authors allude to, guideline-adherent treatment, patient education, co-ordinated care and dedicated follow-up, multidisciplinary (MDT) input and collaboration, were all elements likely to have contributed to the significant reduction in all-cause mortality evident in this post-hoc analysis.(1)

The interest in integrated care for the management of AF has garnered significant attention over the last 6-7 years, propelled by the findings of the original paper by Hendriks et al.(3) In the original study, the primary outcome, a composite of cardiovascular hospitalisation and cardiovascular mortality, was significantly lower in the integrated care arm over a mean follow-up of 22-months compared to usual care (51 (14.3%) vs. 74 (20.8%), respectively; adjusted HR 0.63; 95% CI 0.44-0.90).(3) Individually, cardiovascular hospitalisations (13.5% vs. 19.1%, respectively; HR 0.66; 95% CI 0.46–0.96, p=0.029) and cardiovascular mortality (1.1% vs. 3.9%; HR 0.28; 95% CI 0.09–0.85; p=0.025) were significantly less in those receiving integrated care compared to usual care. This was a pivotal paper as integrated care as a concept for the management of AF was untested prior to the paper by Hendriks et al.(3) and

their new data (1) add weight to the call to adopt integrated care as the management approach for AF.

All major clinical guidelines on the management of AF have subsequently advocated a more holistic approach to patient care but the guidelines have thus far failed to describe exactly what 'integrated care' for AF should include.(4-6)

Why the lack of a standardised definition? Since 2012 only a few studies have tested 'integrated AF care' interventions.(7-10) These studies have varied in their design (2 randomised controlled trials (RCT),(8, 9) one cluster RCT,(10) and one 'before-and-after' study (7)), setting (primary care (8); hospitals(7, 9, 10)), composition, content and delivery (mode, personnel) of the intervention, primary outcomes (proportion on appropriate oral anticoagulation (OAC),(10) composite of death or unplanned readmission,(9) death, CV hospitalisation and AF-related emergency department (ED) visit,(7) unplanned ED visit or cardiovascular hospitalisation(8)), length of follow-up, and perhaps fundamentally, all have lacked a theoretical basis for the intervention (i.e., behavioural change theory). The findings have also been inconsistent, with two studies showing benefit of integrated AF care,(7, 10) while two have not.(8, 9)

A nurse-run, physician-supervised AF clinic incorporating group education on AF symptoms, investigations and treatment demonstrated a significant reduction in the composite endpoint of death, CV hospitalisation and AF-related ED visit (17.3% vs. 26.2%; odds ratio (OR) 0.71; 95% CI 0.59-0.9; p=0.049) in this 'before-and-after' study.(7) An international, multi-centre study (IMPACT-AF) examined the change in the proportion of patients on OAC at 1-year following a comprehensive package, including patient and healthcare professional education, with regular monitoring and feedback on OAC rates to HCPs.(10) Unsurprisingly, there was a significant increase in OAC prescription from baseline to 1-year among those receiving the intervention compared to usual care (68-80% vs. 64-67%, respectively; OR 3.28; 95% CI 1.67-6.44 between groups), most likely driven by feedback to physicians on OAC rates.(10) The SAFETY study(9) found no difference in the co-primary

endpoint of death or unplanned readmission between patients receiving nurse-led care (home visit, prolonged follow-up, with MDT support as required) vs. usual care (76% vs. 82%, respectively; HR 0.97; 95% CI 0.76-1.23; p=0.85). Most recently, a primary care based intervention, comprising a clinical decision support system (guideline-based physician monitoring with optional patient self-monitoring),(8) did not demonstrate benefit over usual care in reducing unplanned ED visits or CV hospitalisation (HR 1.02, 95% CI 0.73-1.41; p=0.93) or major bleeding (HR 0.91, 95% CI 0.32-2.60; p=0.87) (Data unpublished, presented at American Heart Association 2018).

One approach is to streamline the decision-making management approaches to allow them to be uniformly applicable across the whole AF patient pathway, starting with primary care and linking with secondary care (including cardiologist and non-cardiologists), and understandable for the AF patients, to enable them to engage and manage their care. Importantly, the approach should be simple, practical and easily operationalised.

The ABC (Atrial Fibrillation Better Care) pathway(11) for the management of AF focuses on important outcomes for patients (and physicians), namely reduction in stroke/thromboembolism with appropriate anticoagulation, symptom control or elimination, and management of cardiovascular comorbidities, to reduce hospitalisation and other adverse outcomes, and to improve quality of life. Independent studies have demonstrated that compliance with ABC pathway translates into improvement in hard end-points such as death, stroke, and CV events.(12-14) One prospective clinical trial is currently in progress.(15)

However, a truly integrated AF management, in addition to comprehensive assessment and systematic implementation of guideline-adherent therapy, would require other essential components, including appropriate interdisciplinary/MDT expert input, co-ordinated care, continual appraisal of the care pathway, supported by electronic platforms to guide decision-making and capture data for service evaluation,(16) and fundamentally, patient education and empowerment,

and family/carer involvement. The ABC pathway is adaptable to help operationalise this, spanning multidisciplinary healthcare professionals, healthcare providers, patients and families/carers.

Clinical decision support tools for healthcare professionals and patients have been developed and technological innovation has led to a huge number of apps and other e-health and m-health resources, most of which have not been formally tested in prospective trials. Essential components of integrated care for AF need to be clearly defined and supported by evidence. In order to provide integrated care for patients we must make a deliberate effort to change organisations, practice and behaviour to systematically implement and achieve the full benefit of clinical interventions and make these changes sustainable within different healthcare systems. Simply providing educational initiatives to a selected group of healthcare professionals, without consideration of bespoke needs, behavioural change approaches or patient engagement is probably inadequate. It is not only healthcare providers' practice and behaviour that needs to change, but also that of patients (and perhaps their families/carers).

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## References

1. Hendriks J, Tieleman RG, Vrijhoef HJM, Wijtliet P, Gallagher C, Prins M, et al. Integrated specialised atrial fibrillation clinics reduce all-cause mortality: Post-hoc analysis of a randomised clinical trial. *Europace*. 2019;this issue.
2. Pokorney SD, Piccini JP, Stevens SR, Patel MR, Pieper KS, Halperin JL, et al. Cause of Death and Predictors of All-Cause Mortality in Anticoagulated Patients With Nonvalvular Atrial Fibrillation: Data From ROCKET AF. *J Am Heart Assoc*. 2016;5(3):e002197.
3. Hendriks JM, de Wit R, Crijns HJ, Vrijhoef HJ, Prins MH, Pisters R, et al. Nurse-led care vs. usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation. *Eur Heart J*. 2012;33(21):2692-9.
4. Brieger D, Amerena J, Attia J, Bajorek B, Chan KH, Connell C, et al. National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Diagnosis and Management of Atrial Fibrillation 2018. *Heart Lung Circ*. 2018;27(10):1209-66.
5. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37(38):2893-962.
6. Lip GYH, Banerjee A, Boriani G, Chiang CE, Fargo R, Freedman B, et al. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. *Chest*. 2018;154(5):1121-201.
7. Carter L, Gardner M, Magee K, Fearon A, Morgulis I, Doucette S, et al. An Integrated Management Approach to Atrial Fibrillation. *J AM Heart Assoc*. 2016;5(1).
8. Cox JL, Parkash R, Abidi SS, Thabane L, Xie F, MacKillop J, et al. Optimizing primary care management of atrial fibrillation: The rationale and methods of the Integrated Management Program Advancing Community Treatment of Atrial Fibrillation (IMPACT-AF) study. *Am Heart J*. 2018;201:149-57.

9. Stewart S, Ball J, Horowitz JD, Marwick TH, Mahadevan G, Wong C, et al. Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: pragmatic, multicentre, randomised controlled trial. *Lancet*. 2015;385(9970):775-84.
10. Vinereanu D, Lopes RD, Bahit MC, Xavier D, Jiang J, Al-Khalidi HR, et al. A multifaceted intervention to improve treatment with oral anticoagulants in atrial fibrillation (IMPACT-AF): an international, cluster-randomised trial. *Lancet*. 2017;390(10104):1737-46.
11. Lip GYH. The ABC pathway: an integrated approach to improve AF management. *Nat Rev Cardiol*. 2017;14(11):627-8.
12. Pastori D, Pignatelli P, Menichelli D, Violi F, Lip GYH. Integrated Care Management of Patients With Atrial Fibrillation and Risk of Cardiovascular Events: The ABC (Atrial fibrillation Better Care) Pathway in the ATHERO-AF Study Cohort. *Mayo Clin Proc*. 2019;94(7):1261-7.
13. Proietti M, Romiti GF, Olshansky B, Lane DA, Lip GYH. Improved Outcomes by Integrated Care of Anticoagulated Patients with Atrial Fibrillation Using the Simple ABC (Atrial Fibrillation Better Care) Pathway. *Am J Med*. 2018;131(11):1359-66.e6.
14. Yoon M, Yang PS, Jang E, Yu HT, Kim TH, Uhm JS, et al. Improved Population-Based Clinical Outcomes of Patients with Atrial Fibrillation by Compliance with the Simple ABC (Atrial Fibrillation Better Care) Pathway for Integrated Care Management: A Nationwide Cohort Study. *Thrombosis and haemostasis*. 2019. Jul 2. doi: 10.1055/s-0039-1693516. [Epub ahead of print]
15. Guo Y, Lane DA, Wang L, Chen Y, Lip GYH, m AFAITi. Mobile Health (mHealth) technology for improved screening, patient involvement and optimising integrated care in atrial fibrillation: The mAFA (mAF-App) II randomised trial. *Int J Clin Practice*. 2019:e13352.
16. Berti D, Hendriks JM, Brandes A, Deaton C, Crijns HJ, Camm AJ, et al. A proposal for interdisciplinary, nurse-coordinated atrial fibrillation expert programmes as a way to structure daily practice. *Eur Heart J*. 2013;34(35):2725-30.