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Evaluation of Huawei smart wearables for detection of atrial fibrillation in patients following ischemic stroke: The Liverpool-Huawei stroke study



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Background Atrial fibrillation (AF) often remains undetected following stroke. Documenting AF is critical to initiate oral anticoagulation, which has proven benefit in reducing recurrent stroke and mortality in patients with AF. The accuracy and acceptability of using smart wearables to detect AF in patients following stroke is unknown.

Methods The aims of the Liverpool-Huawei Stroke Study are to determine the effectiveness, cost-effectiveness and patient and staff acceptability of using Huawei smart wearables to detect AF following ischemic stroke. The study plans to recruit 1,000 adults aged \geq 18 years following ischemic stroke from participating hospitals over 12 months. All participants will be asked to wear a Huawei smart band for 4 weeks postdischarge. If participants do not have access to a compatible smartphone required for the study, they will be provided with a smartphone for the 4-week AF monitoring period.

Results Participants with suspected AF detected by the smart wearables, without previous known AF, will be referred for further evaluation. To determine the effectiveness of the Huawei smart wearables to detect AF, the positive predictive value will be determined. Patient acceptability of using this technology will also be examined. Additional follow-up assessments will be conducted at 6 and 12 months, and clinical outcomes recorded in relation to prevalent and incident AF post-stroke. The study opened for recruitment on May 30, 2022, and is currently open at 4 participating hospitals; the first 106 participants have been recruited. One further hospital is preparing to open for recruitment.

Conclusions This prospective study will examine the effectiveness and acceptability of the use of smart wearables in patients following ischemic stroke. This could have important implications for detection of AF and therefore, earlier prophylaxis for recurrent stroke. The study is registered on https://www.isrctn.com/ (Identifier ISRCTN30693819). (Am Heart J 2023;257:103–110.)

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Submitted July 21, 2022; accepted December 2, 2022

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Clinically diagnosed atrial fibrillation (AF) after a stroke is associated with a significantly increased risk of future stroke or systemic embolism, particularly in the presence of additional stroke risk factors. It is important to identify AF in order to initiate thromboprophylaxis with oral anticoagulation, which has proven benefit in reducing recurrent stroke and mortality in patients with AE²

In general, AF detection is more likely if we "look longer; look barder and look with more sophisticated methods...." Continuous bedside electrocardiogram (ECG)-monitoring during stroke unit admission for three days detects AF in approximately 7% of patients. More sophisticated systems have higher detection rates of paroxysmal AF, but devices such as event-triggered loop recorders are inconvenient, and implantable loop recorders are expensive and require surgical implantation. ³⁻⁶

AF is prevalent in approximately a quarter of patients following stroke.⁷ With recent advances in AF-specific mobile health,⁸ and an increasing variety of AF screening options,¹ it is now an opportune time to improve AF detection, alleviate patient burden, and reduce health care costs. Indeed, a non-invasive, clinically effective, cost-effective, and patient-acceptable long-duration ECG-monitoring system post-acute stroke is needed. In a recent cohort study, the prognosis of single time-point ECG screen-detected AF was not benign, and oral anticoagulant use reduced the risk of stroke in such patients.⁹

Photoplethysmography (PPG) involves optically measuring changes in tissue blood volume through the skin. The majority of smart watches and bands measure heart rate with PPG technology, and as such, there are potential benefits of widespread adoption, with easily accessible and user-friendly technology to screen for AE¹⁰ The Huawei Heart Study monitored >187,000 people aged ≥18 years in China for suspected AF using PPG signals via Huawei smart wearables. 11 Although, the Huawei Heart Study used 14-day monitoring for AF, the mean age of the participants was 35 years, and, therefore, the detection of suspected AF was low (0.23%). Of the participants with suspected AF, 62% were followed-up and compared to clinical evaluation, ECG or 24-hour Holter monitoring, and the PPG signals had a positive predictive value (PPV) of 91.6% (95% confidence interval 91.5%-91.8%). 11 Other large-scale studies to examine the detection of AF using smart wearables have also been conducted using Apple and Fitbit technology which examined >419,000 and >455,000 individuals respectively. 12,13 The mean ages in these studies were higher than the Huawei Heart Study at 41 and 47 years, but the detection of AF was remained low at 0.52% and 1.0%. A real-time comparison of the smart wearables compared to a 7-day ECG patch was made in both of these studies, and 34% and 32% of the participants with suspected AF had AF detected by the ECG patch, but including only those with an irregular pulse notification during the 7-day followup period, the PPVs were calculated at 84% and 98%, respectively.

Several risk prediction models for AF have been developed. These include the C₂HEST risk score, ^{14,15} the Atherosclerosis Risk in Communities (ARIC) score, ¹⁶ the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE)-AF score, ¹⁷ the Framingham Heart Study, ¹⁸ the HAVOC¹⁹ and the HATCH²⁰ scores. Currently, no single model to stratify people by risk of AF can be recommended for use in clinical practice for people following stroke. Further research is needed to determine an optimal model that is feasible to use as part of patient care pathways.

The aim of the Liverpool-Huawei Stroke Study is to conduct a prospective evaluation of Huawei smart wearables in patients following ischemic stroke to detect prevalent and incident AF. Within a population following ischemic stroke, the specific objectives are to: (1) determine effectiveness by determining the PPV of Huawei smart wearables to detect prevalent and incident AF; (2) identify clinical predictors of prevalent and incident AF and determine the accuracy of risk prediction models for AF; (3) identify clinical predictors of other important outcomes, such as recurrent stroke, mortality and cognitive impairment; (4) determine cost-effectiveness via an economic evaluation of screening procedures with Huawei smart wearables; and (5) determine patient and staff acceptability of screening procedures through an embedded process evaluation.

Materials and methods

Study design

The study is a pragmatic prospective observational study to determine the effectiveness, cost-effectiveness and patient and staff acceptability of using Huawei smart wearables to detect AF following ischemic stroke. The results of the study will not be used to obtain UK Conformity Assessed (CA) or Conformitè Europëenne (CE) marking for the smart wearables, which is needed to meet the requirements of medical device regulations in the UK and EU respectively. The study plans to recruit a minimum of 1,000 adult participants across the participating hospitals.

Patient population - inclusion and exclusion criteria

Participants will be included if they are aged ≥18 years and are a current inpatient at a participating hospital at the time of baseline data collection for ischemic stroke; confirmed by a stroke physician and/or imaging (computerized tomography [CT] or magnetic resonance imaging [MRI]). Participants will be excluded if they are unable to provide informed consent or are receiving palliative or end-of-life care. Patients with AF known at baseline will not be excluded as the aim of the Liverpool-Huawei Stroke Study is to evaluate the Huawei smart

American Heart Journal
Volume 257
Harrison et al 105

Figure 1



The Huawei smart band 6 which will be used in the Liverpool-Huawei Stroke Study.

wearables to detect known (prevalent) AF and undetected (incident or newly diagnosed) AF.

Treatment or intervention

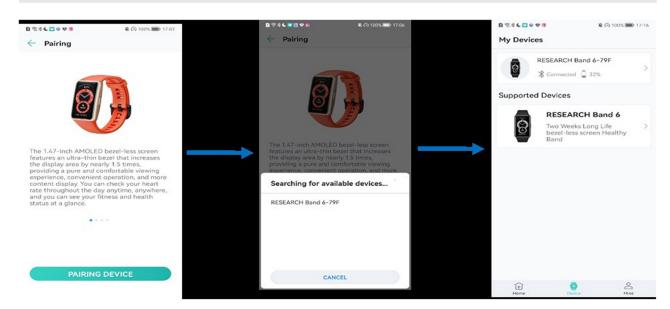
All participants will be provided with a Huawei smart band 6 (Figure 1) which will be paired to a compatible smartphone (Figure 2). The smartphone will have a Huawei smartphone application installed which will monitor for suspected AF based on the PPG technology of the smart band. The smart wearables will be continuously monitoring for suspected AF, but the participants

will also be asked to perform 2 manual measurements for arrhythmia detection per day (Figure 3). Participants who do not have access to a compatible smartphone will be provided with one. Participants will be asked to wear the Huawei smart band for 4 weeks post discharge. As the smartphone application will be the same whether the smartphone is borrowed or owned by the participant, this should have no impact on data collection.

The research team at the University of Liverpool will monitor the data received from the smart wearables daily (Monday-Friday) and when a notification of suspected AF is received, the participant's base hospital team will be informed the same day via email. Participants with suspected AF, identified via the Huawei smart wearables, with no previous diagnosis of AF will be referred to a cardiologist for further evaluation in line with the standard operating procedure (Supplementary Figure 1). This further evaluation will take place at the participant's base hospital or at Liverpool Heart and Chest Hospital and will include 12-lead ECG, and if AF is not confirmed, at least 5 days of Holter monitoring. Once the clinical evaluation is completed, the stroke research team at the participant's base hospital will input the ECG and Holter monitor results in to the electronic case report form. If AF is confirmed, appropriate treatment will be initiated in line with usual care practices. 21 AF diagnosis and treatment will not be based solely on the suspected AF notifications received from the smart wearables.

The evaluation with 12-lead ECG and at least 5 days of cardiac monitoring will in the majority of cases be

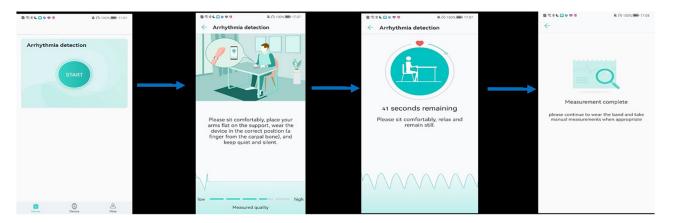
Figure 2



Screenshots from the Huawei Heart Health Study smartphone application which will be used in the Liverpool-Huawei Stroke Study, showing pairing of the smart band to the smartphone.

American Heart Journal Month 2023

Figure 3



Screenshots from the Huawei Heart Health Study smartphone application which will be used in the Liverpool-Huawei Stroke Study, showing completion of a manual measurement for arrhythmia detection.

conducted after the monitoring period with the Huawei smart wearables has finished. Therefore, the comparison between the smart wearables and the clinical evaluation will not be in real-time. This is a limitation of the study, but the extended monitoring which will be conducted in the clinical evaluation is beyond the current recommendations to detect AF following stroke (short-term ECG recording followed by continuous ECG monitoring for at least 72 hours).² Furthermore, asking the participants to use another device such as a Holter monitor at the same time as using the Huawei smart wearables may increase study withdrawals, and a key aim of the study is to examine the acceptability of participants using the smart wearables without any other cardiac monitoring technology simultaneously.²² This pragmatic approach better reflects current clinical practice, and is comparable to the followup for individuals in the Huawei Heart Study where the confirmation of AF was 87.0% in those with AF detected by the smart wearables. 11 Another limitation of the study is the study design does not include a control group, but this was not possible within the current study.

Participants will be able to keep the smart band after the 4-week data collection period but will be asked to return the smartphone (if given). Participants who did not need to borrow a smartphone may continue to use the Huawei smart band and continue to provide data for the study for secondary analyses at 6 months, after which, the monitoring of Huawei smart band data will be terminated. The 4-week monitoring period is shorter than some previous studies examining detection of AF using smart wearables, ¹² but these previous studies have relied on the participants already owning compatible smartphones. It is not possible within the current study to provide each participant with a smartphone for a longer duration as the phones need to be re-used for other par-

ticipants, and this will be noted as a limitation of the study design when reporting the study findings. However, strengths of the study are that participants who do not own a compatible smartphone are not excluded. The provided phones also have a data plan, so would facilitate data capture and are not only relying on WiFi access. Those who do own a smartphone will be invited to contribute data from the smart wearable for up to 6 months.

The research team will complete site initiation visits and train all nurses at the participating sites to deliver the intervention. Educational resources will be provided. The research nurses will show participants and their family/carers how to use the Huawei smart band, Huawei smartphone application, and smartphone as required. Family members may be asked to help the participants with using the smart wearables at home.

Primary outcomes

The primary outcome is detection of AF by the Huawei smart wearables by examining the proportion of participants with at least one suspected AF notification reported by the smart wear. The PPV of the smart wearables will be calculated by comparing to confirmed diagnosis of AF using clinical evaluation (12-lead ECG and at least 5-day Holter monitoring).

Secondary outcomes

Health and well-being characteristics collected at baseline as potential clinical predictors of prevalent and incident AF following stroke will be investigated (Table I). Cost-effectiveness of the Huawei smart wearables and participant and staff acceptability of using the smart wearables will be examined. A modelled cost-effectiveness analysis from a UK health funder perspective will be performed comparing the cost of

American Heart Journal
Volume 2.57

Harrison et al 107

Table 1. Overview of data to be collected at baseline and follow-up timepoints.

| Measures | Baseline | 1-3 months | 6-months | 12-months |
|---|----------------|------------|----------|-----------|
| ECG (AF screening) | X*† | | | |
| Blood pressure | Χ [†] | | | |
| Diagnosed medical conditions | Χ [†] | | | Χ |
| Cardiovascular history | Χ [†] | | | |
| National Institutes of Health Stroke Scale (NIHSS) | Χ [†] | | | |
| Modified Rankin Scale | Χ [†] | | | |
| Cognitive function measured with the Montreal Cognitive Assessment (MoCA) | Χ [†] | | | Χ |
| Blood sample results | Χ [†] | | | |
| Echocardiogram results | Χ [†] | | | |
| Prescribed medications (at time of hospital discharge for baseline) | Χ [†] | | | |
| Stroke-related diagnostic tests including CT and MRI imaging and blood samples, where available. | Χ [†] | | | |
| Functional independence measured with the Barthel Index | Χ | | Χ | Χ |
| Fatigue Assessment Scale | Χ | | Χ | Χ |
| Depression measured with the Patient Health Questionnaire (PHQ)-9 | Χ | | Χ | Χ |
| Anxiety measured with the General Anxiety Disorder (GAD)-7 | Χ | | Χ | Χ |
| Health-related quality of life measured with the EQ-5D-5L without the visual analogue scale of the EQ-5D-5L | Χ | | Χ | Χ |
| STOP-BANG sleep apnoea questionnaire | Χ | | Χ | Χ |
| Modified European Heart Rhythm Association (mEHRA) symptom score | X* | | Χ* | X* |
| Treatment burden questionnaire | X* | | Χ* | X* |
| Participant 'intervention acceptability' survey | | Χ | | |
| Staff 'intervention acceptability' survey | Χ | | | |
| Participant interviews | | Χ | | |
| Staff interviews | | | Χ | |

^{*} Collected at baseline and when confirming suspected AF as indicated by Huawei smart wearables and completed by participants with suspected/confirmed AF.

Huawei smart wearable-based screening for AF with AF diagnosed by standard post-stroke care. The prevalence of AF detected in patients following ischemic stroke receiving usual care from the participating hospitals will be examined to inform the cost-effectiveness analysis. Patient and staff acceptability will be determined through a mixed-methods process evaluation. Quantitative data will be collected to investigate how long participants wore the bands for in total, how many days and for how long they wore them for each day, and whether there are differences in participant characteristics between "adherers" and "non-adherers." In addition, a series of surveys and semi-structured interviews will be conducted with participants and staff to examine their experiences of using the smart wearables.

In addition to measures identified in Table I, the full cohort will be examined using linkage with other available data sources at 12-month follow-up. Outcomes of interest will include all-cause mortality and mortality from cardiovascular causes, as well as cardiovascular outcomes including recurrent stroke, incident AF, transient ischemic attack (TIA), myocardial infarction, and heart failure.

Data collection

Anonymised Huawei data from the smart wearables, linked with the participant ID, will be uploaded to cloud storage in the United Kingdom or European Union. The

Huawei smart band 6 will be completely disconnected from the Huawei infrastructure.

At baseline, participant data collected as part of usual care will be recorded and additional questionnaires will be completed regarding the health of the participant. Data will be recorded in an electronic case report form using Research Electronic Data Capture (REDCap; https://www.project-redcap.org). Follow-up assessments will occur at 6 and 12 months, to repeat some of the questionnaires. The follow-ups will be completed within a 2-week window before or after the 6 and 12-month dates. Additionally, consent will be requested at baseline to link to the participant's hospital episode statistics and mortality data for 12 months from the date of admission to the hospital, held by the National Health Service (NHS) Digital.

Sample size considerations

The PPV of the Huawei smart wearables to detect AF was previously shown to be 91.6% in the general population in China. ¹¹ The PPV of the Huawei smart wearables has not been previously examined in a population following ischemic stroke. A previous systematic review in a post-stroke population has estimated the incidence of new AF following stroke at approximately 24%. ⁷ However, 8 different diagnostic methods up to a mean 74.8 days following stroke were included to calculate this estimate. Therefore, fewer cases of AF may be detected, but

[†]Collected at all participating sites as part of usual care. For the echocardiogram, results will be used if the person had an echocardiogram within the preceding six months.

prevalent AF cases have been included. With an expected 24% prevalence of AF and a conservative estimated PPV of 80% for this population, a sample size of 1,000 would provide accuracy of $\pm 5\%$.

Statistical analyses

The PPV of suspected AF detected with the PPG algorithm with the Huawei smart wearables will be calculated by comparing to confirmed diagnosis of AF using clinical evaluation. The specificity of the smart wearables will not be determined as it was beyond the scope of the current study to conduct further clinical evaluation to detect AF for the participants who did not receive a notification of suspected AF. However, in participants with known permanent AF, we plan to explore the specificity of the PPG-based smart wearables for AF detection.

Predictors of incident AF and other outcomes including mortality and recurrent stroke will be determined using multivariate competing-risk analyses in order to account for potential high probability of mortality amongst the cohort. The accuracy of risk prediction models for AF developed in previous studies will also be determined in this cohort including the C₂HEST²³, ARIC, ¹⁶ CHARGE-AF,¹⁷ Framingham Heart Study,¹⁸ HAVOC¹⁹ and HATCH risk prediction scores.²⁰ Receiver operating characteristic curves will be constructed, and C-statistics (ie, area under the curve) with 95% confidence intervals will be estimated as a measure of model performance. In addition, machine learning approaches including k-Nearest Neighbors, random forest, and decision tree will be used to further examine if the accuracy of risk prediction models can be improved. For all analyses, subgroup analysis based on known AF status at the time of enrolment to the study will be performed. The inclusion of prevalent AF patients allows us to test to specificity and sensitivity of the PPG-based smart wearables in this population which is likely to be older than the general population screen tested in the Huawei Heart Study and with other co-morbidities.

Sub-studies

Additional studies will be conducted with sub-samples of the study participants. First, a sub-study will assess the utility of biomarkers, in conjunction with clinical parameters in the prediction of AF in patients following ischemic stroke. This will involve obtaining a blood sample for biomarker analysis (at baseline and follow-up) and an assessment of sarcopenia (at baseline), comparing between participants who developed and did not develop AF throughout the duration of the study. Biomarkers to be examined include thyroid hormones, thrombosis and fibrinolysis (including point-of-care Global Thrombosis Test), cardiac biomarkers. In addition, multivariate biomarkers of muscle mass and physical function loss (ie, sarcopenia) will be assessed, including total body muscle

mass and fat mass, physical function assessments (walking test, grip strength, and timed up and go), and plasma metabolite for semi-targeted metabolomics to identify "AF-sarcopenic" phenotype.

A second sub-study will examine associations between the physical activity, sedentary behavior and cerebrovascular health and stroke severity/recovery and secondary cardiovascular events in acute ischemic stroke participants. Cerebrovascular function will be measured by transcranial doppler at an outpatient follow-up visit. Physical activity and sedentary behavior following discharge will be measured using an ActivPAL activity monitor which is a small device worn on the thigh.

Discussion

The Liverpool-Huawei Stroke Study aims to determine the effectiveness of Huawei smart wearables to detect prevalent and incident AF in adults following ischemic stroke. The cost-effectiveness and participant and staff acceptability of using the smart wearables in individuals following ischemic stroke will also be examined. Additionally, the study aims to collect data about the health of the participants following ischemic stroke at baseline, and at 6 and 12-month follow-ups to identify clinical predictors of AF and other important outcomes for this population.

AF-related strokes are associated with greater mortality and morbidity, longer stays in hospital and lower rates of discharge compared to strokes without AF.²⁴ Approximately 40% of ischemic strokes are classified as Embolic Stroke of Undetermined Source (ESUS), with no apparent cause identified following routine clinical or short-term 12-lead ECG evaluation, inpatient monitoring, or 24-hour Holter monitor.²⁵ Although prolonged ECG monitoring is recommended in cases of suspected ESUS, there is currently no consensus on the recommended duration, nor data on patient acceptability or cost effectiveness of this approach.

Other non-invasive approaches to monitor for AF include the Ziopatch which is a single-lead ECG skin patch that provides up to 14 days of continuous ECG data. A randomized controlled trial of 116 patients following stroke showed superiority compared to a 24-hour Holter monitor (detection of 1 participant in the Holter monitor group compared to 8 participants in the Ziopatch group).²² The Ziopatch is recommended by the National Institute for Health and Care Excellence in the UK as an option for people with suspected cardiac arrhythmias who would benefit from ambulatory ECG monitoring for >24 hours.²⁶ The current smart wearables may offer some advantages over this technology such as costs may be lower, the data can be monitored in real-time rather than waiting for the end of the monitoring period, and a smart band may be more acceptable to patients over a longer time frame as people are more familiar with American Heart Journal
Volume 257
Harrison et al 109

wearing bands or watches. However, the Huawei smart wearables will not be compared directly to the Ziopatch in this study.

Detection of AF post-stroke is critical to initiate appropriate monitoring and treatment to reduce risk of recurrent stroke. Contemporary management of AF patients requires appropriate characterization and evaluation, ²⁷ followed by a holistic or integrated care approach including the Atrial Fibrillation Better Care (ABC) pathway²⁸ as follows: A: Avoid strokes with anticoagulants; B: Better symptom management with person-centered decisions of rate and rhythm control; and C: Cardiovascular and comorbidity management.^{2,28,29} Adherence to the ABC pathway has been associated with fewer major events in patients with AF including patients with multiple comorbidities, polypharmacy, and prior hospitalization.^{30,31}

Risk prediction models for AF have previously included demographic factors and details of cardiovascular disease history, and some models have incorporated details of structural changes to the heart. Relatively little research has been conducted to examine the risk of AF in individuals following stroke. The C₂HEST score has been shown to perform well in discriminating risk of incident AF in people post-stroke (C index 0.734) and performed significantly better than the Framingham risk score (C index 0.720).³² The HAVOC score has also shown good discrimination for AF in a population following cryptogenic stroke or TIA.¹⁹ Nonetheless, difficulties have been identified in defining and characterizing cryptogenic stroke.^{33,34},

Recruitment for the Liverpool-Huawei Stroke Study opened on May 30, 2022. As of October 21, 2022, 4 hospitals in Merseyside had begun recruitment for the study and 106 participants had been recruited. One additional hospital in North West England was preparing for site initiation and to commence recruitment.

Conclusion

Detection of AF following stroke is critical to initiate appropriate treatment pathways to reduce risk of recurrent stroke. AF often remains undetected, but smart wearables may be useful for longer, non-invasive monitoring to improve detection of AF following stroke. Huawei smart wearables have been shown to have a high positive predictive value for detecting AF in the general population. In this study, the effectiveness, costeffectiveness and patient and staff acceptability of using Huawei smart wearables to detect AF in people following ischemic stroke will be determined. In addition, this study will identify clinical predictors of AF and other important clinical outcomes including mortality, cardiovascular events and recurrent stroke in individuals following ischemic stroke. Improving risk prediction of AF and other outcomes for people following stroke is important to identify, target screening and provide intervention strategies for those at high risk.

Study organization and funding

The study is co-ordinated by academic researchers and clinical collaborators at the Liverpool Centre for Cardio-vascular Science. The study steering committee provides overall governance for the project. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

The study has received the approval from Health Research Authority Research Ethics Committee (21/EM/0214), and the University of Liverpool is the sponsor for the project (UoL001642). This academic-led independent study is supported by funding from Huawei Technologies France.

Disclosures

SLH has received research funding from Bristol-Myers Squibb (BMS). BJRB has received research funding from BMS/Pfizer. YZ has been a consultant for Roche and has received a research grant from Remark Holdings and IntelliCloud. DAL has received investigator-initiated educational grants from BMS, has been a speaker for Bayer, Boehringer Ingeheim, and BMS/Pfizer and has consulted for BMS, and Boehringer Ingelheim. GYHL: Consultant and speaker for BMS/Pfizer, Boehringer Ingelheim and Daiichi-Sankyo; no fees are received personally. DS has received a research grant from the European Society of Cardiology Council of Stroke. GMcD has received funding and research support from Roche Diagnostics and Abbott. IJ has received research funding from Astra Zeneca and BMS. All other authors have no competing interests to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj. 2022.12.004.

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