



# Congress Review

## Review of the European Society of Cardiology (ESC) Congress 2019 with the World Congress of Cardiology (WCC) 2019

Location: Paris Expo Porte de Versailles – Paris, France  
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The beating heart of France, complete with an abundance of unmistakably Parisian architecture, created the beautiful backdrop to this year's European Society of Cardiology (ESC) congress, as they were joined by the World Congress of Cardiology (WCC). Amongst the eclectic array of art, history, and culture, Paris in the height of summer is an image synonymous with romance, creating the perfect setting for an influx of attendees with a vested interest in affairs of the heart.

This year, the ESC congress was, as always, an incomparable event for cardiologists around the world. As the world's biggest cardiology event, they had to open with a bang: featuring instruments from across the world, playing to the rhythm of cardiovascular health. They shone a spotlight on global cardiovascular health at the event, with particular focus on differences in prevalence, strategies for prevention, clinical manifestations, diagnostic modalities, and cardiovascular disease management across the globe.

The EMJ team, along with the 30,000 attendees at the event, were spoilt for choice, with >500 sessions on offer across the 5-day event. For those who were unable to attend the event, and those who did attend and want to re-experience the highlights from ESC, we have selected a range of late-breaking research stories, abstract presentations, and congress sessions to cover in our annual review of ESC.

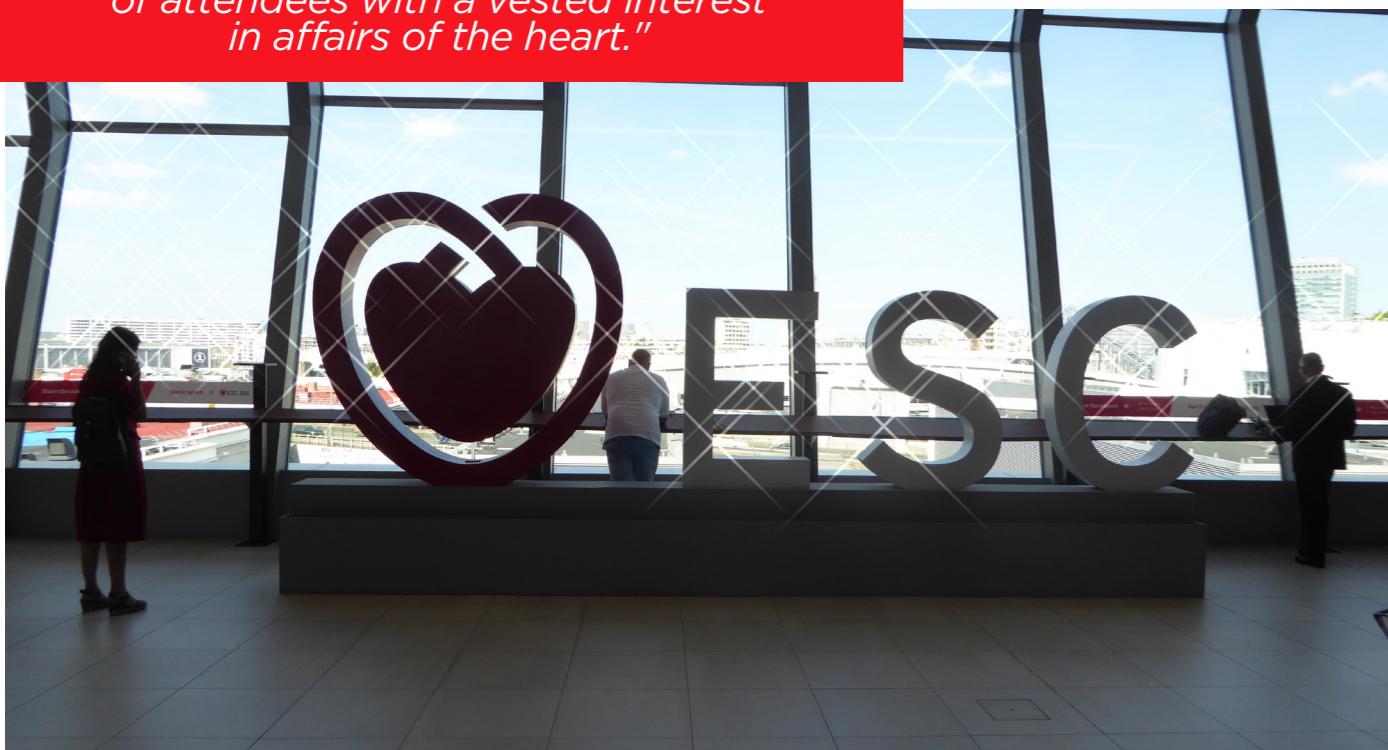
A host of late-breaking research was presented at ESC: from a decline in sport-related cardiac arrest death due to increased incidence of bystander resuscitation to a link between microbes and the destabilisation of coronary plaques. Caregivers were also a hot topic at the event, with research presented on depression in this group as a predictor of health problems in the future. Another study of interest explored the use of ticagrelor and aspirin in the reduction of ischaemic events in patients with stable coronary artery disease and diabetes.

Our hand-picked selection of abstracts from ESC have been written up in summaries, penned by the authors themselves to provide a first-hand account of the research. These explore a range of cardiovascular topics including antiplatelet therapy and oral anticoagulation in transcatheter aortic valve replacement; artificial intelligence in echocardiography; and the regulation of a catecholamine-dependent altered cAMP signalling in a patient-specific induced pluripotent stem cell Takotsubo-model.

ESC's spotlight on global cardiovascular health was a big focus of the Congress, further exploring the worrying statistic that eight out of ten cardiovascular disease deaths occur in low and middle-income countries. This is an important area for focus for ESC, and they are actively working to improve cardiovascular health worldwide: they are uniting 57 national cardiac societies, 28 sub-speciality communities, and >100,000 individual members.

As the digital era seemingly takes over every aspect of our lives, health is no exception; consequently, digital health was an extremely hot topic at ESC this year, with particular focus on wearable devices, data protection and ethics,

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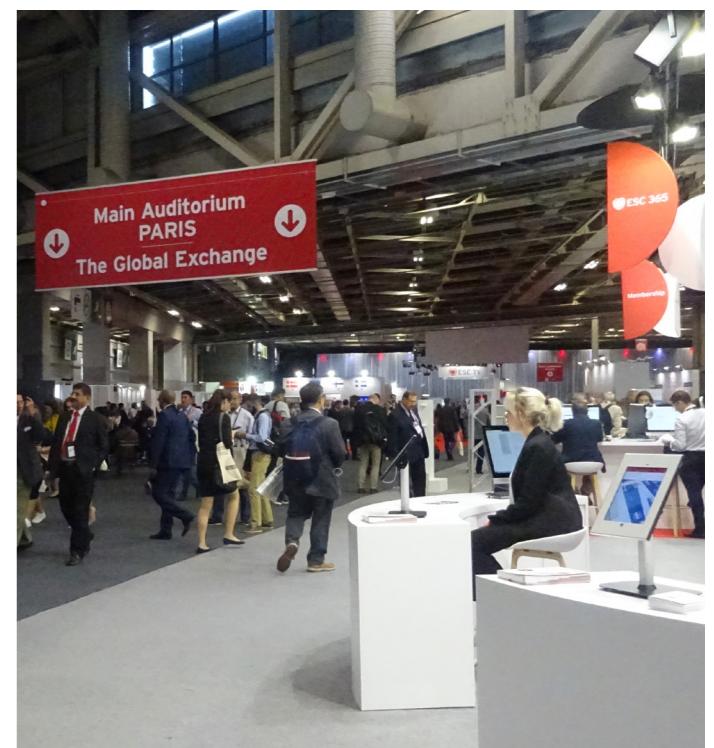


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and implementation of digital health into daily practice. This topic forms one of our congress features, as we consider the impact of an increasingly digital world on healthcare.

2019 saw ESC updating five sets of their guidelines, and these were a prominent focus at the congress. Their guidelines on chronic coronary syndromes were published on the 31<sup>st</sup> August, covered in our congress review. The baleful impact of pollution and noise on patients with coronary syndromes were exemplified: a first for the guidelines.

ESC, along with the WCC, put on a fantastic event this year and we really were spoilt for choice in choosing the content for our review of the congress. Looking ahead to next year, Amsterdam, the Netherlands, will play host to ESC 2020, which is sure to be another unmissable event on the calendar of anyone with a keen interest in cardiology. But for now, without further ado, we present our review of ESC 2019.



ESC 2019 REVIEWED →

## Additional Non-Culprit Lesion Intervention Offers Greater Cardiovascular Outcomes

RESULTS from the COMPLETE trial presented in an ESC press release dated 1<sup>st</sup> September 2019 concluded that complete revascularisation reduced clinical events in patients with ST-segment elevation myocardial infarction (STEMI) compared to patients that did not receive additional revascularisation of non-culprit lesions.

Multivessel coronary artery disease is defined as the presence of multiple narrowed arteries, non-culprit arteries, following myocardial infarction (MI), in addition to the causative artery, known as the culprit artery. Percutaneous coronary intervention (PCI) is used to widen the culprit artery to reduce adverse clinical outcomes such as cardiovascular death or MI. As many as 50% of STEMI patients are afflicted by multivessel coronary artery disease; this trial ascertained the preventative effect of additional non-culprit lesion PCI against major cardiovascular events, the results of which had not yet been explored in any single, large study.



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The trial enrolled 4,041 patients from 31 countries with STEMI and multivessel coronary artery disease who were randomly allocated to one of two groups: complete revascularisation with PCI of angiographically significant non-culprit lesions, or revascularisation alone. Random allocation was organised by proposed timings of non-culprit lesion PCI as before or after primary hospitalisation. The first co-primary outcome was cardiovascular death or MI and the second co-primary outcome encompassed ischaemia-driven revascularisation.

After a median of 3 years, the follow-up indicated that 158 patients (7.8%) in the group who received complete vascularisation of both culprit and non-culprit lesion PCI exhibited first co-primary outcomes compared to 213 patients (10.5%) in the culprit-lesion only group (hazard ratio 0.74; 95% confidence interval: 0.60–0.91; p=0.004). Furthermore, the second co-primary outcome occurred in 179 patients (8.9%) in the complete revascularisation group and in 399 patients in the group that did not receive complete vascularisation (hazard ratio 0.77; 95% confidence interval: 0.59–1.00).

"COMPLETE is the first randomised trial to show that complete revascularisation reduces hard cardiovascular events compared to culprit-lesion only PCI in patients with STEMI and multivessel coronary artery disease," commented principal investigator of the study Prof Shamir R. Mehta, Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada. "These findings are likely to have a large impact on clinical practice and prevent many thousands of recurrent heart attacks globally every year," Prof Mehta reflected.

## Microbes may Contribute to the Destabilisation of Coronary Plaques

ACCORDING to the results presented at ESC, in a press release dated the 31<sup>st</sup> of August, micro-organisms in the body may contribute to the destabilisation of coronary plaques and subsequent heart attack.

Previous research indicates that factors such as age, diet, medications, smoking, and pollution have an adverse impact on cell physiology, the immune system, and metabolism and that these effects are mediated by micro-organism in the intestinal tract. Therefore, the study, which took place at the Catholic University of Sacred Heart, Rome, Italy, investigated the impact of the microbiota to the instability of coronary plaques.

*"The varying chemicals emitted by these bacteria might affect plaque destabilisation and consequent heart attack."*

In the study, 30 patients with acute coronary syndrome and 10 patients with stable angina were enrolled. Isolated gut bacteria from faeces samples and coronary plaque bacteria extracted from angioplasty balloons were compared and revealed a difference in the microbiota between the two sites. While faecal bacteria showed a heterogeneous composition and a noticeable presence of *Bacteroidetes* and *Firmicutes*, the composition of coronary plaque bacteria primarily consisted of microbes with proinflammatory characteristics belonging to *Proteobacteria* and *Actinobacteria*. These findings suggest a selective retention of proinflammatory retention in atherosclerotic plaque that could provoke an inflammatory response and plaque rupture.

Further discovered in the analyses was a difference in gut microbiota between the two patient groups. *Firmicutes*, *Fusobacteria*, and *Actinobacteria* were primarily present in those with acute coronary syndrome, while



*Bacteroidetes* and *Proteobacteria* were predominant in those with stable angina. Dr Eugenia Pisano, Catholic University of Sacred Heart, noted: "we found a different make-up of the gut microbiome in acute and stable patients. The varying chemicals emitted by these bacteria might affect plaque destabilisation and consequent heart attack. Studies are needed to examine whether these metabolites do influence plaque instability."

Dr Pisano concluded that, while this was a small study, the results proved valuable because they implicate that microbiota in the gut and coronary plaque might have pathogenetic functions in the plaque destabilisation process and may become potential therapeutic targets.



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## Environmental and Psychosocial Aspects of Heart Disease and Pollution and Noise Reduction Advised in ESC Guidelines

THE ESC guidelines on chronic coronary syndromes were published on the 31<sup>st</sup> August. For the first time, the baleful impact of pollution and noise on patients with coronary syndromes were exemplified.

Chairperson of the Guidelines Task Force and director of the Turku PET centre, Turku, Finland, Prof Juhani Knuuti said "air pollution and environmental noise increase the risk of heart attack and stroke, so policies and regulations are needed to minimise both." Compared to the previous document, lifestyle changes have a bigger focus to prevent worsening of chronic coronary syndromes because unhealthy behaviours will have contributed to the development of coronary artery disease (CAD).

As a continuation of the preceding stable CAD guidelines, the document further covers chronic coronary syndromes. Patients are advised to quit smoking, avoid passive smoking, and eat a vegetable, fruit, and whole grain rich diet and limit saturated fat and alcohol consumption. Furthermore, because CAD patients have a

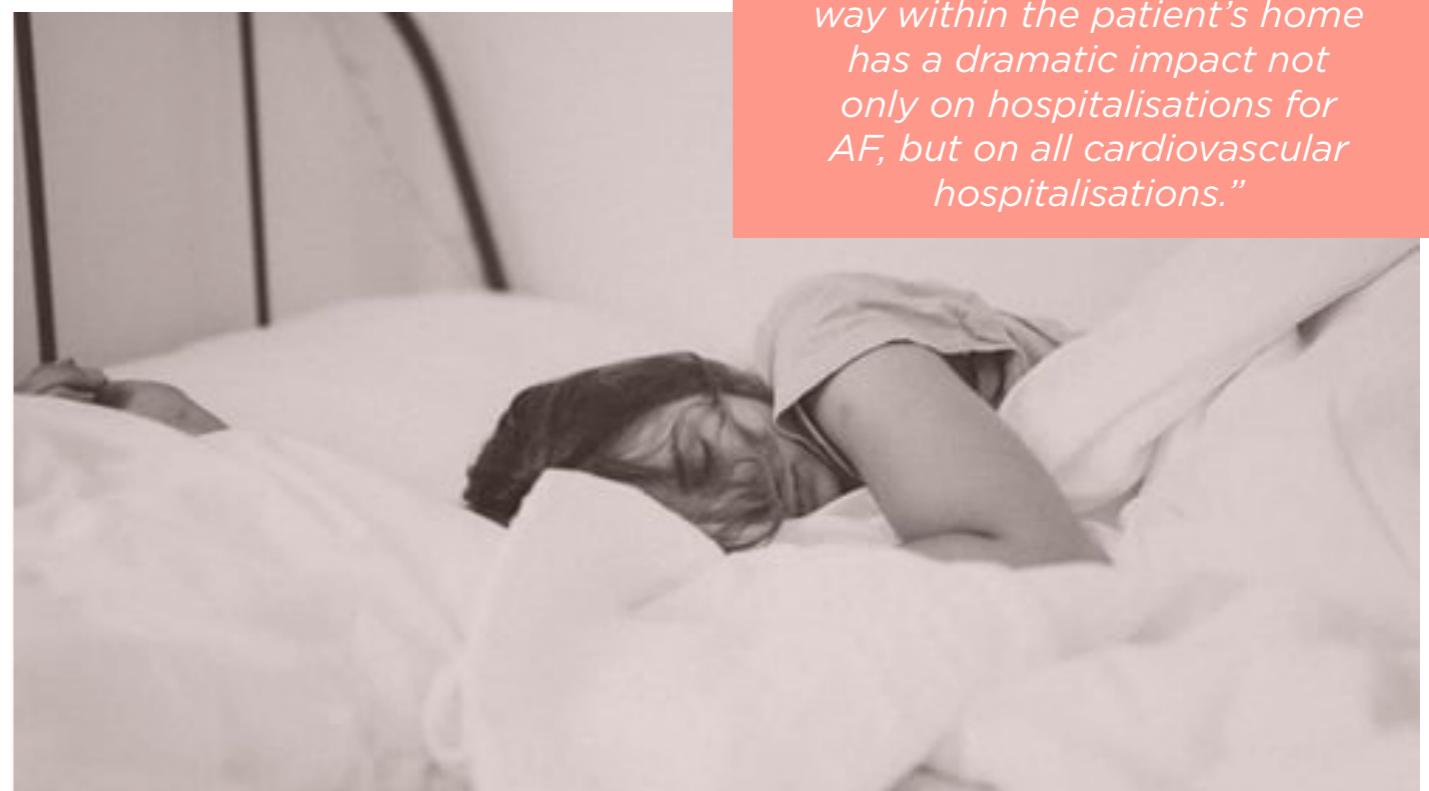
2-fold higher risk of mood and anxiety disorders, improvements in lifestyle and adherence to medications presents as a challenge. For this reason, counselling is encouraged for those with depression, anxiety, or stress. Prof Knuuti also states that "patients need to take medications as prescribed even if they have no symptoms. Promoting behaviour change and medication adherence should be part of each appointment with general practitioners or specialists including nurses and cardiologists."

As the diagnosis of chronic coronary syndromes has significantly advanced since the release of the previous guidelines, the most encountered clinical scenarios were also outlined. Fellow Chairperson of the Guidelines Task Force and professor in interventional cardiology at the Lambe Institute for Translational Medicine, Galway, Ireland, Prof William Wijns stated that "each of these scenarios requires different diagnostic and therapeutic approaches. But in general, treatment of a chronic coronary syndrome demands long-lasting healthy habits, medication adherence, and interventions in selected patients."

## Hospitalisations of Atrial Fibrillation Patients Reduced Through Home-Based Education

AN AGEING population, accompanied by the acquisition of lifestyle-related comorbidities such as sleep apnoea and obesity, has led to an increased prevalence of atrial fibrillation (AF) to which healthcare services must tackle. Accounting for more hospitalisations than either heart attack or heart failure, there has been a shift in focus towards managing the disease through the provision of home-based education as a means of lessening the patient and clinician burden. Now, findings presented in a press release, on the 1<sup>st</sup> September, at ESC, attest to the effectiveness of this approach.

In the HELP-AF study, 627 AF patients from 6 hospitals from Adelaide, Australia, were enrolled and allocated the HELP-AF programme or usual care within 2 months of their emergency presentation. The intervention arm received two educational home visits by a pharmacist or nurse: the first 2 weeks after enrolment, and the second 6 weeks after that. The sessions revolved around education into:



1. Management of future AF episodes.
2. Optimal medicine use to manage symptoms and stroke risk.
3. The role of personalised lifestyle modification.

Over 24 months, the HELP-AF group presented with 233 unplanned hospitalisations compared to 323 in the usual care group, with an incident ratio of 0.74 (95% confidence interval: 0.62-0.89; p=0.001). Following adjustments for multi-variables, the education programme reduced total unplanned hospitalisations by 26%, cardiovascular hospitalisations by 49%, and AF-related hospitalisations by 31%.

Principal investigator Prof Prash Sanders from the University of Adelaide, Adelaide, said: "the study shows that education delivered in a structured and individualised way within the patient's home has a dramatic impact not only on hospitalisations for AF, but on all cardiovascular hospitalisations."

The standardised design of the protocol and its prospectively easy replication in other countries and settings holds great promise for helping provide the personalised therapeutic attention that this patient demographic clearly needs.

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## Ticagrelor and Aspirin Combination Reduces Ischaemic Events in Diabetics with Stable Coronary Artery Disease



*"In addition to heart attack and stroke, acute limb ischaemia and major amputations were also reduced with ticagrelor"*

MILLIONS of patients worldwide are at high risk for heart attack, stroke, and amputations as a result of their diabetes and stable coronary artery disease, a common development seen in diabetic patients. Usually, aspirin is prescribed to reduce risk, but cardiovascular events still occur at a high rate; however, in late-breaking results from the THEMIS trial reported in a ESC press release dated 1<sup>st</sup> September 2019, reduced ischaemic events were seen in patients given a combination of ticagrelor and aspirin.

The THEMIS trial took place at 1,315 sites across 42 countries worldwide and involved 19,220 participants aged ≥50 who had Type 2 diabetes mellitus and stable coronary artery disease. The risk of thrombotic events was compared in those randomly given aspirin and placebo to those given the combination of aspirin and ticagrelor.

## Depressive Symptoms can be Predictive of Health Problems in Caregivers

SIGNS of depression in caregivers of stroke patients may be predictive of future health problems, as shown in a study presented at the ESC Congress, with the WCC, in Paris, France, and reported in a ESC press release dated 1<sup>st</sup> September 2019. The research brings to light the importance of recognising and addressing caregivers' mental health.

Caregivers of stroke survivors can undergo a heavy emotional and physical burden, as stroke can often leave patients with long-term disability. "More attention needs to be paid, especially early on, to managing depressive symptoms in caregivers. They must realise that self-care is not selfish," explained study author Prof Misook L. Chung, University of Kentucky College of Nursing, Lexington, Kentucky, USA.

This study comprised 102 participants who were caring for a stroke survivor. The sample had a mean age of 58 years, were two-thirds female, and around 70% were spouses of the patient. Questionnaires were answered on two



occasions: 6–10 weeks after hospital discharge and 1 year later.

Depressive symptoms, such as trouble focussing and diminished appetite, were reported less frequently over the period of the study: 32.4% compared to 30.4%. A total of 57.8% of the participants reported no mental distress, while 20.6% experienced persistent symptoms of depression over their first year of caregiving. One-third of the participants marked their physical health as either fair or poor after 1 year; additionally, 43% reported feeling that they had experienced a deterioration of their health.

Caregivers experiencing symptoms of depression were seven times more likely to have health problems following 1 year of care-giving than those who did not have depressive symptoms. Poor family functioning, lack of interpersonal support, and heavier care duties were all reported by those with persistent depressive symptoms.

As this study relied on self-reporting techniques, the findings are limited and further research is needed to identify a concrete link; however, the research does suggest earlier interventions and longer-term follow up are needed. Prof Chung concluded: "Self-care intervention programmes should include depressive symptom management for caregivers."

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"There was a significant reduction in the primary endpoint of cardiovascular death, heart attack, and stroke with ticagrelor versus placebo. In addition to heart attack and stroke, acute limb ischaemia and major amputations were also reduced with ticagrelor. Major bleeding was significantly increased," commented senior author

Prof Deepak Bhatt of Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA.

In patients that received ticagrelor, the incidence of primary efficacy outcome was lower (7.7% versus 8.5%; hazard ratio 0.90; 95% confidence interval: 0.81–0.99;  $p=0.038$ ). However, the primary safety outcome of thrombolysis in myocardial infarction major bleeding was increased in the ticagrelor group (2.2% versus 1.0%; hazard ratio 2.32; 95% confidence interval: 1.82–2.94;  $p<0.001$ ).

Prof Bhatt concluded that it is crucial to define subgroups that would benefit from ticagrelor plus aspirin, of whom are patients at high ischaemic risk, but low bleeding risk. Furthermore, substantial gains for the reduction of a full spectrum of coronary, cerebral, and peripheral ischaemic events was seen in ticagrelor plus aspirin.

## Patients with Heart Failure have a Similar Risk of Dementia-Type Lesions to Stroke Patients

COGNITIVE impairment is experienced by 50% of older patients with heart failure. Also associated with dementia, this type of brain damage, called white matter lesions (WML), is just as common in those with heart failure as it is in patients with a history of stroke. These results from the LIFE-Adult-Study were reported in a ESC press release on the 2<sup>nd</sup> September 2019.

Conducted in Leipzig, Germany, between 2011 and 2014, the population-based cohort study involved 10,000 randomly selected residents aged 18–80. Information on health conditions, including heart failure and stroke, was obtained through health assessments and physical examinations of the participants. Further investigation of the brain with the use of MRI was performed in 2,490 participants.

In the majority of the subgroup, 87% had no or mild WML, and 13% had moderate or severe WML; the latter is associated with cognitive impairment and dementia. A 2.5-times greater risk of WML was observed in heart failure compared to those

without. There was a similar trend in stroke patients, who had a 2-times greater risk compared with participants with no history of stroke.

Furthermore, the duration of heart failure was linked with the severity of the lesions: more lesions were present in the brains of patients with a long-standing heart failure diagnosis compared to those who were newly diagnosed. The risk of WML increased from 1.3 for those with a diagnosis of <3 years to a risk of 2.9 for a diagnosis >6 years.

Despite this association, study author Dr Tina Stegmann of Leipzig University Hospital, Leipzig, Germany, commented: "It is still unclear what the pathological pathways are. Some investigators have identified changes in brain structure in patients with heart failure and cognitive dysfunction, but the findings are inconsistent." She concluded that "studies are needed to see if WML could be a therapeutic target for treating cognitive decline in patients with heart failure."

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## HOPEful Results for Patients with Hypertension

*"Adopting the HOPE 4 strategy to better control hypertension and reduce other risk factors could help achieve the United Nations' target for a one-third reduction in premature cardiovascular mortality by 2030."*

LATE-BREAKING results from the HOPE 4 trial were reported in a ESC press release dated 2<sup>nd</sup> September, showing that an intervention programme targeted at patients with hypertension in Colombia and Malaysia successfully reduced cardiovascular risk over 1 year.

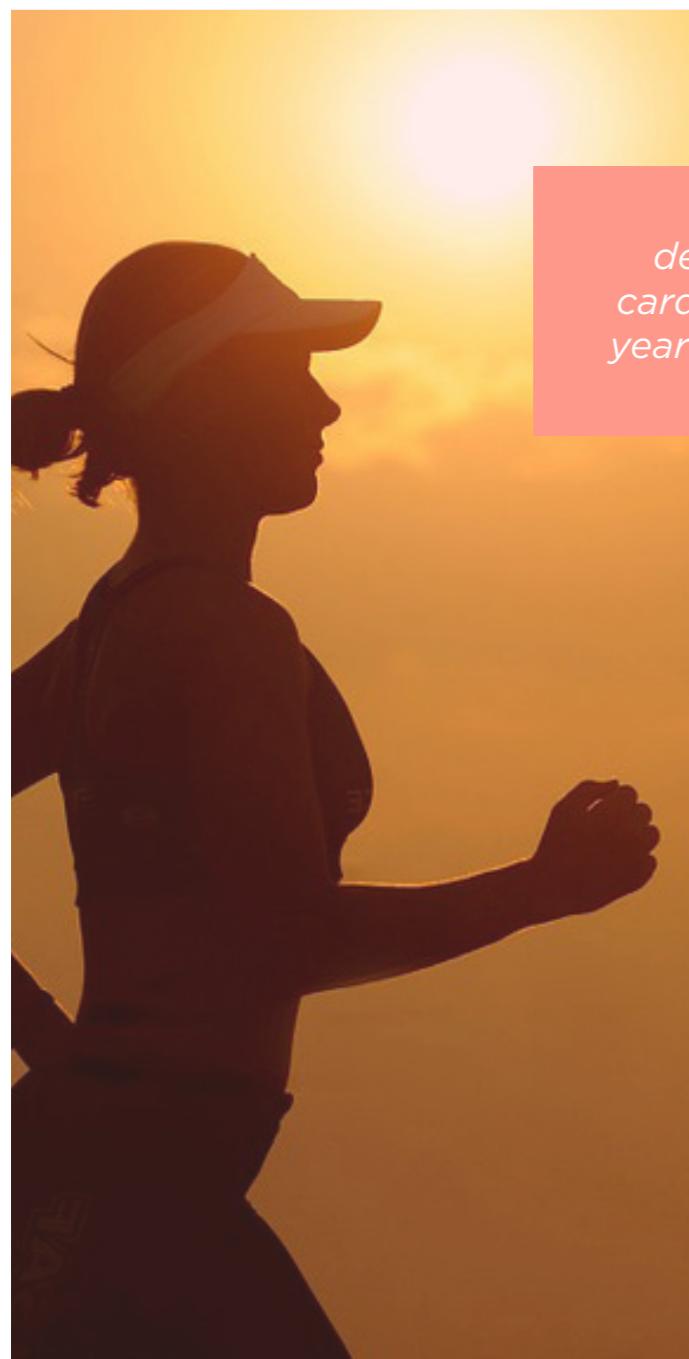
The trial enrolled 1,371 patients aged ≥50 years from across the 2 countries. The patients all had new or poorly controlled hypertension. There were 30 separate communities involved, 16 of which were randomised to receive standard of care as a control group, and 14 that took part in the intervention programme for 1 year. This included undergoing screening to detect eligible patients, implementation and monitoring of treatments, as well as control of risk factors by non-physician health workers using tablet-based management algorithms and counselling, free statins and antihypertensive medications (overseen by physicians), and partnering with a treatment supporter, such as a friend or relative to assist with adherence to medications and lifestyle changes. Treatment supporters attended 74% of visits to the health workers or physicians while also giving ongoing support outside of these visits.

The Framingham Risk Score was the measure used to determine the effectiveness of the intervention, specifically the change in this score from baseline to 12 months. In the intervention group, this score was reduced by an absolute 11.2% in that time, a 75.0% greater reduction than that seen in the control arm. Furthermore, systolic blood pressure saw an absolute 11.5 mmHg greater reduction and serum low-density lipoprotein was reduced by 0.4 mmol/L more in the intervention versus the control group.

Prof Salim Yusuf, Executive Director of the Population Health Research Institute of McMaster University and Hamilton Health Sciences, Hamilton, Ontario, Canada, and Principal Investigator of the study, commented: "This strategy is pragmatic, effective, and scalable, and has the potential to substantially reduce cardiovascular disease globally, compared to current methods that are solely physician based." He added: "Adopting the HOPE 4 strategy to better control hypertension and reduce other risk factors could help achieve the United Nations' target for a one-third reduction in premature cardiovascular mortality by 2030."

## Bystander Resuscitation Increase Leads to Fewer Sports-Related Cardiac Deaths

DECREASED rates of death due to sports-related sudden cardiac arrest has been attributed to an increase in bystander cardiopulmonary resuscitation (CPR), as found by research reported in a ESC press release dated 2<sup>nd</sup> September 2019 in Paris, France.



*"We observed an important decrease in deaths due to sudden cardiac arrest during sports over a 12-year period which was related to more frequent CPR."*

Death, as a result of cardiac arrest from sport, decreased from 4.3 to 3.4 deaths in every 1 million inhabitants. Prof Xavier Jouven, Paris-Sudden Death Expertise Centre, Paris, discussed the findings: "We observed an important decrease in deaths due to sudden cardiac arrest during sports over a 12-year period which was related to more frequent CPR. The static incidence is probably caused by difficulties in early identification of individuals at high risk for sudden cardiac arrest during sports."

"To further improve survival from cardiac arrest, CPR should be taught to the general public and particularly to sports medicine practitioners," concluded Prof Jouven. "An AED should be available in all sports venues. Preventing sudden cardiac arrest remains the ideal goal – in the future, smartwatches and internet-connected T-shirts may alert us to warning signs occurring minutes or hours before, allowing early resuscitation and prevention."

The study considered two registries initiated by the Paris-Sudden Death Expertise Centre. Cases of individuals who had experienced cardiac arrest, during or immediately following sport in Paris (and surrounding suburbs), from the time periods 2005–2010 (n=158) and 2011–2016 (n=162), were included in the analysis.

Incidence was stable across the 2 time periods: an estimated 6.9 cases per 1 million inhabitants. Average age was not significantly different between the periods (from 49 to 52 years of age), nor was percentage of men (from 94% to 96%) or prevalence of known heart disease (from 14% to 17%). In the later time period, bystander CPR increased to 81%, significantly higher than in 2005–2010 at a rate of 46%. Similarly, automated external defibrillator use was up from 1.3% to 11.9%. Athlete cardiac arrest survival rates increased from 20% to 60%.



## Antithrombotic Regimen Following Coronary Stenting Optimised Through Genotyping

FOR HEART attack patients undergoing coronary stent implantation, bleeding and clotting risks can be simultaneously reduced following oral P2Y<sub>12</sub> inhibition through use of genotype guidance. This message was delivered in a ESC press release dated 3<sup>rd</sup> September 2019, and has potentially wider implications for the field.

ESC guidelines advise dual antiplatelet therapy with aspirin and a P2Y<sub>12</sub> inhibitor for 1 year in patients following primary percutaneous coronary intervention (PCI) with ST-segment elevation myocardial infarction (STEMI). Ticagrelor, prasugrel, and clopidogrel are the most common inhibitors prescribed; however, they are subject to differing costs and availability, and the former two exhibit safety constraints in regard to propensity to bleeding events, a major concern in the treatment of these patients.

*CYP2C19* gene functionality has been linked to clopidogrel effectiveness. Investigators from St. Antonius Hospital, Nieuwegein, the Netherlands, hypothesised that genotyping would allow identification of patients better suited for clopidogrel treatment (i.e., \*1/\*1 noncarriers), and those better suited for ticagrelor/prasugrel treatment (i.e., \*2 and \*3 loss-of-function allele carriers), in regard to thrombotic complication reduction.

The POPular Genetics trial involved 2,488 STEMI patients being randomly allocated to standard treatment or genotype-guided arms.

*"This study demonstrated that a CYP2C19 genotype-guided strategy benefits patients with STEMI undergoing primary PCI by reducing the risk of bleeding without increasing the risk of thrombotic events,"*

The former was treated with ticagrelor or prasugrel for 1 year, whereas the latter had genotype testing performed as soon as possible after PCI through blood sample testing. Patients without loss-of-function mutations (\*1/\*1) received clopidogrel for 1 year.

Patients in the genotype-guided arm experienced significantly fewer bleeding events (9.8%) than those in the standard treatment arm (12.5%) (hazard ratio: 0.78; 95% confidence interval: 0.61–0.98; p=0.04). Similar clinical endpoints were achieved in both arms (5.1% in the genotype-guided arm, and 5.9% in the standard treatment arm), meaning noninferiority was proven.

*"This study demonstrated that a CYP2C19 genotype-guided strategy benefits patients with STEMI undergoing primary PCI by reducing the risk of bleeding without increasing the risk of thrombotic events,"* commented first author Dr Danny Classens, St. Antonius Hospital.