Achievable reductions in LDL-C and SBP more than halve the lifetime risk of CVD

Most cardiovascular (CV) events are preventable with sustained combinations of lower low-density lipoprotein cholesterol (LDL-C) and lower systolic blood pressure (SBP).

Professor Brian Ference (University of Cambridge, Cambridge, UK) delivered this message yesterday in a Hot Line presentation of results from the UK Biobank study, which was published simultaneously in the Journal of the American Medical Association.1 “Randomised trials and Mendelian randomisation genetic studies have shown that the benefits of reducing LDL-C and reducing SBP accumulate over time. It seemed likely, therefore, that long-term combined reductions in both LDL-C and SBP could reduce the lifetime risk of CV disease (CVD),” says Prof. Ference. Given the number of patients involved and the projected timescale required—several decades—conducting a randomised trial to investigate this hypothesis is just not feasible. To fill this evidence gap, Prof. Ference explains, the team used genetic variants associated with lower LDL-C and lower SBP as instruments of randomisation.

More than 400,000 participants enrolled in the UK Biobank were included in the study. Patients were initially randomised into higher and lower plasma LDL-C groups, based on a 100-exome variant score, and then further randomised into higher or lower SBP groups, according to a 61-exome variant SBP score. The primary endpoint was the incidence of major coronary events defined as the first occurrence of a non-fatal myocardial infarction, coronary revascularisation or coronary death. There were no differences in baseline characteristics between the resulting four randomised groups: a reference group, a group with lower LDL-C, a group with lower SBP, and a group with combined lower LDL-C and lower SBP.

Based on the reference group, the lower LDL-C group had a 14.7 mg/dL lower LDL-C and a 27.0% lower risk of major CV events (OR 0.73), while the lower SBP group had a 2.9 mmHg lower SBP and an 18% lower risk (OR 0.82). Importantly, the group with both lower LDL-C and SBP had both 14.7 mg/dL lower LDL-C and 3.1 mmHg lower SBP, and a 39% lower risk of major CV events (OR 0.61). Of note, the effects of lower LDL-C and lower SBP on the risk of CV events were independent, additive and dose-dependent. Any combination of lower LDL-C and lower SBP was associated with a correspondingly lower lifetime risk of CVD.

With greater reductions of 1 mmol/L (38.7 mg/dL) lower LDL-C and 10 mmHg lower SBP, there was an 80% lower lifetime risk of CVD and a 68% lower risk of CV death. “Because benefits accumulate over time,” says Prof. Ference, “even small differences in LDL-C and SBP can lead to large reductions in the lifetime risk of CVD, if the reductions are maintained long term.” He thinks this has important implications for the impact of lifestyle changes. “These modest changes in LDL-C and SBP are in the range of those you might expect to see with prescribed diets, such as the Dietary Approaches to Stop Hypertension (DASH) diet. Not only do the results underline the importance of lifestyle changes, they also suggest that recommendations for such changes can be substantially simplified to focus on the common goal of achieving and maintaining a combination of reduced lipids and blood pressure.” The optimal regimen should be tailored to the individual. “There is no universal ‘best’ regimen to follow. Instead, the ‘best’ modification for any individual is the one that leads to the greatest LDL-C and SBP reductions for that person. Crucially, this regimen should also be one that the individual can adhere to long-term.”

Prof. Ference concludes, “To prevent avoidable CV events, we need to encourage patients to minimise their risk by adopting healthy lifestyle choices early in their life and then sustaining them over time. If larger reductions in LDL-C and SBP are required to reduce lifetime risk, early initiation of medication can be considered—further research is required to identify who would benefit most from early treatment.”


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2019 ESC Clinical Practice Guidelines
Diabetes - in collaboration with EASD

Initially studied for their glucose-lowering abilities, evidence from CVOTs indicates that

certain sodium-glucose co-transporter-2

(SGLT2) inhibitors and glucagon-like peptide

receptor agonists (GLP-IRAs) can reduce the risk of myocardial infarction, stroke and

cardiovascular death in patients with type 2 diabetes who are at high cardiovascular risk.

“These data have changed the treatment algorithm for patients with atherosclerotic CVD or

high/very high cardiovascular risk and the new guidelines provide recommendations for

drug-naive and metformin-treated patients,” notes Prof. Birkeland. “CVOTs also provide the basis for new recommendations to reduce the risk of hospitalisation for heart failure, which is particularly common in patients with
diabetes and heart failure.” Furthermore, SGLT2 inhibitors are now recommended to reduce progression of diabetic kidney disease based on results from a large-scale outcome trial in

patients with type 2 diabetes and albuminuric chronic kidney disease.

Other changes to medication recommendations relate to antidiabetic therapy. Aspirin for primary prevention is not recommended in patients with diabetes at moderate cardiovascular risk; however, aspirin (75-100 mg/day) may be considered for primary prevention in patients with diabetes at very high/high risk in the absence of clear contraindications. Non-vitamin K antagonist oral anticoagulants (NOACs) are now preferred over vitamin K antagonists (VKAs) for the management of atrial fibrillation, a common comorbidity in patients with diabetes.

Professor Massimo Francesco Piepoli (Guglielmo da Saliceto Hospital, Piacenza, University of

Parma, Italy), ESC Guideline Review Coordinator, is keen to emphasise the central role of lifestyle

changes in the new guidelines. “Lifestyle is very important to prevent both the conversion of

pre-diabetes to diabetes and also to prevent the cardiovascular complications of diabetes. Excess bodyweight is a risk factor for the development of metabolic disorders, including diabetes, and we know that even modest weight loss can delay CVD progression, in diabetes in particular. Reducing calorie intake to induce weight loss is recommended as it may lead to improvements in glucose levels, lipid levels, blood pressure, quality of life and life expectancy. Smoking cessation should be our first recommendation to all our patients and alcohol consumption should be as low as possible. Other lifestyle guidance includes adoption of a Mediterranean diet supplemented with olive oil and/ or nuts to reduce CVD risk, and regular exercise, preferably moderate-to-vigorous physical activity of ≥30 minutes/week, to prevent and control diabetes.”

In the 2019 ESC Guidelines, lifestyle changes are also recommended to manage hypertension.


Creating Europe’s largest continuous cardiovascular registry: EuroHeart

European Unified Registries On Heart Care Evaluation and Randomised Trials

The ESC, acting as a central coordinator, plans to support countries to develop their own national quality-of-care registries and to use the information to drive a data powerhouse to secure high-quality care across Europe.

“There has really been nothing like this before in Europe,” says Professor Lars Wallentin (Uppsala University, Uppsala, Sweden). “The ESC does of course have the infrastructure, but each country will be responsible for setting up, running and monitoring its own nationally harmonised registry infrastructure,” says Prof. Wallentin.

In July 2019, the ESC Board approved the launch of a two-year pilot phase of EuroHeart, which will involve two to four countries to assess the feasibility of implementation of EuroHeart in different healthcare systems. “This is a very exciting time for the ESC,” says Professor Chris P. Gale (University of Leeds, Leeds, UK). “But we know it won’t be easy. The biggest challenge is not IT and it’s not data. The biggest challenge is in fact people and culture. It is about people understanding and wanting to engage in a programme of quality improvement using an IT platform. And it is about people being willing to collect the data and enter it in routine practice.

In the pilot phase, it will be the countries with the most enthusiasm and with the infrastructure and support to deliver the programme, from their governments, healthcare authorities and National Cardiac Societies, that will be selected.”

The final decision regarding the countries selected to participate in the pilot phase is expected to be made by the end of the year, allowing the system to be put into development early in 2020. After the pilot study, and if successful, EuroHeart could be rolled out to other countries.

Projecting 10 years into the future, Prof. Gale thinks the biggest successes of EuroHeart will be the routine, system-wide collection of information for every patient with cardiovascular disease and the possibility to automatically review their care. In addition, he welcomes the opportunity to offer patients, where appropriate, entry into pragmatic randomised clinical trials to test new interventions. This would be in line with one of the ESC’s key advocacy strategies to develop smarter, more integrated approaches to trials using less expensive data.

“EuroHeart also has the potential to provide tremendous benefits for cardiologists, including automated reporting of care delivery, and the ability to engage with the wider ESC membership and to initiate or join in with research and quality improvement. And if we are routinely monitoring new healthcare technologies and medical devices within countries, we will have a huge amount of data to inform us whether these devices and technologies are doing what they should be doing,” states Prof. Gale.

EuroHeart will exemplify the very best collaboration between the ESC and National Cardiac Societies; national knowledge and experience, harnessed by the ESC at a ‘European’ level, to improve outcomes for patients.

Confronting cardiovascular risk in patients with diabetes – Spotlight on dual antiplatelet therapy

Tuesday 3rd September | 13:00 – 14:00 | Centre Stage (Level 2)

Welcome and Introduction
Marc Bonaca (US)
The prothrombotic nature of diabetes
Kausik Ray (UK)
Current practice of dual antiplatelet therapy in patients with diabetes
Harald Darius (Germany)
Recent data and future direction on dual antiplatelet therapy in patients with diabetes
Gabriel Steg (France)
Discussion
All faculty
Summary and Close
Gabriel Steg (France)

Supported by an unrestricted educational grant from AstraZeneca. This scientific programme has not been influenced in any way by its sponsor.
### Lipid modification to reduce cardiovascular risk: 2019 ESC/EAS Clinical Practice Guidelines for the management of dyslipidaemias

**What’s Your Diagnosis?**

**BROUGHT TO YOU BY THE EUROPEAN ASSOCIATION OF CARDIOVASCULAR IMAGING (EACVI)**

**Solution: L-transposition**

L-transposition of the great arteries (L-TGA). The aorta arises from a morphologically right ventricle (prominent trabeculations), which, however, is congenitally switched to the left side. The pulmonary artery (PA) arises from a morphologically left ventricle (prominent trabeculations), which, however, is congenitally switched to the right side. The aorta and PA are both connected to a morphologically left atrium.

Stephen Achenbach, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

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**Prof. Heinz Drexel**

“Although it is only three years since the previous ESC/EAS Guidelines on the management of dyslipidaemias were published, a substantial body of new evidence has accumulated,” says Professor Heinz Drexel (University Hospital of Bern, University of Bern, Bern, Switzerland), Guideline Review Coordinator for the European Atherosclerosis Society (EAS).

“New up-to-date ESC/EAS Guidelines are needed to help physicians provide the very best approaches to efficiently and safely modify lipid levels and reduce the risk of atherosclerotic cardiovascular disease (ASCVD) as far as possible.”

“Emerging data from observational studies, randomised controlled trials and Mendelian randomisation studies now unequivocally demonstrate a causal effect of low-density lipoprotein cholesterol (LDL-C) in the development of ASCVD,” says Prof. Drexel. “Moreover, several recent large-scale trials of ezetimibe or proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, reductions that are associated with the subtilisin/kexin type 9 (PCSK9) inhibitors, ezetimibe or proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, reductions that are associated with the statin intolerance. In observational studies, statin intolerance is frequent when LDL-C goals on a maximum tolerated dose of a statin are not achieved.”

In the 2019 ESC/EAS Guidelines, Lipid modification to reduce cardiovascular risk, including all cardiovascular risk factors, not only LDL-C, is also reinforced in the 2019 ESC/EAS Guidelines. Concerning other lipids, Prof. Drexel says, “There has been much interest of the effects of omega 3 polyunsaturated fatty acids to reduce elevated triglyceride levels but there has been some inconclusive evidence. However, based on the results of the recent REDUCE-IT trial, icosapent ethyl (2x2 g/day) should now be considered in combination with a statin in high-risk (or above) patients with triglyceride levels from 1.5 to 5.6 mmol/L (135–499 mg/dL) despite statins.”

The new ESC/EAS Guidelines state that lipoprotein(a) measurement should be considered at least once in each person’s lifetime, if possible, to identify people who have very high levels of triglycerides (<600 mg/dL, 1430 mmol/L) and who may have a very high ASCVD risk. Lipoprotein(a) measurement should also be considered in selected patients with a family history of premature ASCVD, and for reclassification in people who are borderline between moderate and high risk.

Other new recommended ways to evaluate risk and potentially re-classify include non-invasive cardiovascular imaging. Arterial ultrasonography to assess plaque burden or computed tomography to assess coronary artery calcium score can now be considered risk classifiers in individuals at low or moderate risk.

Inflammation, statin use in older patients and the cost effectiveness of lipid-modifying interventions are just some of the other revised or new concepts covered in the 2019 ESC/EAS Guidelines. As a final note, Prof. Müller says, “The new guidelines are not solely focused on pharmacological approaches to modify lipids. A lifetime approach to ASCVD risk is advocated. In addition to patients at high and very high ASCVD risk, everyone should be encouraged to adopt or sustain a healthy lifestyle to improve their plasma lipid profile.”

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**Prof. Christian Müller**

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Stephen Achenbach, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

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**Stephan Achenbach, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany**

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Professor Pascal Meier (904/Pascalmeier; Hospital Grumbden, University of Zurich, Chur, Switzerland)
ESC Social Media Ambassador

“Twitter brings the world of cardiovascular medicine directly to you whether or not you travel to a Congress. The ESC Ambassadors won’t stop tweeting when the Congress closes. We will continue to be active, exploiting the reach of social media to keep disseminating cardiovascular news and updates from the ESC.”

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- Be scientific and unique on Twitter Today, 13:00 – 14:00, Global Exchange 2 – ESC Plaza

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Shape the conversation
A population-based salt-substitution strategy slashes hypertension risk

**A simple strategy for reducing salt intake on a population scale halved the number of people developing hypertension. This startling statistic was just one of the findings reported by Professor Jaime Miranda (Universidad Peruana Cayetano Heredia, Lima, Peru) in a Hot Line Session yesterday.**

Reducing blood pressure (BP) is key to reducing the risk of heart disease and stroke, and it has been known for decades that reducing sodium intake and increasing potassium can lead to reduced BP. The health threat of salt is such that World Health Organization Member States agreed to a reduction of 30% in global salt consumption by 2025. “Public health interventions, such as limiting the salt content of processed foods, are valuable steps towards this goal,” says Prof. Miranda. “But they take time. We wanted to do something quicker and simpler to reduce salt intake on a wide scale.”

Basing their study in six villages in Tumbe, Peru, where the main salt intake was due to addition during cooking, Prof. Miranda’s team evaluated the effects of offering a low-sodium salt (“Salt Lic,” 75% sodium and 25% potassium) to households, street vendors and food stores to replace 100% sodium salt. Interestingly, the salt was introduced via a social marketing strategy on the grounds of being highly desirable, rather than being healthy, explains Prof. Miranda. “We knew that if we said it was a healthy option, people would assume that it would taste bland and would not be interested in using it.” A randomised trial was neither feasible nor ethical, so a stepped-wedge design was employed, involving incremental initiation of villages for salt substitution at 5-month intervals and using the non-recruited villages at each stage as the control group. BP was measured at baseline, again every 5 months, at each new initiation, and at the end of the trial. The trial, which involved 2,376 participants, continued for three years (2014-2017).

Salt substitution led to an average population-wide reduction of 1.23 mmHg (95% confidence interval [CI] 0.38–2.07) in systolic BP and of 0.72 mmHg (95% CI 0.10–1.34) in diastolic BP.

“On the surface, these appear to be modest reductions in BP,” says Prof. Miranda. “But this is on a population-wide scale, including patients at all levels of hypertension risk. Studies have shown that a decrease of as little as 2 mmHg in systolic BP can translate into reductions in stroke mortality and cardiovascular mortality by 10% and 7%, respectively. So the benefits for the population are actually enormous.” This is particularly true for individuals without hypertension. “There was a massive effect of salt substitution on preventing the development of hypertension, with a 55% reduction in the risk of hypertension among those hypertension-free at baseline (p<0.001). And in high-risk patients, including those with hypertension at baseline and older people, the absolute reductions in BP were at least double those seen in lower-risk subgroups.”

How did the group know that Salt Lic was being used by people and not just left in the cupboard? “We tested urinary levels of sodium and potassium in a random sub-sample of the group at baseline and at the end of the study,” Prof. Miranda explains, “and confirmed that the changes were in line with use of the salt substitute.” There is a word of caution here regarding the use of the sodium/potassium salt in people with kidney disease, who should be managed closely by their renal consultant.

“Our salt-substitution approach proved to be an extremely effective way of reducing salt intake and hypertension across communities,” says Prof. Miranda. “We think that it could be applied in other societies, although the impact may differ depending on societal behaviour. For example, in our study, the prime source of salt intake was through cooking. In other societies, where salt is consumed mainly via processed foods, the effect of replacing household salt is likely to be smaller across all groups. But the benefits still exist.” He concludes that, “Multiple strategies are required to reduce salt consumption in the general public and our population-based method could make a major contribution to these efforts to reduce BP and impact on stroke and cardiovascular mortality.”


**Hope, hype and harms of genome editing for heart disease**

Professor Serena Zacchigna (University of Trieste and International Centre for Genetic Engineering and Biotechnology, Trieste, Italy), who co-chaired yesterday’s symposium ‘Genome editing for heart disease’, discusses the possibilities, challenges and limitations of this powerful tool.

“Genome editing involves altering the sequence of endogenous DNA using technologies that break and then repair the DNA, in order to either disrupt a DNA sequence or to replace an existing DNA sequence with a new one,” she explains. Editing is achieved with nucleases, the most recently introduced of which is CRISPR-Cas9. “The advantage of CRISPR-Cas9 over previous technologies, such as the TALENs (Transcription Activator-Like Effectors Nucleases), is that it is cheaper and faster, and this has widened the opportunities to use genome editing technology,” says Prof. Zacchigna. She describes the main ways that genome editing can be used in cardiovascular diseases. “In terms of treatment, in diseases with a genetic basis, genome editing will allow the correction of the causal mutation/s and, if used in utero, prevent the onset of some diseases.” The technique is also invaluable for creating in vivo and ex vivo disease models that mimic the human condition in order to improve understanding of it, help to develop effective treatments and move towards personalised medicine. Prof. Zacchigna sees hopes and challenges for genomic editing. “The hope is to be able to expand the controlled use of this technology across countries worldwide. The challenge is doing this in a situation where different countries have different regulations, where there is no consensus on how best to regulate the technology, there are no agreements on its applications and the risks have yet to be properly defined and quantified.”

“International consensus is needed to address the challenges facing genome editing.”

Prof. Zacchigna wants to ensure that genome editing is made accessible to all countries, not just those with the most resources. “Because these technologies provide tremendous opportunities for research and treatment, collaboration and cooperation between countries is important to promote informed use. More-developed, better-funded countries can support developing countries by sharing the technology, promoting debate and defining the regulations.”

According to Prof. Zacchigna, many of the issues and concerns surrounding genome editing—including the use of viral vector delivery systems to modify gene function and whether to restrict its use to somatic cells or to also allow manipulation of germ cells—have already been discussed in the context of gene therapy. “Of course,” she says, “there are also some other perspectives to consider, such as gene drive technology, used for example in pest control, which increases the probability that an artificially modified gene will be passed on to offspring. This highlights the need to identify the risks, find ways to limit them and also ensure that we have systems in place to control the technology.”

Currently, one of the main limitations to genome editing is reliable targeting. “It is currently difficult to predict where other mutations, away from the desired locus, might occur and it is expensive to track them using whole genome sequencing. Higher specificity CRISPR-Cas9 variants are more likely to be smaller across all groups. But the benefits still exist.” He concludes that, “Multiple strategies are required to reduce salt consumption in the general public and our population-based method could make a major contribution to these efforts to reduce BP and impact on stroke and cardiovascular mortality.”

**Replay the video and slides on ESC 365:** [www.escardio.org/365](http://www.escardio.org/365)
How will data protection impact remote monitoring?

When patients get a pacemaker or a defibrillator with the option for remote monitoring, they need to sign a consent form regarding the treatment of their personal data for all purposes that are non-therapeutic. But what exactly are these ‘other’ purposes, and where does the information go? Who is ultimately responsible for looking after and ensuring the security of data from cardiac implantable electronic devices (CIED)? The doctor? The hospital? The manufacturer?

A joint Task Force from the Regulatory Affairs Committee of the ESC Advocacy Committee and the European Heart Rhythm Association (EHRA), has been looking into the situation. The objective is to understand the roles of the different stakeholders and to assess whether any risks or liabilities exist for patients and clinicians in light of the new EU General Data Protection Regulation (GDPR), which, since May 2018, harmonises data privacy laws across Europe. The main findings and recommendations will be presented at a symposium this afternoon.

Co-Chair of the Task Force for EHRA, Professor Jens Cosedis Nielsen (Aarhus University Hospital, Aarhus, Denmark) explains, “Someone has to take responsibility for the handling of personal data, and we are recommending that this should be a joint venture between the hospital and the manufacturer. Within this agreement, the physician should at best act on behalf of the hospital with no individual responsibility. Nevertheless, he/she should be well informed so that—as primary contact for patients—he/she can answer any questions. As this is unexplored territory, the Task Force will develop a list of recommendations to guide hospitals and manufacturers in the definition of their respective obligations under GDPR.”

Session Co-Chair and Co-Chair of the Task Force for Regulatory Affairs, Professor Josef Kautzner (Institute for Clinical and Experimental Medicine, Prague, Czech Republic) describes additional levels of complexity. “Hospitals and manufacturers have obligations to hold records for a certain period of time, but there is some contradiction with GDPR, which states that data can be deleted at the patient’s request,” he says. “Are hospitals and manufacturers technically even equipped to comply with such provisions?”

And what do patients expect from remote monitoring? Patients are not required to have remote monitoring of their device, as it is not the primary function, but they can consent to have this extra service and they can also change their minds. Patients may have concerns and sometimes they ask that only specific parameters are monitored, which may not be feasible. We have also been trying to clear up uncertainties about the medical benefits of remote monitoring—is it useful for the patient? The evidence will be discussed as part of the symposium.”

Another important issue under discussion is the consent forms used by patients. Now essential, many hospitals use forms from manufacturers and there is no standardisation as Professor Ruben Casado Arroyo (Université Libre de Bruxelles-Erasmes Hospital, Brussels, Belgium) will explain in his presentation. At the moment, the consent forms available from manufacturers are very different and there is a need for greater consistency in the information they contain. The Task Force, which counted a patient with a CIED among its members, is developing an informed consent template that aims to comply with GDPR requirements, while meeting the needs of patients in terms of readability and addressing patient concerns such as what happens to their data and who they can contact for more information. The Task Force has faced quite a challenge capturing sufficient information in a succinct easy-to-understand format that takes into consideration the average age of the patient base and their wide range of educational abilities.

“We should also be concerned about the security of patients’ data,” says Session Co-Chair and EHRA President, Professor Hein Heidbuchel (University Hospital Antwerp, Antwerp, Belgium). “The potential for devices to be hacked was thrown into the spotlight in March this year with a warning from the US FDA that this is a real possibility with some devices. We have sought the advice of international experts on whether companies and hospitals need to look closer at cybersecurity. The Task Force will be reporting back. The goal of the Task Force is to provide all involved in remote monitoring with very concrete guidance on its instalment.”

Prof. Nielsen and Prof. Kautzner emphasise that everyone working with implantable electronic devices may benefit from attending today’s session. “These are very difficult issues, but it is our role to question the system and to ensure not only that it works well, but also that physicians and all healthcare providers are well informed about the regulations to ensure state-of-the art treatment and care of their patients.”

Don’t miss!
- Remote monitoring of cardiac implant electronic devices: new ESC Recommendations
- Launch of new Oxford Master’s in Digital Health Area 1 - Digital Health Area

Regulatory Affairs is an important part of ESC Advocacy. Find out more at: www.escardio.org/The-ESC/Advocacy

Launch of a new MSc in Clinical Trials

With its finger firmly on the pulse of the cardiovascular community, the ESC’s European Heart Academy together with the University of Oxford and the support of the ESC Working Group on Cardiovascular Pharmacotherapy are ready to launch a new Masters course in Clinical Trials.

“With the Diploma of Advanced Studies in Cardiac Arrhythmia Management (DAS-CAM), a joint collaboration with the European Heart Rhythm Association and Maastricht University Medical Centre; and an MSc in Health Economics, Outcomes and Management in Cardiovascular Sciences with the London School of Economics.

“We now have over 500 alumni across these courses and their enthusiasm has amazed and delighted me,” says Prof. Elliott. “We want to encourage these motivated individuals to use the skills they’ve learned to push the ESC further and help it meet the needs of the cardiology community, and most of all, the needs of our patients.”

Don’t miss!
- Launch of new Oxford Master’s in Clinical Trials
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- Launch of new Oxford Master’s in Clinical Trials
HOPE 4 study: Community-based intervention programme reduces CVD risk in low–middle income countries

Early detection of modifiable cardiovascular risk factors followed by lifestyle modifications and evidence-based medications can substantially reduce the risk of cardiovascular disease (CVD).

“Hypertension is the leading cause of CVD and, despite proven medications, blood pressure remains poorly controlled around the world,” says Doctor Jon-David Schwalm (Population Health Research Institute of McMaster University and Hamilton Health Sciences, Hamilton, Ontario, Canada). “We urgently need simple and scalable strategies that can be used to tackle one of the largest contributors to the global disease burden.”

To this end, the Heart Outcomes Prevention and Evaluation 4 (HOPE 4) study was conducted and results were presented by Dr. Schwalm at a Hot Line Session yesterday and simultaneously published in The Lancet. This 12-month, cluster randomised controlled study, undertaken in Colombia and Malaysia, looked at whether a community-based, comprehensive and integrated intervention programme, compared with usual care, could improve long-term cardiovascular risk, and focused on blood pressure and also lipids in people with newly diagnosed or poorly controlled hypertension.

The intervention package in HOPE 4 was informed by extensive health system appraisals and combined a 3-pronged approach: 1) community screening, treatment and control of CVD risk factors by non-physician health workers (in conjunction with local physicians) using mobile health tablet-based simplified management algorithms and counselling programmes; 2) provision of anti-hypertensive and cholesterol-lowering medications to eligible participants; and 3) involvement of family/friends to support the participant-nominated family member/friend providing encouragement and support,” says Dr. Schwalm.

Senior author, Professor Salim Yusuf (Population Health Research Institute of McMaster University and Hamilton Health Sciences, Hamilton, Ontario, Canada) explains that the HOPE 4 study design differs from previous community-based intervention packages. “At the start of the study, we conducted an extensive analysis that included systematic reviews of barriers to effective hypertension management, coupled with in-depth mixed-methods situation analyses in each country. Examples of unique barriers identified included traditional health beliefs with in-depth mixed-methods situation analyses in each country. Examples of unique barriers identified included traditional health beliefs in Malaysia and fragmentation of provision of care in Colombia. The analyses informed the development of a strategy appropriate for these countries. “Importantly,” Prof. Yusuf continues, “the intervention approach was designed to be feasible within the existing country infrastructure. The use of locally sourced medications and task shifting with non-physician health workers contribute to a strategy that we believe is pragmatic and scalable for expansion nationally, as well as for implementation in other countries of all income levels.”

Dr. Schwalm and Prof. Yusuf conclude, “HOPE 4 programme has the potential to make a significant impact on the global disease burden.”

The intervention package was also associated with a change in blood pressure control status (systolic blood pressure <140 mmHg) that was more than double compared with the control group (69% vs 30%; p<0.0001). Improvements in the intervention vs control group were also seen with low-density lipoprotein cholesterol levels (mean change from baseline to 12 months -0.60 vs -0.19 mmol/L; p<0.0001).

The latter includes increased levels of physical activity and greater consumption of fruits and vegetables, which may be largely attributable to the involvement of a participant-nominated family member/friend providing encouragement and support,” says Dr. Schwalm.

“The latter includes increased levels of physical activity and greater consumption of fruits and vegetables, which may be largely attributable to the involvement of a participant-nominated family member/friend providing encouragement and support,” says Dr. Schwalm.

We saw a greater than 40% reduction in the primary outcome of mean Framingham Risk Score 10-year CVD risk estimate among people participating in the community-based intervention vs the usual care group (-11.17% and -6.40%, respectively; p<0.0001).”

The intervention package was also associated with a change in blood pressure control status (systolic blood pressure <140 mmHg) that was more than double compared with the control group (69% vs 30%; p<0.0001). Improvements in the intervention vs control group were also seen with low-density lipoprotein cholesterol levels (mean change from baseline to 12 months -0.60 vs -0.19 mmol/L; p<0.0001).

The latter includes increased levels of physical activity and greater consumption of fruits and vegetables, which may be largely attributable to the involvement of a participant-nominated family member/friend providing encouragement and support,” says Dr. Schwalm.

The ESC is proud to welcome 365 newly elected cardiovascular experts to the Fellows of the ESC (FESC) community. All healthcare professionals who have distinguished themselves in scientific, clinical or nursing excellence in the cardiovascular field are welcome to apply for next year. The deadline for FESC applications is 30 September 2019.
Sessions of the day

7:30
- Balance: Hot topics in out-of-hospital cardiac arrest management
  - Colette: Optimising exercise training in cardiac patients
  - Hugo: General cardiology crash course - Part 4
  - Apron: A career in Basic Science - Sales from the road
  - Duras: Morning insights into pacing
  - Camus: Precision medicine: novel biomarkers for patient risk stratification

8:30
- Nevissa: Meet the Experts - Imaging tools for in vivo myocardial tissue characterisation
- Amsterdam: Expert Advice - Tips and tricks in imaging your patient with valvular heart disease
- Helsinki: Chronic coronary syndrome: Essential Update
- Tbilisi: Expert Advice - Evolving evidence in the treatment of secondary mitral regurgitation
- Zagreb: Meet the Experts - Challenges in adult congenital heart disease care
- Tallinn: How should I treat challenging patients with severe aortic stenosis?
- Duras: Controversies in coronary revascularisation: left main disease and diabetes

9:00
- Digital Health 1
  - Global: Big data in cardiovascular medicine: hope or hype?
  - Corner 1: Atherosclerosis and Aortic Stenosis
  - Corner 2: Lipids / Cardiovascular risk prediction / Lifestyle

9:30
- Centre Stage
  - Budapest: Diabetes and heart failure: a complex relationship
  - Pragre: Evolving concepts in lipidology
  - Douras: Challenging decision-making in anticoagulation therapy
  - Sarajevo: Expert Advice - Therapeutic options in advanced heart failure

10:00
- ESC TV Stage
  - Meet the Trialist - GALACTIC

10:10
- Science Doc 1
  - Agra 2: Blockbusters from the Young in myocardial and pericardial disease

10:15
- Science Doc 2
  - Agra 1: Blockbusters from the Young in cardiovascular interventions

10:30
- Science Doc 3
  - Agra 2: Remote Monitoring in Arrhythmias

10:40
- Science Doc 4
  - Agra 3: Meet the Task Force of the 2019 ESC Guidelines on Acute Pulmonary Embolism

10:50
- Science Doc 5
  - Duras: Practical tips to optimise stroke prevention with non-vitamin K antagonist oral anticoagulants (NOACs).

11:00
- Science Doc 6
  - Agra 1: Vascular protection: when do patients need more? Sponsord by Bayer AG

11:10
- Science Doc 7
  - Colette: Benefits and risks of anticoagulation in elderly atrial fibrillation patients. Sponsored by Daichi Sankyo Europe GmbH

11:15
- Science Doc 8
  - Agra 2: Living an active life with angina. Illusion or reality? Sponsored by Servier

11:30
- Science Doc 9
  - Agra 3: Expert Advice – Challenging percutaneous coronary interventions

11:45
- Science Doc 10
  - Duras: Contemporary antithrombotic strategies in STEMI and multivessel disease

12:00
- Science Doc 11
  - Cambridge: Functional mitral regurgitation in heart failure - Time to score or not to score risk assessment in primary prevention.

12:15
- Science Doc 12
  - Duras: Latest insights into cholesterol management for the post-2019 ESC/EAS dyslipidaemia guidelines: expert discussions on practical implications. Organised by PACE-CME, supported with educational grant from AstraZeneca

12:30
- Science Doc 13
  - Duras: Impact of novel guidelines: transforming diabetes management in cardiology. Organised by PACE-CME, supported with an educational grant provided by Novo Nordisk

12:45
- Science Doc 14
  - Agra 1: Meet the Trialist - CLARIFY!

13:00
- Science Doc 15
  - Nevissa: Latest developments in devices for cardiac rhythm management. Sponsored by Medtronic

13:15
- Science Doc 16
  - Duras: Latest insights into cholesteryl ester transfer protein (CETP) - Spotlight on dual antiplatelet therapy (EBAC Accredited). Supported by an unrestricted educational grant from AstraZeneca

13:30
- Science Doc 17
  - Rome: Improving outcomes with non-vitamin K antagonist oral anticoagulants (NOACs): Focus on atrial fibrillation patients with acute coronary syndrome (AADC) and/or undergoing percutaneous coronary intervention (PCI). Sponsored by The Bristol-Myers Squibb/Pfizer Alliance

13:45
- Science Doc 18

14:00
- Science Doc 19
  - Agra 2: How wider use of combinations will improve control of the main cardiovascular risk factors. Sponsored by Servier

14:15
- Science Doc 20
  - Agra 2: Cardiovascular disease prevention: what do we know? - EAPC

14:30
- Science Doc 21
  - Rome: Functional renal revascularisation in heart failure - Time to treat! Sponsored by Abbott Structural Heart

14:45
- Science Doc 22
  - Amsterdam: DOAC-related bleeding: what every cardiologist needs to know. Organised by Medscape Education, supported with an educational grant from Portola Pharmaceuticals, Inc.

15:00
- Science Doc 23
  - Sofia: Targeting dyslipidaemia in the Asia Pacific Region. Sponsored by Sanofi

15:15
- Science Doc 24
  - Prague: Influenza as a trigger of cardiovascular events: new evidence and role of the vaccination. Sponsored by Sanofi Pasteur

15:30
- Science Doc 25
  - Duras: Advances in implantable cardiac monitors for diagnosing heart rhythm disorders. Sponsored by BOSTRON & Co. KG

15:45
- Science Doc 26
  - Pristina: The TARGET BP clinical program - Investigating alcohol-mediated renal denervation. Sponsored by Ablative Solutions Inc.

16:00
- Science Doc 27
  - Global Exchange 1: Be scientific and unique on Twitter

16:15
- Science Doc 28
  - Agra 1: Confronting cardiovascular risk in patients with diabetes - Spotlight on dual antiplatelet therapy (EBAC Accredited). Supported by an unrestricted educational grant from AstraZeneca

16:30
- Science Doc 29
  - Duras: How should I treat challenging patients with severe aortic stenosis?

16:45
- Science Doc 30
  - Duras: Expert Advice – Cardiac imaging for risk stratification

17:00
- Science Doc 31
  - Agra 2: Meet the Trialist - Initialisation: Community wide reductions in blood pressure and hypertension incidence

17:15
- Science Doc 32
  - Duras: Latest insights into cholesterol management for the post-2019 ESC/EAS dyslipidaemia guidelines: expert discussions on practical implications. Organised by PACE-CME, supported with educational grant provided by Amgen, Pfizer and Sanofi-Aventis

17:30
- Science Doc 33
  - Agra 2: Impact of novel guidelines: transforming diabetes management in cardiology. Organised by PACE-CME, supported with an educational grant provided by Novo Nordisk

17:45
- Science Doc 34

18:00
- Science Doc 35
  - Hugo: A cross-specialty focus – Who are the appropriate patients for SGLT2Is? Sponsored by MSD

18:15
- Science Doc 36
  - Hugo: Latest insights into cholesterol management for the post-2019 ESC/EAS dyslipidaemia guidelines: expert discussions on practical implications. Organised by PACE-CME, supported with educational grant provided by Amgen, Pfizer and Sanofi-Aventis
16:00

Amsterdam

Role of cardiac imaging in current guidelines: what’s new?
Nicosia

Imaging aortic stenosis: beyond echo Doppler
Sofia

Heart failure management in the intensive care unit: Essential Update
Tbilisi

How should I treat acute pulmonary embolism?
Tallinn

Clinical issues in thoracic aortic disease
Prague

Smoking cessation - What’s new?

16:40

Amsterdam

Multimorbidity: cardiac imaging in clinical practice: Essential Update

Nicosia

Meet the Experts - Atrial fibrillation in patients with acute coronary syndromes: how annoying!

Sofia

Right ventricular function from mechanics to prognosis

Tbilisi

The brain in hypertension

Prague

Cellular cross talk in heart failure

Zagreb

Understanding and treating low gradient aortic stenosis

Prag

Burden of ischemic heart disease in women: focus on sex-specific coronary pathophysiology

The ESC Textbook of Cardiovascular Diseases of the aorta: predictors of events and risk modifiers

In 90 seconds

Get a chance to win a prize*
The rapid advance of technology is securing an ever-greater role for imaging in the diagnosis and management of cardiovascular disease. European Association for Cardiovascular Imaging (EACVI) Past Secretary, and a speaker at a symposium this afternoon, Associate Professor Chiara Bucciarelli-Ducci (University of Bristol, Bristol, UK) gives her views on novel applications for cardiac imaging in ESC Clinical Practice Guidelines.

“The latest ESC Guidelines on acute myocardial infarction in patients presenting with ST-segment elevation (STEMI), the role of non-invasive imaging has been refined with ST-segment elevation (STEMI) was introduced for the first time and discussed. The Fourth Universal Definition of Myocardial Infarction puts greater emphasis on CMR and injury and damage based on the pattern of myocardial oedema and scarring. 1

In the ESC Guidelines on the diagnosis and management of chronic coronary syndromes (CCS), six clinical scenarios are presented and the application of various diagnostic tests in different patient groups to rule-in or rule-out coronary artery disease (CAD) have been updated. 2 The main-and much awaited novelty is the introduction of coronary computed tomography (CT) in the diagnostic work-up of patients with suspected CAD and angina or dyspnoea. The specific recommendations in imaging are:

1) Non-invasive functional imaging for myocardial ischaemia or coronary CT angiography (CTA) is recommended as the initial test to diagnose CAD in symptomatic patients in whom obstructive CAD cannot be excluded by clinical assessment alone (Ia).

2) It is recommended that selection of the initial non-invasive diagnostic test is done based on the clinical likelihood of CAD and other patient characteristics that influence test performance, local expertise and the availability of tests (Ic).

3) Functional imaging for myocardial ischaemia is recommended if coronary CTA has shown CAD of uncertain functional significance or is not diagnostic (Ib).

Imaging is recommended also for risk stratification, preferably stress imaging or coronary CTA (if permitted by local expertise and availability) or alternatively, exercise stress electrocardiogram (ECG) (if significant exercise can be performed and the ECG is amenable to the identification of ischaemic changes) in patients with suspected or newly diagnosed CAD (Ib).

Among the novel concepts in imaging in valvular heart disease is the introduction of the heart team in which the cardiovascular specialist interacts with the patient and the heart team in which the cardiovascular specialist interacts with the patient and the cardiovascular imaging imager is an integral part. What’s new in aortic stenosis imaging is the additional clarity on assessing patients with suspected aortic stenosis and assuring its severity, as well as the extension of the diagnostic work-up for transcatheter aortic valve implantation (TAVI) in patients at low risk following the PARTNER 3 and Evolut trials. Also, the limitations of the 50% cut-off for left ventricular ejection fraction as a measure of left ventricular function in aortic stenosis is appraised along with the role of global longitudinal strain by echocardiography and myocardial scar detection by CMR. Following the MITRA-FR and COAPT trials, the role of echocardiography for secondary mitral regurgitation has been further developed and used to interpret the possible explanations about the different results.

I hope you can join me and Professors Knutti, Bax and Popescu as we discuss the very latest role of imaging in acute and chronic coronary syndromes, heart failure and valvular heart disease.”


Don’t miss!
• Role of cardiac imaging in current guidelines: what’s new?
Today, 14:30 – 15:40; Amsterdam – Village 1
Abstract of the day:

**Pericarditis increases one-year mortality**

Incident pericarditis triples the risk of dying within one year, according to a presentation this morning from Ms. Flora Lind Sigvardt (Gentofte University Hospital, Copenhagen, Denmark) (Abstract S036).

Using data from nationwide Danish registries (1996-2016), the study assessed the one-year mortality of 8,077 patients with a first-time diagnosis of pericarditis. Results were adjusted for baseline comorbidities, including cardiovascular conditions and chronic obstructive pulmonary disease, and were compared with data from the general population, partnering each study patient with eight age- and sex-matched controls.

Explaining why her group decided to conduct the study, Ms. Sigvardt says, “Clinically it’s an interesting patient group: they are relatively young—40-45 years old—and present with symptoms similar to those of acute myocardial infarction. After treatment and discharge, follow-up of non-complicated episodes tends to be minimal, about one week. This is because it is thought that there are no apparent long-term risks associated with the condition, apart from subsequent recurrences. A Danish study has previously suggested that pericarditis may be a marker of occult cancer but there are currently no data on mortality rates after a non-complicated event and epidemiology in general is inconclusive.”

“In our study, we found that absolute one-year mortality rates in patients with and without pericarditis were 2.9% vs 0.8%, respectively (p<0.001). Furthermore, in the year after the first episode of pericarditis, hospital admission rates for a variety of conditions were significantly increased compared with the general population: recurrent pericarditis (10.6%), other cardiovascular disease (4.6% vs 1.2%), respiratory disease (3.4% vs 0.7%) and malignant disease (1.4% vs 0.5%).”

Ms. Sigvardt adds that the causes of the increased mortality and morbidity are not yet known and require further investigation. As far as the working clinician is concerned, she thinks greater vigilance is required. “Because patients have higher cardiovascular and non-cardiovascular hospital admissions in the first year, doctors need to look more closely at underlying comorbidities. They should also consider extending follow-up and educating patients about signs and symptoms that may indicate recurrence or suggest the presence of another condition.”


**Don’t miss!**

- Increased 1-year mortality among patients discharged following hospitalization for pericarditis – a nationwide cohort study
  
  Today, 10:10 – 10:50, Agora 2 – Poster Area

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**ESC Asia with APSC & AFC**

**Expanding the boundaries of cardiovascular medicine**

8 – 10 November 2019, Singapore

The meeting is not all about guidelines. It will also feature a number of other sessions, including high-quality abstracts from the region, explains Professor Michel Komajda (Saint Joseph Hospital, Paris, France), Scientific Committee Co-Chair and Organising Committee Chair. “There will be presentations by Asia-Pacific investigators of abstracts reported at ESC Congress 2019 along with local best-graded abstracts not included in the Paris programme due to restrictions on numbers.”

“We hope to attract many regional young cardiologists to this shared endeavour.”

Prof. Komajda continues, “Specific sessions for young cardiologists include a clinical case competition and advice on writing acceptable congress abstracts and scientific articles. We are also providing young cardiologists and allied professionals with a lower registration fee to encourage them to take advantage of this incredible opportunity to hear from, and network with, the very best in Europe and Asia-Pacific. During my term as ESC President 2010-2012, one of our goals was to extend the ESC mission beyond European borders and expand relationships with sister societies, particularly in Asia. I am delighted that this goal has become reality at ESC Asia!”

Register for ESC Asia by 16 September and save on the registration fee!
The 2019 ESC Rene Laennec Lecture on Clinical Cardiology was delivered yesterday by Professor Isabelle Van Gelder (University of Groningen, University Medical Center Groningen, Groningen, Netherlands).

Enormously respected for her work in improving the understanding and treatment of atrial fibrillation and its sequelae, Prof. Van Gelder is the Principal Investigator of over twenty clinical trials, a Task Force member of the upcoming 2020 ESC Clinical Practice Guidelines for the management of atrial fibrillation and Associate Editor of EP Europace.

While doing her PhD in arrhythmia research in the 1980s, Prof. Van Gelder’s interest was piqued by atrial fibrillation, particularly the diversity of patients and their symptoms. “Some patients were very symptomatic and others had no symptoms at all. At that time, the standard clinical approach for all patients was restoration of sinus rhythm, but this was difficult to maintain and patients also had to suffer the side effects of antiarrhythmic drugs. I wanted to know if it was actually necessary to restore sinus rhythm in asymptomatic patients,” she says. Prof. Van Gelder counts the series of RACE trials that emerged from her subsequent research as being among her greatest career achievements. “The first RACE trial showed that rate control was not inferior to rhythm control in reducing the risk of death and morbidity. Published at the same time as the US AFFIRM study—which reported similar results—these findings changed the way atrial fibrillation is treated, and had the dual benefit of sparing patients the side effects of unnecessary treatment and reducing treatment costs.” The RACE 2 and RACE 3 trials followed, demonstrating the benefits of lenient vs strict rate control strategies and of treating underlying conditions, respectively. It is this latter area that Prof. Van Gelder focused on in her lecture, “Atrial fibrillation: not just an arrhythmia.” “We need to identify, and then treat, patients’ comorbidities; this is essential for reducing the adverse outcomes of atrial fibrillation, such as heart failure, stroke and dementia.”

“We must learn to look not only at their ECG, but also at the whole patient.”

Prof. Van Gelder talks about the challenges facing atrial fibrillation research, “We have learned a lot, but there is still much progress to be made,” she says. “We need to know if the duration of atrial fibrillation plays a part in prognosis and to better understand the role of personalised therapy. For example, do we treat atrial fibrillation patients with hypertension and diabetes differently to those with heart failure? And a really pressing challenge is dealing with sex differences in atrial fibrillation. At the moment, fewer than 3% of participants in atrial fibrillation trials are women; in the recent CASTLE-AF trial, the proportion was only 14%. So, how do we know if the results from even large trials are applicable to women?” A further challenge is screening: “One in four people over the age of 55 years will have atrial fibrillation. We need to find ways to increase awareness among general practitioners and the general population and to capture the data more easily.” Finally, lifestyle factors should be incorporated into all treatment plans.

It is these challenges that will form the basis for the future of research in atrial fibrillation, at least in the short-term, with the main emphasis being on individualising the disease and personalising treatment. In addition to incorporating new technologies into treatment, Prof. Van Gelder thinks that different subspecialties should cooperate more closely. “Atrial fibrillation never comes alone. Combining the views of different specialists will give doctors a more complete picture and will help patients to get better treatment in a more efficient situation.”

ESC Grants: Increased opportunities for training and research

Prof. Tomasz Guzik

Access to quality training and the chance to conduct innovative research are important both for personal growth and for the advancement of the field of cardiology; however, these come at a cost. But this is where the ESC can help!

Each year, the ESC pledges a minimum of 3% of its expenditures and for 2018, this was nearly €1.8 million for its members. Describing some of the grants available, Chair of the ESC Research and Grants Committee, Professor Tomasz Guzik (University of Glasgow, Glasgow, UK and Jagiellonian University, Krakow, Poland) says, “The ESC provides Research Grants of €25,000 each to allow young members with novel ideas to conduct their research in different countries around the world. The Society also funds the clinically oriented Training Grants and Nursing Grants, helping young professionals to develop their skills in centres of excellence. In addition, ESC Congress Educational Grants are offered to healthcare professionals and researchers who have limited access to funding or difficulties obtaining financial assistance to attend. Eight members are awarded ESC Grants for Women in Leadership to enable them to attend the innovative Women Transforming Leadership Programme.”

“The ESC has increased the number of research and training grants available and, in 2019, the Society will announce a number of new grant categories, including the ESC Homecoming Grant, for people returning from post-doctoral fellowships abroad, and the ESC Springboard Grant, to fund the initiation of collaborations,” says Prof. Guzik.

Anyone who is eligible is encouraged to apply, although ESC Grants are rightly difficult to obtain. “The ESC Research and Grants Committee conducts a rigorous, independent, objective assessment process to grade and rank applications,” explains Prof. Guzik. “Members need to submit a comprehensive, well-planned application to be in with a chance of being awarded a grant.”

Why is ESC doing this? “One of the ESC’s main pillars is research and ESC Grants contribute towards this strategic priority,” says Prof. Guzik. “Over the past few years we have monitored the grants, and practically every one of them has resulted in a journal publication. At the same time, the grants are helping young members at a crucial time in their career progression. Strength in research is due to strength in people—ESC Grants are investments in terms of developing individuals and also consolidating the future of the Society.”

ESC Congress News - Tuesday 3 September
Sleep, stress and socioeconomic status - how do they impact on cardiovascular health?

Prof. Massimo Piepoli

As well as lifestyle factors, such as lack of physical activity, tobacco use, unhealthy food habits and excess body weight, other less well-considered factors have been linked to adverse cardiovascular (CV) health. Professor Massimo Piepoli (Guglielmo da Saliceto Hospital, Piacenza, University of Parma, Italy), Editor-in-Chief of European Journal of Preventive Cardiology, describes some interesting new findings:

“Poor sleep quality has been linked to elevated blood pressure and the development of hypertension, but here at ESC Congress yesterday, Sasaki et al presented an observational study of 3,313 elderly people showing a relationship between visit-to-visit blood pressure variability and sleep quality (Abstract P4403). This finding is pertinent given that visit-to-visit blood pressure variability is already known to be associated with incident CV disease (CVD) independent of mean blood pressure.

Sleep-disordered breathing is known to be associated with increased CV risk but is not part of standard scales used for risk stratification. On Sunday, Korostovtseva et al presented a Russian population-based study which showed that subjects with self-reported snoring were more often at high-to-very-high risk of fatal CV events according to SCORE risk charts than non-snorers (Abstract P1554). The same relationship was not seen with self-reported sleep apnoeas, but this may have been due to the subjective assessment based on the questionnaire.

It furthermore appears that impaired sleep and work stress are a deadly combination. A Russian population-based German study evaluated the effect of impaired sleep and work on 1,959 hypertensive employees.1 Over a mean follow-up of 17.8 years, compared with individuals with low work stress and non-impaired sleep, subjects with work stress (hazard ratio [HR] 1.56; 95% confidence interval [CI] 0.81–2.98) or impaired sleep (HR 1.76; 95% CI 0.96–3.22) had an increased risk of CVD, while participants with both work stress and impaired sleep had the highest risk of CVD mortality (HR 2.94; 95% CI 1.18–7.33).

The impact of income level is also highlighted at ESC Congress 2019. Liao et al examined the effect of income level on adverse events in patients with atrial fibrillation (Abstract P3775). Multivariate Cox regression analysis showed that higher income was significantly associated with a lower risk of adverse events. After propensity matching, high income level was associated with a lower incidence of ischaemic stroke (adjusted HR 0.83), intracerebral haemorrhage (adjusted HR 0.78), major bleeding (adjusted HR 0.85) and mortality (adjusted HR 0.57).

A recent study in the European Journal of Preventive Cardiology investigated socioeconomic status and CV mortality2. After a median follow-up of 10 years, CV death was significantly higher among middle and low socioeconomic status groups (HR [95% CI]; for middle 1.192 [1.68–2.99] and for low 1.73 [1.50–2.00]) compared with the high socioeconomic status group after adjustment. An upward shift of socioeconomic status was associated with a lower risk of CV death (HR 0.46; 95% CI 0.40–0.52), while a downward shift was not a significant predictor. Socioeconomic status may have an influence on the use of preventive medications such as statins and antiplatelet agents. Improvement of quality of life may also be an appropriate prevention strategy for CV health and an increase in income may be one of the socioeconomic factors that can positively influence the quality of life.

A progressive improvement in the level of education was accompanied by reduced premature CV mortality, according to a study from Norway.3 A large proportion (over two-thirds) of the gap in premature deaths between people with the highest and the lowest education was mediated by the modifiable CV risk factors, including smoking, systolic blood pressure, total cholesterol, body mass index, triglycerides and physical activity. While public campaigns attempt to improve the public knowledge on the risks of ‘bad behaviours’, recent evidence suggests that low educational levels represent an important barrier.”

References

Cardiovascular Disease Scorecards: Painting the picture of heart health in Africa

The Cardiovascular Disease Scorecard is a tool that allows stakeholders, including members of the World Heart Federation (WHF), to assess strengths and gaps in national cardiovascular disease (CVD) programmes and policies.

The CVD Scorecard provides a core set of indicators that allows WHF, its members and other stakeholders to understand the epidemiological situation in a country, monitor progress in the implementation of CVD prevention and management programmes, identify policy gaps to highlight where action is needed, and prioritise advocacy for particular policies or programmes.

Since 2018, the Pan-African Society of Cardiology (PASCAR) has been supporting WHF in implementing this project in Africa, and collaborating with the National Cardiac Societies and partners across the continent in the data collection and verification process. A clear picture of the current state of CVD prevention, control and management is being created across 12 African countries including Ethiopia, Mozambique, Nigeria, South Africa and Sudan.

As well as advising national Ministries of Health, the CVD Scorecards provide a consolidated source of the most recent available CVD data by country to be utilised by cardiologists and other healthcare professionals. Data are collected from open data sources, published journal articles and government documents. The dataset covers various aspects of CVD with four focus areas: the national burden of CVD and its risk factors, health system capacity and treatment coverage, policy and governance environment for prevention and protection from risk factors, and the efficacy of CVD advocacy and involvement of civil societies.

By measuring the national response to CVD, priorities can be defined and progress mapped. Ultimately, countries can be held accountable for their actions to promote better heart health outcomes and to meet the World Health Organization goal of reducing premature CVD mortality by 25% by 2025.

PASCAR and WHF welcome collaboration and input on the CVD Scorecard project. For more information, or to get involved, contact info@worldheart.org.
ESC Gold Medal Award winner: It's in the genes

Prof. Christine Seidman

Professor Christine Seidman (Thomas W. Smith Professor in Medicine and Genetics at Harvard Medical School and Director of the Cardiovascular Genetics Center at Brigham and Women's Hospital, Boston, MA, USA) is an internationally recognised scientist and physician in cardiology.

In addition to being awarded the 2019 ESC Gold Medal, which honours individuals who have gained outstanding achievements in original research and scientific excellence, Prof. Seidman has also received the 2019 Vanderbilt Prize in Biomedical Science. Other honours she has been bestowed include the Joseph A. Vita Award and Basic Research Prize from the American Heart Association and the Bristol-Myers Squibb Award for Distinguished Achievement in Cardiovascular Research.

Prof. Seidman is best known for her elucidation of the genetic causes of hypertrophic cardiomyopathy, a condition about which inspired her to specialise in cardiology and more specifically cardiovascular genetics. Prof. Seidman describes her delight in studying an organ that literally 'sings/murmurs' to you. “I have always been fascinated in the physical examination of hearts as well as the diverse spectrum of heart diseases, from acute onset problems such as arrhythmias to chronic conditions such as angina.” She continues, “At the time I was trained, there was particularly interested in heart muscle function and the changes this undertaking in response to disease, such as hypertrophy or dilatation. Improvements in imaging techniques including echocardiography allowed us to define changes in heart morphology in the absence of symptoms, paving the way to recognising that some of these conditions were being driven by a genetic mechanism. Around the same time, I became aware of advances in molecular genetics in other fields of medicine and saw a potential application for these new techniques in cardiology.”

Prof. Seidman’s ensuing research using linkage analysis to compare the presence of polymorphisms in the genome of affected families vs unaffected families has been fundamental in identifying the genetic causes of hereditary cardiomyopathies and congenital heart diseases. However, Prof. Seidman is keen to emphasise that these successes are not hers alone but the result of the hard work and dedication of her whole research group, which she runs in collaboration with her husband, Professor Jonathan Seidman. Working together, the research team has developed mechanistic models of hypertrophic cardiomyopathy in mice, and more recently in cardiomyocytes derived from induced pluripotent stem cells, which have provided insights into the mechanisms by which these gene mutations develop into heart disease. “Only once the causes and mechanisms of disease are understood, can we hope to define and develop more effective therapies,” she explains.

How does Prof. Seidman see the future for cardiomyopathy research? This method of genetically providing a possible heart disease, the identification of small molecules that show promise as targeted therapies is an area that she feels holds enormous potential. One such therapeutic agent is already being investigated in clinical trials for the treatment of hypertrophic cardiomyopathy.

“In addition, the potential to correct gene mutations at the molecular level is rapidly emerging and includes correction of the precise nucleotide abnormality or the use of RNA interference technology to prevent translation of the mutated gene.”

Prof. Seidman is hopeful, “Both of these strategies may enable future prevention or cure of potentially devastating diseases, which can manifest as sudden death in people of all ages including the very young. Furthermore, the implications of prevention and cure extend beyond the patients themselves, given the burden to immediate family members who may have inherited the gene mutation.”

In Prof. Seidman’s opinion, “Research collaboration—within and between countries, and between scientists and physician researchers—is vital to achieving therapeutic advances in cardiology.”

In addition, she feels it is important to reach across all areas of science and technology to find the tools that can be applied in cardiology, allowing progress to span from the bedside back to the bench. This is something Prof. Seidman will touch on at an Advances in Science session today. In her presentation, Prof. Seidman will discuss her research experience in cardiology, from identifying gene mutations to understanding disease mechanisms to the development of potential medicines, and present how this could provide a research template for other heart muscle diseases.

Don’t miss!
• The potential of genetic testing in dilated cardiomyopathy

ESC Paul Hugenholtz Lecture for Innovation
Collecting data and establishing evidence the smart way

Prof. Stefan James

Following the first ever ESC Paul Hugenholtz Lecture for Innovation in 2018, this year’s lecture was given by Professor Stefan James, Scientific Director of Uppsala Clinical Research Center, Uppsala, Sweden and President of the Swedish Society of Cardiology.

Prof. James has been involved in the executive leadership of multiple global mega trials using experiences he gained from international collaborations. He has also served on multiple ESC guideline committees and worked with dedication to facilitate implementation of guidelines into clinical practice.

Prof. James has a longstanding interest in how data can be collected and used in new and innovative ways to enable patients to receive the best evidence-based care. He says, “Gathering data should be fun and not just something that we are forced to do. Simple systems should be built that are valuable to the individuals inputting the data as well as the investigators running the studies. We need to try to create a ‘learning healthcare system’ in which more data are collected from all patients and used in a clever way. The learning healthcare system is a virtuous circle of evidence generation, guideline production, clinical implementation and real-world investigation.”

“Embedding a learning system within the regular healthcare system will allow us to use information from every patient to build a continuous platform for improvement and innovation.”

He continues, “In Sweden, we have a strong tradition of data collection. The Swedish church began keeping complete local registers in the 15th century and in 1947, the personal identification number was introduced for all permanent residents. The publicly funded healthcare system, together with personal identification numbers and national registers of statistics, have allowed Sweden to establish many quality registries.” Prof. James has been active in building and running some of these registries, including SWEDEHEART (Swedish Web-system for Enhanced and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies).

Although prospective, randomised, controlled clinical trials (RCTs) have transformed cardiology in many areas, only a small proportion of guideline recommendations are based on RCT evidence. Furthermore, RCTs are becoming increasingly large, complex, selective and prohibitively expensive to conduct. Prof. James and collaborators have pioneered a new concept in randomised trial design: registry-based prospective randomised clinical trials (RRCTs).

Prof. James continues, “With RRCTs, by incorporating randomisation into a clinical quality registry, we are able to combine some of the critical attributes of a prospective RCT with the practical features of a large-scale registry. This methodology provides a possibility to examine minimally selected consecutive enrolment, with efficient patient identification and follow-up. RRCTs are relatively inexpensive to conduct and may more readily promote adoption of evidence into practice than RCTs.”

The first large-scale implementation of the RRCT concept was in the TASTE trial, which prospectively evaluated whether routine intraoperative thoracic aspiration before primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction could reduce short-term mortality. The SWEDEHEART registry was used to identify patients eligible for inclusion using only a limited number of selection criteria. Patients were randomly assigned treatment directly in the registry clinical report form. No additional study-related activities were included, and endpoint data were automatically collected from national registers. The trial showed no significance difference in outcome between the groups but provided Prof. James and investigators with the experience needed to design and conduct additional RRCTs.

Prof. James explains, “RRCTs have now become a very successful way of generating randomised prospective data. From early studies, such as TASTE, we have been able to complete and publish a number of trials that have had a great impact on international guidelines and helped to change clinical care. By running more RRCTs using different cardiovascular and non-cardiovascular registries within and outside of Sweden, we are hoping to further develop the system. In Scandinavia, there is a data collection culture, which we have been able to build upon. We are eager to spread this approach to other countries across the world so that investigators better understand the opportunities and limitations and can speed up the process of prospective randomised trials and evidence generation.”

Prof. James concludes, “I have been fortunate to learn from great masters in the field like Lars Wallentin—his ideas and those of my other mentors like Robert Califf and Robert Harrington have helped to create this pathway for smart evidence generation. It is important to emphasise that progress can only be achieved through collaboration—I believe that if we work together in the same direction, then we can achieve even better results. ESC Congress is a perfect arena for this collaboration.”


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ESC Congress News - Tuesday 3 September

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Machine learning (ML) is becoming increasingly integrated into modern life, and offers the possibility to revolutionise clinical medicine and research, but what exactly is it?

Doctor Luis Eduardo Juarez-Orozco (University Medical Center Groningen, Groningen, Netherlands) describes it as a family of algorithms with the characteristic ability to progressively improve their performance in a particular task (such as classification or prediction), the more data they receive. He explains, “ML has fostered the new wave of artificial intelligence that we are witnessing in so many areas of knowledge. This intelligence explosion originates from the recent convergence of three very specific forces, namely: the enormous increase in our capacity to access and store data, the exponential growth in our computational capabilities and the existence of complex problems which can be targeted by new ML algorithms. Indeed, the very complexity of biological systems make medical issues an ideal target for ML.”

So how can ML be used in cardiology?

Dr. Juarez-Orozco, Doctor Jan-Walter Benjamins (University Medical Center Groningen, Groningen, Netherlands) and colleagues presented an excellent example at the International Conference on Nuclear Cardiology and Cardiac CT (iCNiC) 2019, with further data presented at ESC Congress 2019 on Sunday (Abstract P218). The study compared the performances of an ML algorithm based on 82 data variables—derived from coronary computed tomography (CT) angiography scans, positron emission tomography (PET) scans and medical records—with risk scores based on 9 clinical variables, calcium score or expert image interpretation to predict myocardial infarction (MI) or death in 951 patients with chest pain. During follow-up (1 month–9.6 years), 24 MIs and 49 deaths occurred, while 11.5% of patients underwent early revascularisation. Novel deep learning-based survival analyses of these PET/CT data out-performed calcium score and categorical expert interpretation (concordance indices of 0.75, 0.73 and 0.68, respectively). Furthermore, combining PET/CT with clinical variables enhanced prediction, independently from the effect of early revascularisation.

“In our study, ML increased the statistical ability to predict death or MI in patients evaluated for chest pain complaints. The system repeatedly analysed the data in search for higher-dimensional patterns that could better identify the patients who ultimately develop an event,” notes Dr. Juarez-Orozco. “With ML, we will soon be able to derive individual-patient risk estimations with a greater accuracy than traditional risk scores. This could allow a better understanding of disease progression to events, personalised treatments, and hopefully, it may ultimately lead to better outcomes for patients.”

A Rapid Fire Abstract presentation yesterday discussed proof-of-concept findings regarding the prediction of events (death or heart failure hospitalisation) using 17 clinical parameters and similarities in longitudinal strain patterns of 12 left ventricular (LV) regions and an LV volume curve (Abstract 4302). An unsupervised ML-based algorithm (multiple kernel learning) was trained using data from 2,123 subjects enrolled in the AIRC population based cohort. Using the same descriptors, data from 105 untreated patients from the TOPCAT trial and 429 untreated patients from the MADIT-CRT trial were projected onto the learned multi-dimensional space. Event rates tracked with multi-dimensional location, indicating that ML integration of complex echocardiographic patterns and clinical parameters has predictive capabilities.

ML may also help in the prognostic assessment of asymptomatic patients. A presentation on Saturday reported that ML-based integration of clinical parameters with quantitative CT measures of coronary artery calcium and epicardial adipose tissue significantly improved the prediction of long-term risk of MI and cardiac death in 2,071 asymptomatic subjects from the EISNER trial (Abstract 30). Patients with a high ML risk score had a high risk of suffering an event (hazard ratio 9.25; p<0.001).

Timely detection of subclinical LV remodelling and dysfunction is important in the risk stratification of asymptomatic subjects. Yesterday, a moderated poster discussed how ML algorithms used to combine routine clinical and laboratory data showed high accuracy in predicting LV diastolic dysfunction area under the Receiver Operating Characteristic curve (AUC 89%-93%) and LV hypertrophy (AUC 70%-79%) (Abstract P3489). Top selected ML classifiers for predicting LV diastolic dysfunction included age, body mass index, blood pressure components, blood sugar, leptin, uric acid, lipid profile and blood cell counts. These classifiers may be useful to preselect individuals at risk who would benefit from in-depth echocardiographic examination, monitoring and prevention strategies.

Dr. Juarez-Orozco concludes, “By enhancing the complexity of our analytical approaches, ML gives us the power to harness novel insights into long-known problems in cardiology and enhance data-driven applications that may possibly help many more patients than we are currently able. I believe the last time medicine saw such a phenomenon was with the explosion of genomics and the start of the digital revolution!”


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63 topics. 770 chapters. 792 authors. These are the statistics behind ESC CardioMed, the dynamic online sister version of The ESC Textbook of Cardiovascular Medicine.

“Text books are still the backbone of learning in cardiovascular medicine,” says ESC CardioMed Editor, Professor Thomas Lüscher (Imperial College London, London, UK), “but they must be adapted and complemented if we are to keep up with today’s incredibly fast pace of progress and the needs of the contemporary cardiology community. For in-depth learning on a certain topic or for a quick question that needs a quick answer, as an electronic and fully searchable encyclopedia, ESC CardioMed can provide the information needed—in the clinic, at home and on the move.”

Keeping such a comprehensive resource updated is a huge task, as ESC CardioMed Editor, Professor John Camm (University of London, London, UK), explains, “The editors discuss necessary revisions every week and, in addition, authors consider updates three times a year. The ESC Clinical Practice Guidelines Task Forces help to ensure that ESC CardioMed is fully aligned with the ESC Guidelines, quite a challenge given their reach across all sections. And we are particularly excited about the ‘On the radar’ section, which is in development—it will give readers hot-off-the-press information about recently published or presented data from key randomised clinical trials.”

And all this will soon come with a new dimension to further aid learning.

A perpetual goal for ESC Publications is to find improved ways to communicate science to its members and beyond. As such, the ESC has teamed up with 3D Tech Omega Zeta who are specialists in the development of 3D and interactive medical and scientific content. “3D Tech Omega Zeta’s enhancements to ESC CardioMed are a valuable first step into a future where discovery is driven by virtual artificial intelligence environments,” believes Mr. Michael Alexander, ESC Publications Head. Mr. Jacobo Beut, CEO of 3D Tech Omega Zeta explains further: “Whereas classic 2D illustrations present anatomy at face-value, 3D Tech Omega Zeta’s interactive models and mechanism-of-action videos allow learners to interact with and experience scientifically accurate life-like human organs and their components, modelled from DICOM (Digital Imaging and Communications in Medicine), as well as providing them with the opportunity to dive deeper into complex processes that occur at a cellular and molecular level.” By greatly reducing the experiential learning limitations between 2D medical images and cardiovascular reality, the ESC and 3D Tech Omega Zeta are confident that these new enhancements will increase understanding and retention.

ESC CardioMed is absolutely free to all ESC Professional Members and Fellows. Come to the Professional Members’ Lounge to hear more about the resource from Prof. Lüscher and Prof. Camm and to see demonstrations of ESC CardioMed and the new 3D features in action.

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• Make the most of your benefits: ESC CardioMed is evolving - New 3D enhancement: 14:45 - 15:00

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