My return economy class airfare to London was kindly sponsored by Aspen Pharmaceuticals. This report is based on my impressions of the various sessions I attended.

Five updated ESC Guidelines were launched during the meeting: non-ST segment elevation acute coronary syndrome, pulmonary hypertension, ventricular arrhythmias and sudden cardiac death, pericardial diseases, and infective endocarditis. The full texts of all ESC Guidelines are available at escardio.org/guidelines. Year-long access to the presentations at ESC are available at escardio.org/ESC365.

Hypertension

The PATHWAY studies were undertaken by the British Hypertension Society. PATHWAY-2\(^1\) investigated the optimal treatment for drug-resistant hypertension adding an \(\alpha\)-blocker, \(\beta\)-blocker, spironolactone and placebo in 4 consecutive 12 week cycles to an ACE or ARB + calcium channel blocker + thiazide diuretic in patients with uncontrolled hypertension. 60% of patients treated with spironolactone achieved control of their BP. The response with adding spironolactone (25 mg daily) was superior to adding a beta-blocker or alpha-blocker. The BP response was inversely related to the renin level.

PATHWAY-3 examined the differences between HCTZ (25-50 mg), amiloride (10-20 mg) and their combination at half-dose levels (HCTZ 12.5-25 mg + amiloride 5-10 mg) on blood pressure, serum potassium, plasma glucose and uric acid in patients with hypertension and at least one characteristic of the metabolic syndrome (99% were obese). The greatest fall in blood pressure occurred with the lower dose combination while the serum potassium was unchanged. Plasma glucose rose in the HCTZ only group, but was lower with amiloride alone or in combination. Uric acid rose on HCTZ.

Prof Bryan Williams, University College, London presented PARAMETER trial which compared the angiotensin receptor-neprilysin inhibitor LCZ696 (valsartan / sacubitril) to ACE inhibition over 12-weeks in elderly patients with an elevated systolic pressure and a wide pulse pressure. LCZ696 achieved a 4 mm Hg greater reduction in central systolic pressure with a greater fall in night time BP and in NTproBNP. A greater percentage of patients on ACE inhibition required additional medications to achieve control.

ATTEMPT-CVD\(^2\) compared the ARB telmisartan with alternative antihypertensive therapy over a 3-year period. The endpoints were CV events, UACR, and BNP. Identical BP control was achieved with little difference in UACR (urinary albumin creatinine ratio) and BNP. There was a non-significant reduction in CV events with the ARB.
Coronary Artery Disease

1. Miscellaneous

The IMPROVE-IT study evaluated simvastatin 40 mg + ezetimibe 10 mg vs. simvastatin 40 mg in post-ACS patients and demonstrated a small benefit in favour of the combination. Guigliano presented a subgroup analysis of patients with and without diabetes. The effect in the diabetes sub-group was markedly greater when compared to those without diabetes; there was a significantly greater reduction in the primary end point driven by a 24% reduction in MI and a 39% reduction in ischaemic stroke.

Another sub-group analysis from the IMPROVE-IT study found no increase in new onset diabetes over 6 years in those treated with the combination.

Dr D Kotecha, Birmingham University, United Kingdom reported that his meta-analysis including the individual data of 13,000 patients from various trials could not show a difference in the effect of beta-blockers in respect of either age or gender.

The PLATFORM Study was presented by Dr Pamela Douglas, Duke University, USA. The investigators assessed the effect of CTA-FFR\textsubscript{CT} (fractional flow reserve by computed tomographic angiography) versus the standard practice of invasive angiography that was planned to rule out obstructive coronary artery disease (OCAD) in moderate risk patients. The trial was fairly small and was not randomized. Of note CTA-FFR\textsubscript{CT} could not be completed in 12% of patients. Follow-up was for 90 days only. In the CTA-FFR\textsubscript{CT} group, only 39% eventually underwent invasive angiography. The rates of detection of OCAD were similar (27% and 30%) whereas the primary endpoint, no OCAD was reached in 73% of in the planned invasive group vs. 12% in those who first had CTA-FFR\textsubscript{CT}.

The FREEDOM trial evaluated revascularisation by coronary bypass surgery vs. PCI in patients with diabetes. A presentation at this meeting examined the effect of baseline blood pressure. The investigators found a dichotomy in the outcomes between CABG and PCI. A lower blood pressure before CABG was associated with worse outcome whereas this relationship was not present in the PCI group. The authors had not considered the possible effects of pre-operative ACE inhibition which might complicate the management of intra-operative hypotensive events.

The 5-year results of the FAME trial, which was not powered for this length of follow-up, nonetheless showed maintained (though non-significant) benefit extending for the entire period. In the group managed with FFR a 1.3% reduction in mortality and 27% reduction in cardiovascular events was observed.

Celecoxib was compared to diclofenac or ibuprofen in arthritic patients who were free from known CVD to assess whether the cardiovascular event rate differed. 7,297 low risk arthritic patients from the UK, Denmark and the Netherlands was studied in the SCOT trial (Standard Care versus Celecoxib Outcome Trial). The observed primary event rate was low at 0.9 events/100 patient years, and was no different with celecoxib in comparison to the other
NSAID’s. Serious adverse events were encountered in 30% of patients in both groups. The withdrawal rate was higher on celecoxib therapy.

2. Acute Myocardial Infarction

The BACC study investigated the value of a 1-hour rule-out strategy for NSTEMI using hs-troponin I. 1045 patients with acute chest pain presenting to the ER were included. A cut-off of 6 ng/L (rather than the 99th percentile) was used. Determination of hs-troponin I was performed at the time of presentation and after 1 hour. Those with values below the cut-off or a differential of <12 mg/L could safely be discharged. However, caution should be exercised in applying these findings generally as the type of test used and local laboratory norms should determine the absolute values and cut-off to be used.

The healing of the everolimus-eluting Absorb bioabsorbable scaffolds was compared to everolimus-eluting metallic stent in 191 patients with STEMI and found to be non-inferior. The 5-year follow-up of the EXAMINATION study which used Xience V drug-eluting stents (DES) in all comers with STEMI found a 4% reduction in the primary endpoint with a reduction in mortality but no change in the incidence of MI and a trend towards reduced revascularization. Most of the benefit of DES was derived within the first year. The MATRIX Duration study which compared stopping bivalirudin at the conclusion of PCI vs. continuing the infusion for 4 hours in STEMI and NSTEMI patients with high risk characteristics could show no benefit of prolonging the infusion.

The ATLANTIC study had evaluated the benefit of immediate (pre-hospital) versus delayed (in cath lab) ticagrelor administration in patients with STEMI and could not demonstrate an early benefit. Pre-hospital administration was associated with more bleeding. Analysis of the trial results at a later time point showed a slight improvement in ST segment resolution and a reduction in new MI and stent thrombosis in the early treatment group.

The BASKET-PROVE II Trial found no difference in non-CABG major bleeding after PCI between prasugrel 10 mg daily (reduced to 5 mg daily in patients >75 years or <60 kg) and clopidogrel. Bleeding was more frequent in patients with ACS. Bleeding was not reduced in the group which received 5 mg prasugrel.

A series of trials which investigated whether the prognosis of AMI / ACS could be improved by a variety of therapies failed to show any improvement viz. ALBATROSS (immediate MRA inhibition with canrenolate and then spironolactone), ARTS HF (finerenone vs. eplerenone), CIRCUS (cyclosporine immediately before PCI), ELIXA (lixisenatide) and pacing the peri-infarct zone.

3. Antiplatelet therapy

Udell surveyed the effects of prolonged dual antiplatelet therapy (L-DAPT) (now published in the European Heart Journal) finding no increase in total deaths, non-cardiovascular deaths, fatal bleeding or intracranial haemorrhage. While there are no guidelines to assist in deciding
whether to prolong DAPT, the decision should be individualised according to the the assessed risk of future ischaemic events and bleeding risk (need for oral anticoagulation, recent bleeding, recent surgery or prior intracranial haemorrhage).

OPTIDUAL sought to establish whether there was benefit in prolonging dual antiplatelet therapy with aspirin and clopidogrel from 12 to 48 months. Two thirds of the almost 1400 patients underwent an elective PCI. It is regrettable that the trial was terminated early. Although not reaching its combined endpoint of death, MI, stroke and major bleeding, there was a strong trend to reduced ischaemic events in the 48 month group without an observed increase in bleeding (2% of patients in both groups).

The PEGASUS trial compared aspirin with aspirin and ticagrelor initiated 1-3 years after an MI. In a sub-group analysis, though there were variations in their baseline characteristics, the benefit of DAPT was greatest in the group commencing the combined treatment within 30 days of stopping prior DAPT. There was less benefit in the group starting treatment after a gap of 30 days to 1 year and no benefit in those who had stopped DAPT for more than a year.

The DAPT trial reported a higher rate of cancer in those on ticagrelor. However it is reported that the site of neoplasm was inconsistent and numbers were small, suggesting the play of chance.

Heart Failure

In a rapid fire session on prognosis in heart failure, the AHEAD score was presented, drawn from the Czech National Registry of Heart Failure. Considering a wide variety of co-morbidities, simply adding 1 point for each of atrial fibrillation (A), haemoglobin <12 gm/dl in women or <13 gm/dl in men (H), age >70 years (elderly = E), abnormal kidney function (A) and the presence of diabetes (D) accurately correlated with the 5 year prognosis, whether assessed on admission for acute heart failure or at discharge. Those with a zero score had an excellent prognosis, whereas those with higher scores would deserve more intensive observation and treatment.

1. Biomarkers in heart failure

In a sub-study of the RELAX-HF trial it was demonstrated that 10% patients presenting with acute heart failure had normal hs-troponin T <14 ng/L. Their 180 day mortality was zero even though their BNP levels were >3000, suggesting that such patients may not require hospital admission.

The concentration of micro-RNA miR-22-3p is inversely related to the occurrence of worsening heart failure independent of the recognised biomarkers CRP, hs-TNT and BNP. Elevated serum ST2 (a biomarker associated with interkeukin 33 signaling when membrane bound) is related to HF mortality. Fibroblast growth factor 23 which regulates phosphate metabolism was shown to be predictive of mortality in HeF-REF but not in HeF-PEF. Prediction was improved by combining FGF23 with BNP.
The obesity paradox, which suggests that obese patients with heart failure have an improved survival, was studied in ambulatory diabetic and non-diabetic patients with heart failure. Patients with diabetes were more obese, were more often male, had more hypertension and were in in worse NYHA class and more chronic kidney injury. Survival was worse amongst the diabetes group. Obese non-diabetic patients had better survival whereas those with the lowest weight in this group did worse. The effect of terminal cachexia should be considered. However, survival was best amongst the very small group of diabetes patients with low body weight.

Hospital admission rate (80% vs 64%) and mortality (30% vs. 16%) were higher over 2 years in depressed patients with HF. However depression could not be shown to be an independent predictor of outcome.

The Swedish Heart Failure Registry found that kidney failure in association with heart failure exerts an effect on outcome independent of age, NYHA class, haemoglobin and diabetes.

The apnoea-hypopnoea index (AHI) is commonly used as a measure of sleep disordered breathing but turns out to be a weak predictor of prognosis in heart failure patients with reduced ejection fraction (HeREF). It was shown that the absolute time that oxygen saturation fell below 90% is a more robust measure with the risk of death rising 16% for every additional hour/night that the “hypoxaemic burden” increases.

The SERVE-HF trial evaluated adaptive servoventilation in 1 300 patients with chronic systolic heart failure (NYHA Class III/IV) with predominant central sleep apnoea. 60% of patients used the intervention for an average of 3-4 hours/night. Treated patients had a 28% increase in all-cause deaths and a 34% increase in CV deaths without improvement in quality of life and a greater reduction in the 6 minute walk test distance.

The OPTILINK study failed to demonstrate a beneficial effect on outcome using remote monitoring of pulmonary water to modify treatment in ICD or CRT-D patients with recently worsening heart failure.

The TECOS trial of sitagliptin was examined for evidence of the increased risk of heart failure previously detected with saxagliptin (significant) and alogliptin (borderline effect). None was found. However patients with diabetes and prior heart failure remain at high risk of recurrence.

Digoxin’s use was subjected to scrutiny in a meta-analysis of 41 trials (7 of which were randomised) including a total of 100 000 patients. In the unadjusted observational studies there was a 76% increase in mortality, whereas in the 7 randomised trials, the effect on mortality was neutral. Hospitalisation for heart failure was slightly reduced in the digoxin group. The authors concluded the digoxin is safe while at the same time recommending that a low dose be favoured.

Persistent or worsening dyssynchrony over a 6 month period of observation in patients with a narrow QRS complex predicted a higher risk of worsening heart failure.
An Australian group investigated the benefit of a comprehensive cardiovascular nurse led, home-based education and management programme encompassing ACS, heart failure and atrial fibrillation. Their interesting finding was that the intervention was effective in high clinical complexity situations but deleterious in those of lower complexity.

Atrial fibrillation

AEGEAN compared an intensive educational programme to promote adherence to and persistence on anticoagulant treatment with usual care and could not demonstrate an improved outcome. Standard of care was associated with a high rate of compliance with treatment.

EAST AF evaluated the use of anti-arrhythmic drug (AAD) therapy for 90 days after AF ablation vs. no AAD. Although early arrhythmias were suppressed, the strategy did not influence outcome.

The 5-year follow-up of the MANTRA-AF trial comparing AAD therapy to AF ablation was reported. Follow-up was 80% in the AAD group and 86% with AF ablation. The results were in favour of AF ablation with more being asymptomatic (94 vs. 85%), having a lower AF burden and being in sinus rhythm (86 vs. 71%). AAD’s were being used in almost ½ of the patients who had ablation.

Isolation of the left atrial appendage in addition to standard AF ablation reduced the risk of recurrent AF but was associated with thrombus development and stroke in a few patients. This technique is not recommended.

Pacing

The LEADLESS II study\(^9\) reported on the Nanostim LP leadless pacemaker implanted in 526 patients with a 96% success rate and freedom from device-related serious adverse effects in 93%. The unit provides rate-responsive VVI pacing. It was projected to be applicable in approximately 15% of patients needing pacing. Vascular complications and pericardial tamponade were noted as potential hazards. The generator life of these pacemakers is estimated at 15 years.

The frequency of sudden cardiac death was identical for CRT-D and CRT-P patients.

The 12-month mortality after pacemaker lead extraction is 6.7%. Fully 20% of patients undergoing lead extraction have not required re-implantation.

Athletes’ Heart

Whereas the T wave inversion in hypertrophic cardiomyopathy occurs in the lateral chest leads, the most common findings in athletes’ heart are T wave inversion in V1-V4 (71%), with J point elevation (83%) and ST segment elevation (80%) in the same leads. This T-wave inversion is encountered in 1-4% of white athletes and 25% of black athletes. The changes are more pronounced in endurance athletes and less pronounced in women and children.
Individuals suspected of athletes’ heart should be intensively investigated to exclude HCM and arrhythmogenic right ventricular dysplasia, amongst other forms of cardiomyopathy.

Valvular Heart Disease

1. Bicuspid aortic valve

Bicuspid aortic valve (BAV) disease is congenital and is associated with a variety of conditions. It is found in 1-2% of patients with a 2:1 male to female predominance. There is no uniform phenotype. 80% of cases are due to fusion of the leaflets between the left and right coronary arteries. A raphe is not inevitably present although it may be difficult to identify. BAV associates with large aortic sinuses, an increase in aortic stiffness, a dilated ascending aorta and a higher rate of aortic dissection. By determining the direction of flow, the particular deformity of the valve may influence the form which aortic dilation takes. The increase in aortic size is influenced by family history, gender, patient age, and body size. BAV is more frequently encountered in aortic coarctation (50%), Turner’s syndrome (30%) and supravalvular aortic stenosis (30%). Both the valvular disease and the aortic dilation have a variable rate of progression. Follow-up studies have demonstrated that the aortic root size did not progress in 43% patients. Degeneration of the BAV constitutes 50% of cases requiring aortic valve replacement (60% under age 70 years and 40% above 70 years). The risk of aortic dissection is low. Eventually 10% of cases may require replacement of the ascending aorta. Elective surgery is recommended if the aorta exceeds 5.5 cm in diameter or is 4.5 cm or greater at the time of other cardiac surgery.

It is difficult to establish the natural history of BAV. Aortic regurgitation (AR) and infective endocarditis occur more frequently in males, who also undergo aortic valve replacement more commonly. Severe AR and a higher NYHA Class predict a worse prognosis in women. The results aortic valve replacement for BAV are worse than that of other pathologies.

2. Aortic stenosis

Otto discussed the role of echocardiography in diagnosing the severity of aortic stenosis (AS) in asymptomatic patients. The aortic velocity predicts the onset of symptoms better than the aortic valve area. In low flow situations the stroke volume index should be calculated. Dobutamine stress echo also may be used in that setting; an aortic velocity >4 m/sec indicates severe stenosis. A less usual presentation of severe AS is that with severe left ventricular hypertrophy and a low stroke volume.

Iung addressed the question of whether it is appropriate to intervene in the asymptomatic patient. Current studies have found that the risk of sudden death in severe AS is <1 in 100 per annum. However there are difficulties in watchful waiting in severe AS, particularly in the elderly who inter alia may require urgent non-cardiac surgery at times which will then constitute a higher, potentially avoidable risk. Extensive valvular calcification and high aortic velocity present a higher degree of risk. Symptoms may be unmasked by exercise testing in 37% of “asymptomatic” patients. An inadequate rise in systolic blood pressure during exercise (<20 mm Hg) is also significant. If exercise echocardiography is employed an increase in the gradient >18 mm Hg is significant. BNP may also be useful is determining the severity
of the problem. However, there is (as yet) no proof that survival is improved by intervention in the truly asymptomatic patient.

Regarding alternative forms of imaging in AS, valvular calcium scoring on CT is independently predictive of both the severity of stenosis and prognosis. Critical levels of calcium score are 1300 in women and 2000 in men. Imaging with Na-FI PET can detect the presence of active calcification which has also been related to prognosis. The demonstration of fibrosis on CMR is related to LVH in the ECG; it predicts a poorer prognosis and response to surgery. Biomarkers such as hs-troponin T also relate to the outcome in AS.

Given the low risk of stroke in recent studies and the reduction in the frequency of significant aortic regurgitation (eg. NOTION valve), transcutaneous aortic valve replacement (TAVR) may soon become an alternative strategy for intermediate risk patients with severe AS. One study reported success with the performance of TAVR under local anaesthesia with only 07.% requiring conversion to general anaesthetic and 37% needing deep sedation. In another study, it was found that subclavian artery access produced the results when femoral access for TAVR could not be used.

3. Tricuspid regurgitation

A Cleveland Clinic symposium discussed tricuspid regurgitation (TR). It was emphasised that the observed frequency varies in accordance with the population studied. However there is a high frequency of TR in heart failure which in turn exerts profound effects on morbidity and mortality. TR is more frequently observed in HeF-PEF. Surgical morbidity and mortality remain high, in the region of 20%. Appreciating that the annular dilatation that drives the TR is the result of expansion around the commissure between the anterior and posterior leaflets as well as the posterior leaflet itself, a percutaneous device is being pioneered which allows the placement of a pledgeted stitch from the atrial surface of the anterior leaflet to the posterior aspect of the posterior leaflet under transoesophageal echo guidance. By drawing this stitch in, the tricuspid valve effectively becomes a bicuspid valve. So far only 9 cases have been attempted, 8 successfully with disappearance of the TR after the procedure.

**Infective endocarditis**

The risk of infective endocarditis (IE) associated dental surgery is reduced from 1 in 500 000 cases without to around 1 in 150 000 with antibiotic prophylaxis. This understanding has led to a downscaling of the guideline recommendations, confining antibiotic prophylaxis to the highest risk patients undergoing the highest risk procedures. As the risk of tooth brushing approximates that of dental surgery, meticulous oral and cutaneous hygiene is recommended.

The new guidelines place strong emphasis on the performance of transesophageal echocardiography (TEE) in the diagnosis of IE, particularly in the presence of a valve prosthesis. TEE should be repeated in 5-7 days if there is continuing uncertainty about the diagnosis. Additional information may be gained from CT, MRI and FDP PET scanning. The stroke risk in IE is highest in the first week after initiating treatment.