Journals on the move: launch of the ESC Journals App

We have all been witnessing the steep upward trend in mobile device usage and their increasing sophistication which will no doubt continue. We used to use our mobile phones to make calls and possibly to send a text message, but now we check our emails, reserve cinema tickets, and, of course, read the latest journal articles via our smartphones and tablets.

At Oxford University Press, we launched mobile optimized sites for the ESC Journals that we publish, over a year ago—providing readers with an enhanced experience when viewing journal content on their smartphones. In 2011, the European Heart Journal received 146,000 visits from readers using mobile devices, more than triple the usage of 2010. Almost 80% of these visits were through either an iPhone or iPad. We have now gone one step further in order to cater to these readers and released an ESC Journal App for both the iPad and iPhone, through which users can stay up to date with the latest articles, regardless of whether they are online or not.

The App provides an excellent user experience for those readers wanting to read the journals on their iPads or iPhones. Articles are easy to read and it is easy to navigate through an issue. Users will find the App’s functionality very intuitive, and where appropriate, users can link though to browsers in order to access further information such as references and wider search options. The App has a range of functionalities; the key ones are:

- Download articles in HTML and PDF
- Save articles to favourites
- Search issue and article
- Easy navigation within and between articles
- Figures can be expanded to full screen and further expanded using finger zoom
- Share figures and tables via email
- Fully linked articles—references can be accessed via the in-app browser

The App is free to download, and for a promotional period, all content through the App is freely available to those with the App.

We will continue to upgrade the App as new functionalities develop. European Heart Journal, Cardiovascular Research, European Journal of Heart Failure, European Heart Journal – Cardiovascular Imaging, and EP – Europace are available through the ESC Journal App.

Figure 1 App view X-ray image. Figures can be expanded to fit the full screen with further finger expansion.

Julia Jeans
Antiplatelet therapy: to tailor or not to tailor?

This hot topic was debated at the Cardiovascular Research Technologies (CRT) 2012 conference in February

Pro: We should tailor antiplatelet therapy based on platelet function testing and genotyping.

Known for being outspoken against routine platelet function and genetic testing, Angiolillo put his personal views aside for the purposes of this debate.

Nobody can argue about the prognostic implications of the presence of high platelet reactivity (HPR). High platelet reactivity or the presence of poor clopidogrel metabolism, based on an individual’s genetic background, is associated with worse outcomes. This is in line with the fact that platelets play a key role in atherothrombotic complications.

Strategies that enhance platelet inhibition in patients with HPR (e.g. acute coronary syndromes) are associated with improved clinical outcomes. This was demonstrated in two major clinical trials—TRITON-TIMI 38 (prasugrel) and PLATO (ticagrelor)—which provide indirect evidence that reducing platelet reactivity can be associated with improved clinical outcomes.

These two trials also showed that patients treated with clopidogrel may have good outcomes and that patients treated with prasugrel and ticagrelor tend to bleed more. Overall, this suggests that antiplatelet therapy can be tailored to provide treatment options associated with less ischaemic events as well as less bleeding.

GRAVITAS is the most important trial providing direct evidence on whether randomizing patients to high-dose or standard-dose clopidogrel according to their levels of platelet reactivity has an impact on clinical outcomes. The trial did not meet its primary endpoint [cumulative incidence of cardiovascular (CV) death, non-fatal myocardial infarction, or stent thrombosis], but the low overall event rate (2.3%) suggests that patients were at such low risk there was little room for improvement using a tailored treatment strategy. In addition, it is known that the treatment strategy that was tested (150 mg clopidogrel) does not achieve sufficient platelet inhibition to intensify antiplatelet therapy.

TRIGGER-PCI was interrupted prematurely due to futility (clinical events were not occurring). Prasugrel improved platelet inhibition but without any impact on clinical outcomes because of a very low-risk patient population.

The take-home message from these earlier trials is that if we are going to consider a strategy of tailored therapy in patients with a low risk of events (e.g. stable or elective patients), clopidogrel is probably a good choice.

However, there is definitely room for improvement in the high-risk acute coronary syndrome patients for whom we still do not have evidence from large-scale prospective randomized trials that tailoring treatment will be of benefit. But, we do have some indirect evidence from the larger PLATO and TRITON-TIMI 38 trials. The ARCTIC trial will provide important insights into this topic.

Con: There is no role for platelet function and genomic testing with the new antiplatelet agents.

Individualizing antiplatelet therapy should ideally be based on a biomarker—platelet reactivity or a genotype test—that precisely measures platelet responsiveness, accurately characterizes low- and high-risk patients, and reliably guides treatment decisions to optimize outcomes in a cost-effective manner. Unfortunately, the quest for such a marker remains elusive as none of the currently available platelet function or genetic tests exhibit these desirable attributes.

While there is good evidence that the pharmacokinetic and pharmacodynamic effects of clopidogrel are modulated by the genotype, the evidence regarding clinical outcomes is somewhat mixed. The outcome most strongly (hazard ratio of 3–4) associated with CYP2C19 loss-of-function genotype is stent thrombosis, a rare but potentially life-threatening event. However, the key question remains whether this statistical association is clinically relevant. Typically, stronger associations (hazard ratios exceeding at least 10 and ideally up to 100) are required to have a clinically meaningful impact on
individualized treatment decisions. Given the rare occurrence of stent thrombosis, the positive predictive value of genotype is only 3–4%. Finally, a randomized controlled trial (RCT) to definitively address the role of genotype is unlikely to be sponsored, given the prohibitive sample size requirement of 20 000–30 000 patients.

With regard to platelet reactivity, while one can argue that it is closer to the final phenotype (CV outcomes) and takes into account the environmental and genetic factors influencing platelet function, testing is limited by biological and methodological variability and lack of standardized criterion for defining HPR. In addition, the prognostic performance is rather modest, outcome- and indication-specific, and dependent on time of assessment post-stenting, thereby requiring repeat testing and potentially rendering the results difficult to interpret during acute periods. Finally, the question remains whether it is a risk marker or a modifiable risk factor, the latter being more important to clinicians. Three large studies have shown that HPR was not modifiable by either increasing the maintenance dose of clopidogrel (GRAVITAS, RECLOSE 2 ACS) or using alternative antiplatelet agents like prasugrel (TRIGGER-PCI) or ticlopidine (RECLOSE 2 ACS).

Guidelines from the European Society of Cardiology and American College of Cardiology/American Heart Association give platelet function and genetic testing a Class IIB (optional), Level C (based on consensus opinion) recommendation. Given the paucity of ischaemic events, I doubt that the question will ever be adjudicated directly via RCTs. Thus, based on the totality of evidence, personalized antiplatelet therapy remains an elusive dream rather than an imminent reality.

Jennifer Taylor, MPhil

The latest science and controversies in cardiovascular nursing

J. Taylor reports on the 12th Annual Spring Meeting

Around 200 abstracts were presented by nurses and allied professionals at the 12th Annual Spring Meeting on Cardiovascular Nursing, held 16–17 March in Copenhagen, Denmark. Topics included arrhythmias, heart failure, prevention, acute care, myocardial infarction, and implantable devices.

The meeting was organized jointly by the ESC Council on Cardiovascular Nursing and Allied Professions (CCNAP) and the Professional Society for Cardiovascular and Thorax Surgery Nurses, based in Denmark.

New scientific findings were presented, showing that poor dental hygiene behaviours in patients with congenital heart disease are increasing their risk of endocarditis. One study collected lifestyle information from more than 400 adolescents with congenital heart disease aged 14–19 years and controls matched for age and gender. It revealed that adolescents with congenital heart disease floss, brush, and visit the dentist less than their peers, but have healthier behaviours when it comes to alcohol, cigarettes, and illicit drugs.

A second study collected the same lifestyle information from 59 adults aged 16–48 years (average age 24 years) with single-ventricle physiology who were matched on age and gender to 172 healthy controls. These patients also had poorer dental hygiene practices, although the finding did not reach statistical significance. A significantly lower proportion of binge drinking was found in patients compared with controls (24 vs. 41%) and patients exercised significantly less than controls (61 vs. 76%).

‘Systematic structured patient education on the importance of dental hygiene is critical for preventing endocarditis in patients with congenital heart disease’, says the supervisor of both studies Professor Philip Moons (Belgium and Denmark).

A study from the Netherlands investigated the impact of depression on mortality during a 7-year follow-up in patients treated with percutaneous coronary intervention (PCI). Depression was assessed in 1234 PCI patients aged 26–90 years (average age 62) from the Rapamycin-Eluting Stent Evaluated At Rotterdam
Cardiology Hospital (RESEARCH) registry 6 months after having a stent implanted. The endpoint was all-cause mortality.

The prevalence of depression was 26.3%. The incidence of all-cause mortality in depressed patients was 23.5 vs. 12.2% in non-depressed patients. After 7 years of follow-up, depressed patients were 1.5 times more likely to have died than non-depressed patients. The findings were independent of age, gender, clinical characteristics, anxiety, and the distressed (Type D) personality.

‘Doctors and nurses have traditionally focussed on medical factors like diabetes or family history of cardiovascular disease when assessing PCI patients’ risk of death, but that’s not the whole picture’, says lead author Nikki Damen. ‘Psychological factors do matter as well, in combination with the medical factors’.

Research from Italy revealed that liking art (music, painting, theatre) improves recovery in stroke survivors. Patients interested in art had better general health, found it easier to walk, and had more energy. They were also happier, less anxious or depressed, and felt calmer. They had better memory and were superior communicators (speaking with other people, understanding what people said, naming people and objects correctly).

The findings were independent of the gravity of stroke. Lead author Dr Ercole Vellone says: ‘The results suggest that art may make long term changes to the brain which help it recover when things go wrong’.

Sessions were also held on hot topics in cardiovascular nursing such as the growing problem of how to manage complex cardiovascular problems in older patients with dementia. Leadership and management in difficult times was the focus of another session, which investigated how to get nurse–patient ratios right and how to motivate and retain experienced nurses.

The meeting attracted around 600 nurses, allied professionals, and technicians from Europe and beyond. Next year’s meeting will be held in Glasgow, Scotland.

Jennifer Taylor, MPhil

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The new European Journal of Preventive Cardiology

A catchier title is expected to attract an increasing number and quality of submissions

The European Journal of Cardiovascular Disease Prevention and Rehabilitation (EJ CPR) became the European Journal of Preventive Cardiology (EJPC) in January 2012.

It was felt by many, including Editor-in-chief Professor Diederick E. Grobbee (Utrecht, The Netherlands), that the journal’s visibility and profile were hampered by its long, complex name. ‘It was too long and not very catchy’, says Grobbee.

‘You might even question whether the name was internally consistent’, he adds. ‘One could argue that rehabilitation is a component of prevention’.

The journal’s previous title makes historical sense. The journal was founded when two European Society of Cardiology (ESC) working groups—Public Health and Epidemiology, and Exercise Physiology and Cardiac Rehabilitation—merged to form the European Association for Cardiovascular Prevention and Rehabilitation (EACPR). Both groups wanted to maintain their identity within the new Association. But Grobbee says: ‘I don’t think that the previous name was chosen with a keen understanding of what suits the market or fits in with the general array of journals in this field’.

European Journal of Preventive Cardiology will continue to be the official journal of the EACPR and the scope, which is broad, will stay the same. It remains an important part of the family of ESC journals and receives the largest transfer of submissions from
The German Centre for Cardiovascular Research

A new model of collaborative science to improve a nation’s research

Germany is one of Europe’s leading nations for cardiovascular research and has hosted internationally competitive basic science and clinical cardiology for many decades. Competition between leading German universities and hierarchy within each institution has resulted in failure to foster a spirit of national collaboration—the whole is less than the sum of its parts. Specific weaknesses include lack of a forum for common ideas, duplication of resources with resulting inefficiency and expense, poorly coordinated interaction with industry, under-developed systems for education and mentoring of research trainees, and under-representation of female scientists. In a bold initiative, the German Federal Government has supported the development of a German Centre for Cardiovascular Research (GCCR) by providing up to €200 million competitively tendered funding over a 5-year period to support designated centres committed to address these deficits and to encourage collaboration between the Universities and other health-care institutions. This initiative will stimulate trans-national cardiovascular science from bench to bedside and is likely to improve cardiovascular health.

At an early stage, it was decided that project applications should be overseen by an expert international review panel with remit to provide independent scrutiny of (i) proposed research programmes, (ii) ability of applicant institutions to deliver collaborative translational research goals and comply with the aims of the overall proposal, and (iii) structure, governance, and leadership. Experience gathered in the process of institutional research evaluation, politics of infrastructural change during foundation of the GCCR, and details of the initiative and selection process are of relevance to other nations and health-care systems and are described here by the international review panel.

Research funding in Germany

In Germany, health research is funded from a variety of sources including the Federal Government via the Federal Ministry of Education and Research (BMBF), the Federal States (‘Laender’), the German Research Foundation (DFG), and foundations within the Association of German Academic Foundations, all linked with
### Partner institutions and locations

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**Figure 1**
industry’s efforts to promote German science and research. Federal financial support is delivered via targeted, short- to medium-term funding for individual projects and programmes and strategic medium- to long-term funding of individual institutions. Thus, the Centres of the Hermann von Helmholtz Association (HGF), the Max Planck Society (MPG), and the Fraunhofer-Society (FhG) and institutions of the Leibniz Association receive support from the Federal Ministry of Education and Research and State government. In contrast, individual universities receive institutional funding via the State government alone.

This structure is unwieldy and impractical when translation of basic scientific research into clinical practice requires coordinated action and co-operation of University Hospitals and non-University research institutions whose total infrastructure, capacity, and proposed study numbers exceed those within a single centre. It also fails to embrace large clinical centres where patients are concentrated but research facilities lacking.

The proposal of new centres for health research

The German Federal Government has prioritized common disorders such as cancer, cardiovascular, metabolic, infectious, pulmonary, and neurodegenerative diseases within its ‘Health Research Framework Programme’ by developing six German Centres of Health Research, defined by networks of expertise between disciplines and institutions to ensure faster more effective research translation. Premier research groups from University Hospitals and non-University research institutions cooperate closely within these Centres to establish groundbreaking new knowledge as quickly as possible and to develop novel therapeutic strategies with emphasis on individualized (‘tailored’) therapy, preventative measures, health-care systems research, partnership with pharmaceutical and medical device industries, and globally networked research efforts.

The German Centre for Cardiovascular Research (GCCR)

Cardiovascular disease is the leading cause of death in Germany, accounting for 43% of overall mortality (363,785 cases) in 2008 and an overall health-care cost of €37 billion per annum. Given the medical and fiscal impact of cardiovascular disease, the Federal Ministry of Education and Research apportioned a budget of up to €40 million per year to the German Centre for Cardiovascular Research.

Selection procedure

In May 2010, the Federal Ministry of Education and Research announced a public call for initiation of four new German Centres of Health Research (including the GCCR) to complement two existing Research Centres for Neurodegenerative Disease and Diabetes Mellitus. Detailed preliminary submissions were received from 23 candidate sites and evaluated in a transparent three-stage process based upon scientific excellence.
infrastructural components, and quality of the proposed science. Initial ranking by the international review panel identified the 11 most promising sites who were invited to present their proposal as a team at a second-stage meeting. From these, seven outstanding partner sites (representing 24 institutions) (Figure 1) were selected to formulate and present a national collaborative proposal to the review panel who provided subsequent recommendations for delivery, administration, and governance at a final meeting.

Mission
This innovative programme fostered by the German Federal Ministry of Education and Research offers a model for national collaborative research which could be successfully adopted in other countries worldwide. The initiative is an essential development for Germany to improve overall public health, exploit commercial opportunities, coordinate scientific personnel and infrastructure, and translate basic science into clinical and commercial applications in prevention, diagnosis, and treatment, while maintaining Germany’s pre-eminence in the competitive international environment.

The GCCR intends to achieve these aims without threatening the autonomy of single institutions, thereby forming a true transnational centre of excellence for cardiovascular research. Close networking, collaborative projects, and long-term equal partnerships between different institutions will be established and accompanied by enhancing existing research structures to accelerate research findings into clinical practice. Generic resources (e.g. large registries, national bio-banks, specialized equipment, and facilities) will be readily available for each partner site allowing development of a cooperative identity. As a consequence, the centre should produce a total output which significantly exceeds the sum of the partners’ individual contributions in a cost-effective programme.

Over the next 5 years, the GCCR will focus on six joint research programmes, each involving at least two partner sites in close collaboration: Vascular disease, Hereditary and Inflammatory Cardiomyopathies, Heart Failure, Arrhythmias, Prevention and Imaging (Figure 2). Sample research goals include unravelling the genetic and epigenetic basis of cardiovascular disease, identification and validation of new biomarkers, development of risk-prediction algorithms and imaging standards for clinical studies, iPS-mediated disease modelling, innovative therapies (including miRNAs, RNA-based correction of genetic defects, new anti-platelet agents, gene therapy and stem cell-based tissue engineering), refined atrial fibrillation ablation, and innovative surgical strategies. Cooperative initiatives involving all partner sites will offer opportunity for collaboration with non-partner institutions (creating the platform for initiation of large national clinical trials), a national experimental development pipeline for accelerated translation of experimental results into clinical practice, and a training programme for the next generation of cardiovascular clinical scientists. In due course, the GCCR will become an internationally visible ‘brand’ for cardiovascular research in Germany, functioning as a nucleus for international collaboration, promoting the ongoing training of young scientists (including those recruited from abroad) and an attractive partner for industry.

A Steering Group involving all partners will coordinate governance and conduct of joint research activities, division of responsibilities, and resources across partner sites (and their sublocations) on the basis of jointly defined priorities. This Steering Group will refer to a high-level international Scientific Advisory Board who will support research activities of the GCCR. An external expert international review panel will evaluate the programme at regular intervals for achievement of scientific excellence and progress against originally agreed strategic objectives.

Perspective and conclusion
Strategic collaboration of leading cardiovascular researchers will strengthen the international position of German science in the short and long term, and attract the most promising young researchers from Germany and abroad. A key challenge will be to develop new working relationships among established scientists who have been in competition with each other (as individuals and institutions) for large parts of their career. The selected GCCR partners have made great progress within 1 year of the programme’s conception, and a refreshing sense of team work and genuine cooperation is already apparent.

This new mode of collaborative working with extensive financial and administrative support from the Federal Ministry of Education and Research promises substantial benefits for the conduct of cardiovascular science in Germany and its translation into clinical practice. We commend it as a model for other nations to emulate.

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