translational work is around embedding this idea into clinical prevention services and it has influenced the approach to research and treatment.

The NCCPO collaborates with national initiatives such as Public Health England's Health Checks Programme, for which Deanfield sits on the Academic Board. 'The problem with undertaking health checks in people who are relatively young,' says Deanfield, 'is that illness may seem to be a long way in the future. It is hard therefore to convince people to do something about their lifestyle.' A big ambition is to combine health checks and the JBS3 approach and early evidence suggests that this can have a substantial impact.

Third is an emphasis on dealing with risk factors after clinical events such as acute coronary syndrome. The centre has a big programme for secondary prevention, working together with primary care to promote evidence based practices. In addition, colleagues have reached out internationally to create an exciting consortium of studies (GENIUS) with genetic and phenotype measures to explore causal pathways (R Patel). Increasingly, collection of robust, longitudinal, outcome data at scale underpins clinical and academic CV progress. 'This is the key to quality improvement, long term safety and efficacy surveillance as well as measurement of value,' says Deanfield.

The NCCPO, at the BHC, hosts the National Institute for Cardiovascular Outcomes Research (NICOR), which consists of NHS England's major national audits of CV diseases and interventions, including heart attacks, coronary interventions, heart failure, cardiac surgery, congenital heart disease, and rhythm management. NICOR developed from initiatives of specialist medical societies, which exploit the unique NHS number each patient is allocated in the UK to allow and enable long-term individual follow-up. Deanfield helped to pull together these registries into a single NICOR structure, which now holds more than 4 million electronic health records on cardiac patients. Being hosted in an NHS environment, and part of a major university (UCL), provides NICOR with a unique opportunity, not only for quality assurance, but also the conduct of exciting research to drive quality improvement. Furthermore, the development of national registries for new treatments within NICOR promises to ensure rapid evaluation and introduction into practice for the benefit of patients. This work has been undertaken in partnership with the NHS and the National Institute for Health and Care Excellence (NICE). The large prospective datasets in NICOR also provide the opportunity to run randomized clinical trials within registries.

This approach has been pioneered by the Swedish national programme, SWEDEHEART, who are collaborating with NICOR at the BHC. Deanfield says: 'The use of registries to recruit and follow patients in a formal clinical trial is very exciting and will allow novel treatments to be evaluated faster at a fraction of the cost of conventional trial designs.'

The creation of the very large clinical and academic facility at the BHC is central to the ambition for 'maintenance of health' and not just 'treatment of disease'. The CV programme is closely linked to other exciting national health initiatives which are part of Barts/QMUL/UCL, including Genomics England (M Caulfield) and the Farr Institute of Health Informatics Research (H Hemingway). 'The BHC is all about bringing different aspects of CV care together, including world class treatment and prevention. Our approach is a real change in culture and is built on managing the whole pathway of CV disease, not only within a Centre of Excellence, but in partnership with our broader medical community,' concludes Deanfield.

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Changing sides

Vincent Mooser MD moved from academia to industry then returned to academia

Physician scientist Vincent Mooser MD, is Head of the Laboratories Department at the University Hospital of Lausanne (CHUV), Switzerland. His research spans institutions on three continents and includes clinical pharmacology, experimental pharmacology, genetics, hypertension, and Lipidology. He left academic life for 10 years in 2002 to join pharmaceutical giant GlaxoSmithKline (GSK), in Philadelphia, USA. During this time, he rose to become vice-president responsible for Genetics in research and development. He returned to CHUV in 2011.

Mooser trained as a doctor and studied internal medicine at the University of Lausanne. He had always been keen to pursue clinical research and his first experience was in the lab of Hans Brunner—known for his work with ACE inhibitors. Mooser spent 2 'exciting' years in Brunner's lab before finding a postdoctoral position in Australia at the University of Melbourne looking at experimental hypertension in rat models. After Australia, he returned to Switzerland and completed his training in internal medicine but his search for knowledge—specifically into the new science of genetics and lipids—would take him away again.

He embarked on a second post-doctorate at UT Southwestern in Dallas, Texas, this time in the lab of the distinguished duo Brown and Goldstein who were jointly awarded the 1985 Nobel Prize in Physiology or Medicine for their discoveries concerning the regulation of cholesterol metabolism. He spent 3 years working in Helen Hobbs lab immersed in genetics and lipids before returning to Lausanne with a research professorship in 1996.

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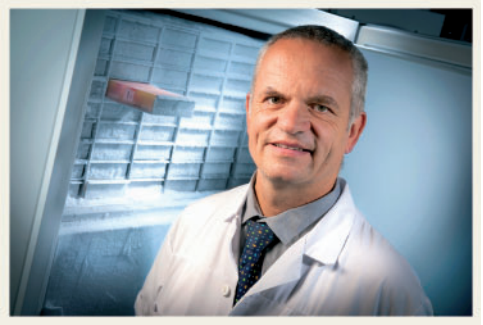
In 2002, the opportunity arose to join GSK as head of the genetics group for cardiovascular diseases (CVDs) based in Philadelphia, USA. Although it was a tempting proposition for a research-focused clinical academic, it was a difficult decision to make. 'I was leaving academia and Switzerland, I had a wife and 3 kids, I was going to a country with a different language and culture, it was the end of my taking care of patients which I really enjoyed, so it was a big risk', he says.

Mooser was recruited to identify genes involved in CVDs and metabolic diseases with a view to developing new drug therapies. His clinical background would prove invaluable in filling the sort of gaps and expertise that was lacking in industry. He set about recruiting geneticists and trying to access the sort of large-scale genetic clinical data which would be readily available in an academic setting, but was absent in industry. When it became difficult to access the data that GSK needed Mooser set up his own 'Framingham' style population-based study with his former colleague Gérard Waeber and his research group in Lausanne. This would be analysed and used extensively and would eventually contribute to over 200 publications.

Mooser was able to bring hands-on clinical research in lipids, hypertension and CVD to GSK and over the next few years he gained footing in the organisation and in 2008 was appointed vice-president in charge of applied genetics worldwide. He says: 'That was a very exciting job because I was in charge of a large genetics group which covered all of GSK's therapeutic areas and spanned the UK, America, Europe and Asia. He remained at the helm until 2011, when he was approached by the University of Lausanne to run the 600-strong lab department in the university hospital.



Moving between the two sectors involves very difficult personal and professional decisions, but Mooser believes the benefits are enormous. 'Industry is driven by success and application and I liked having the goal of finding therapies to treat or prevent diseases. Working with lots of people towards a common goal is a very enriching experience as is being part of a team that addresses the big challenges that industry takes on. One thing that people in academia would tend to underestimate about industry is the amount of expertise and brain-power that resides there but it's necessary given the complicated and enormous challenges of developing a new drug. There is no way you can do that without the brain power of a large group of people working together.

Another thing about industry is that if they don't have expertise internally they go outside and get it. This was wonderful because it meant we could collaborate with outstanding geneticists and groups around the globe. I also liked the fact that once industry has decided to meet particular goals it gets the funding to meet these objectives'.

Medical professionals who join the pharmaceutical industry have much to offer in terms of adding clinical reality to projects. Mooser came to GSK as a fully-formed physician scientist with a broad knowledge of genetics, solid understanding of CVDs, and a strong publication record. He had very useful contacts he could tap into and having trained and worked as a doctor, was able to anchor the process of drug discovery and development into clinical reality that he had first-hand experience of.

Mooser believes that when the two sectors collaborate, they can produce enviable results. He points to the 'COLAUS' study—a joint venture between the University of Lausanne and GSK—which neither side could have completed alone. 'Industry could not have done this sort of study without academia because of the need to access population studies and academia could not have done it without the support of GSK. Industry and academia can be very successful as long as people are very clear what they want to achieve and how they want to achieve it'.

Returning to CHUV in 2011, Mooser discovered that lots of the skills—especially the management skills—he had learned in his ten years with GSK were transferable. He suggests industry takes care to nurture and train its managers to take charge of large groups and organisations and that this approach would benefit physicians who have similar responsibilities. He also returned with a profound understanding of the 'suffering' that goes into each of the steps of drug development and the hard decisions which need to be made at.

The 'so what' question which dominated his working life at GSK has also remained with him. 'Managers were always asking the "so what" question: why are we doing this research? What will be the benefits to the patient? What are the steps we need to meet until people can benefit from this investment? And it was always useful to focus on clinical utility'. In some respects, the two sectors proved to be similar.

Mooser found that although the pharmaceutical industry has the financial power to make things happen, it was still necessary to build a strong case for funding and demonstrate how projects could benefit the company and move drug development along. 'It's estimated that pharmaceutical companies around the world spend around 60 billion dollars on research and development each year, but you need to acknowledge that clinical research is very expensive and you still have to prove yourself to get support'.

Mooser believes that scepticism about working with industry still exists in academia because the goals are different. 'In academia people are primarily paid to work in hospitals and to do research which does not necessarily have the objectives of clinical utility, but industry has to develop drugs which need to be clinically useful and make money'. He suggests that academia would benefit from a better understanding of the reality of drug development and its attendant risks. In a similar vein, it is important for pharmaceutical companies to appreciate fully that they cannot develop drugs without a robust science.

He suggests that new and exciting opportunities for co-operation and collaboration are opening up with new research technologies surrounding genetics and genomics. 'There is more and more evidence that there are some rare mutations in populations and there is a lot that can be learned from these mutations and their impact on humans. Industry doesn't have access to these populations but academia does, so there are opportunities for partnership and for a real paradigm shift as well. Twenty years ago research started from animal

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models but genomics and all these other technologies have opened up the possibility of starting with humans, using animals to engineer the model and then going back to humans with therapies'.

Mooser characterises his decade with GSK as a '10-year sabbatical' but he advises clinicians to think hard before making such a move. Industry, he suggests is much more volatile than academia. But for those who like big and exciting challenges—such as developing new drugs—it can be a wonderful experience.

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Dietary patterns and the secondary prevention of coronary heart disease

A 'Mediterranean' diet is linked to a lower risk of myocardial infarction and strokes in people with coronary heart disease (CHD), but a 'Western' diet is not associated with an increased risk

Evidence from large population studies[1] and two randomized clinical trials [2,3] suggests that a 'Mediterranean dietary pattern' lowers cardiovascular risk. An important question is whether a diet which includes food groups from the 'Mediterranean dietary pattern' would also be associated with improved outcomes when consumed as a part of other varied diets globally. This question was evaluated in 15 482 (98%) patients with stable CHD from 39 countries who participated in the stabilization of atherosclerotic plaque by initiation of darapladib therapy, or 'STABILITY' trial,[4] with results reported in the *European Heart Journal*.[5] At the start of this trial, a simple food frequency questionnaire was used to ask participants how often they ate foods in common groupings during a typical week. From this a 'Mediterranean diet score' (MDS) was calculated from more consumption of whole grains, fruits, vegetables, legumes, fish, modest alcohol, and less meat.

During a median follow-up of 3.7 years' major adverse cardiovascular events occurred in 10.1% of study participants, which included 623 cardiovascular deaths, 698 non-fatal myocardial infarctions, and 267 non-fatal strokes. For the subjects with a MDS $\leq$12, the median score, there was no significant association between the score and adverse cardiovascular events. However, MDSs above this level were associated with a lower risk of major adverse cardiovascular events (hazard ratio 0.93 for each one unit increase, 95% CI 0.90–0.96, $P < 0.0001$), and this association remained after stepwise adjustment for all covariates. Similar associations were observed for cardiovascular death, myocardial infarction, stroke, and all-cause death.

These associations were consistent across diverse geographical regions with widely varying diets. They were also consistent in analysis stratified by country income level and for subjects with more and less education, and categories defined by age, and other clinical risk markers. Of note, MDSs were often higher in non-Mediterranean compared to Mediterranean countries. In a secondary analysis, a simpler healthy diet score based on daily consumption of fruits and vegetables, and weekly consumption of alcohol and fish, was also associated with fewer major cardiovascular events and lower mortality. These observations provide additional support for recommendations in the current European Society of Cardiology secondary prevention guidelines[6] to increase consumption of 'healthy foods', including fruits and vegetables. In the global STABILITY cohort, the majority of patients did not eat fruit and vegetables every day, suggesting many could benefit by increasing consumption of these and possibly other healthy foods.

The STABILITY diet study also evaluated a 'Western diet score' from reported consumption of foods usually considered to be 'unhealthy'; refined grains, sweets and deserts, sugared drinks, and deep fried foods. Somewhat surprisingly there was no association between a higher 'western diet score', or any of the foods included in this score, and either major adverse cardiovascular events or mortality. The method used to assess diet was relatively crude, and the data are observational, so definite conclusions on lack of causality cannot be made. However, the observations are consistent with other studies which also found no clear associations between 'less healthy foods' and cardiovascular risk.

Some recent studies have questioned the evidence to support dietary recommendations to limit salt,[7] saturated fat,[8] and high fat dairy.[9] The STABILITY diet study did not evaluate these questions. Uncertainty regarding dietary advice reflects the difficulty in obtaining reliable unbiased information on causal associations from available nutritional research, which is based predominantly on observational studies and small intervention trials with surrogate outcomes. Large dietary intervention trials which assess clinically important outcomes, such as the PREDIMED trial[2] which confirmed benefit from two 'Mediterranean' dietary interventions, are rare.

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