

Circulation

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European Perspectives in Cardiology



Spotlight: Christina Chrysohoou, MD, PhD, FESC



In Greece, Many Believe That Women Should be Nurses, not Doctors.

Cardiology is a challenging profession, perhaps especially for women in Greece, who may have to overcome prejudice and juggle career and family. Dr Christina Chrysohoou talks to Jennifer Taylor about her life and career to date.

Christina Chrysohoou, MD, PhD, FESC, is a cardiologist at First Cardiology Clinic, Hippokraton General Hospital at the School of Medicine, University of Athens, in Athens, Greece, and is a member of the Hellenic Cardiology Society. Perhaps it is not surprising that she has chosen cardiology as her career path because it follows a deep-seated love of medicine and cardiology in her family, and she is well-known for her work. “I was inspired by my family,” she says. “I come from four generations of doctors.” Her maternal grandfather studied in Paris and was a gynaecologist; her paternal grandfather studied internal medicine in Italy. Her father was a cardiologist, and she describes how her maternal grandfather in particular had a respect for human life. “Many times he offered his services for free,” she says.

Dr Chrysohoou’s decision to pursue cardiology stems from a love of both clinical work—“being close to the patient”—and being able to use the newer developing procedures such as echocardiography, magnetic resonance imaging, and catheterisation. “In cardiology, you have to examine your patients and talk to them every day, whereas in internal medicine, you talk to the patient, but you don’t have the interesting procedures.” She also appreciates how cardiology is more centred on a single system in the body.

She began her studies in 1986 at the age of 18, at Patras University Medical School. Her first job, from 1993 to 1994,

was as a general physician in small villages in Greece, upholding the country’s tradition of graduates doing this type of work for the state for 1 year. Dr Chrysohoou then studied internal medicine for a year, in 1994, at St Anargyroi Oncological Hospital in Athens.

From 1995 to 2000, she pursued her studies in cardiology at First Cardiology Clinic, and began a PhD programme in 2002, during which she looked at echocardiographic evaluation of left ventricular systolic function in patients with coronary heart disease in comparison with apex cardiography.

For the past 4 years, Dr Chrysohoou has specialised in heart failure. This has involved her in treating young patients with beta thalassaemia major (of which there are just 200 in Athens) and using echocardiography for coronary heart disease. “I was really interested in heart failure because the number of patients with heart failure is increasing. Because of secondary prevention and invasive methods, we increase life expectancy, but heart failure is the final stage of disease.”

Outside of her family, her mentors included Steve Singh, MD, with whom she did a postdoctoral fellow-ship from 2004 to 2005 at the cardiology department of the Veterans Affairs Medical Center in Washington, DC, where he is head of the department.

“I liked the way he came close to the patient during the examination, and the way he interpreted the results and came

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Profile of a Young Cardiology Researcher

Eric Morel, PhD, won the poster prize at the Heart Failure Association Research Winter Meeting in Garmisch-Partenkirchen earlier this year. He talks about his work in cardiological research.

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to the final diagnosis,” she says. “He was very calm, and he showed great dignity and respect to patients and students.”

It may have been people like Dr Singh who spurred her on because, as a female cardiologist in Greece, she was in a small minority, with extra hurdles to jump.

“In the medical school, there was some prejudice against women,” she says. “And, some patients believe that men are better doctors and that women should be nurses. This stereotype is particularly entrenched in rural areas of Greece, where women do not have a strong position in the family. Sometimes, the patients call female doctors ‘nurses.’ They cannot accept a woman as a doctor.”

In addition to the stereotypes, lack of convenient child care is a problem that faces women cardiologists. “We are not supported here by the state. We don’t have kindergarten schools near the hospital so we can have our children nearby.” As a result, extended child care has to be paid for, or the grandmother, if she is willing and able, has to fill in the gaps.

“This limits female doctors. I think it’s better for the child not to be an only child, but it’s difficult to have more than 1.” She adds, “An additional problem is that if you work in a university cardiology department, as I do, you are obliged to do some scientific work. We need to work on scientific papers and create scientific projects at home.”

With women having the main responsibility at home in Greece, the fact that the 39-year-old Dr Chrysohoou is married and has a 4-year-old daughter creates considerable time pressures. Every weekday, she wakes up at 6:30 AM and goes to the hospital, returning home at 5 PM. One evening a week, she does a night shift at the hospital, and 1 or 2 afternoons each week, she gives or attends lectures.

“I try to spend the rest of my time between scientific work and family commitments,” she says. It can lead to fatigue, but some respite is provided by holidays and weekends when there is no hospital work. Sometimes she takes a walk and thinks about other things.

Despite these conflicts, Dr Chrysohoou enjoys her work. “I like doing some scientific work because you see fulfillment when someone accepts it for publication or refers to your work.”

She also enjoys the hospital environment, doing clinical examinations, and discussing clinical diagnoses with colleagues. And she takes pride in what she does. “I feel very proud about clinical improvement of our patients, and I try to learn from my mistakes.”

She adds that the work in primary prevention, including rehabilitation, encouraging the Mediterranean diet, and educating people about the effects of passive smoking and the benefits of physical activity, has been an achievement. “I’m proud of our scientific successes. It has given us 70 publications in peer-reviewed journals, and many people have used those publications in their work.”



Hand X-ray of a patient with thalassaemia showing demineralisation. Dr Chrysohoou is troubled by the fact that she cannot do much for these patients.

But, as with any true professional, there is always room for improvement. “I would like to be a better clinical doctor, of course,” she says. “I would like to be able to offer more to patients with heart failure, where sometimes you can’t offer them what you would want to.” She is troubled by the fact that, for patients with beta thalassaemia major (see Figure), “you don’t have much to offer them.”

One of Dr Chrysohoou’s goals is to find a marker—biological, echocardiographical, clinical, or biochemical—for patients with heart failure, that could help prolong their lives. Another goal is to spend more time playing the piano. She has a degree in classical piano from Athens Conservatory, and in high school she played up to 7 hours each day. This has fallen to just a couple of hours per month. “Now, I don’t have much time to play,” she says. Added to that, the building where she lives only permits her to play between 5 and 9 PM, when she is normally playing with her daughter or working.

Jennifer Taylor is a freelance medical journalist.

Viewpoint: Obesity in Europe

The Obesity “Time Bomb” in Europe May Annul Falls in Cardiovascular Disease Mortality

Ian Macdonald, BSc, PhD, joint editor of the *International Journal of Obesity*, believes that the mantra “eat less, exercise more” seems unlikely to stop the American-style obesity that is predicted for Europe. The solution is a new type of clinician, the “obesiologist,” and billions of government money. Dr Macdonald talks to Barry Shurlock, MA, PhD.



Dr Ian Macdonald, professor and director of research, Faculty of Medicine and Health Sciences, University of Nottingham Medical School, Nottingham, United Kingdom, and the joint editor of the *International Journal of Obesity*, believes that the mantra “eat less, exercise more” seems unlikely to stop the American-style obesity that is predicted for Europe. “The messages that need to be delivered to obese patients are clear,” he says, “but to deliver them will probably involve the recognition of new medical specialists and will certainly require a huge investment by governments.”

A metabolic physiologist, Dr Macdonald sketches the scale of the problem. “As a whole, the United States is about 5 to 10 years ahead of Europe, with an overall prevalence of obesity of 25% to 30%, with excesses in ethnic groups such as Hispanic Americans and African Americans, compared to 10% to 15% in Europe.” Wide variations exist, however, in the prevalence of adults who are overweight and obese (defined as a body mass index >30 kg/m²) within Europe (see Figure 1), with low rates in Italy, France, and the Scandinavian countries and higher rates, by almost a factor of 3, in Germany, England, Cyprus, and the Czech Republic. Dr Macdonald points out that in the definition of obesity, clinical judgement is required in the case, for example, of a rugby player, who may be designated obese because of muscle bulk rather than adipose tissue.

“In most countries in Europe,” says Dr Macdonald, “the obesity epidemic is accelerating, though there is evidence that the curve might be flattening out in Sweden, Denmark, and the Netherlands. Eastern European countries are doing poorly because the break up of the Soviet bloc has led to deindustrialisation. He explains, “This means that heavy labour is not being used, and, amongst men especially, there is growing obesity, just like the problems we see with

out-of-work coal miners in northern England.” Dr Macdonald is clear about the reasons for this diversity. “In some countries, such as Italy and France, there is in general a positive attitude towards the way you present yourself and look after yourself. There is a focus on presentation and having a healthy weight. Also, in these countries they still have family-oriented eating, where children learn good habits. This has been lost in other countries, including the United Kingdom.”

However, Dr Macdonald points out that the data for Italy and France are biphasic, and there may be a higher prevalence of obesity in the future, particularly in the rural population and in the elderly. The Scandinavian countries have relatively low levels of obesity because of initiatives to increase physical activity and improve diet. “They are probably more effective than larger countries with similar cultural roots,” he suggests, “because they have relatively small populations.”

Tackling Obesity

Dr Macdonald is upbeat about the measures required to combat obesity. “Simple strategies need to be conveyed to people. Much of it is common sense, though cognitive behavioural

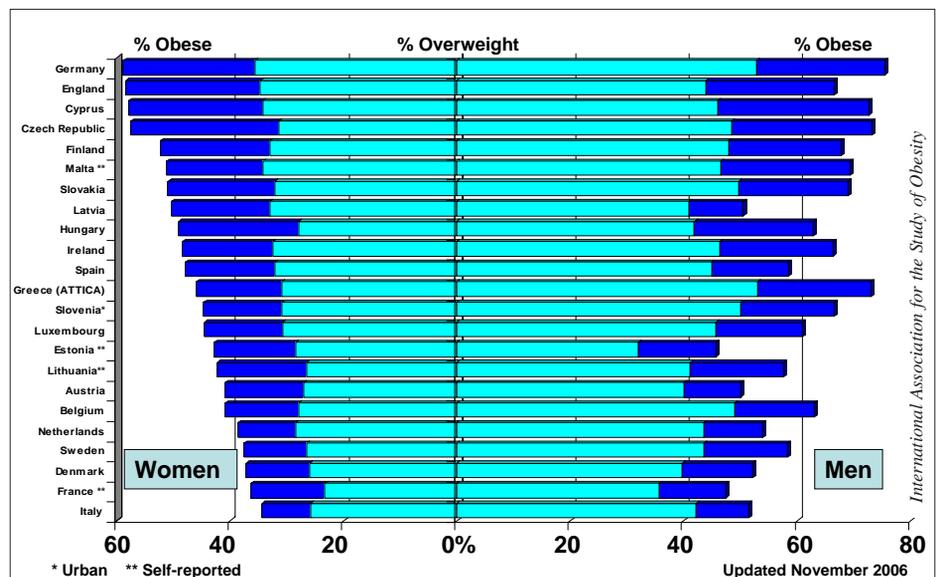


Figure 1. Percentage of adults who are overweight in various European countries.

therapy is also effective. And although 35% to 60% of European women and 50% to 75% of European men are overweight and obese," he continues, "the rest are not, and that tells us that it can be done. Also, the experience of the Finns in the North Karelia Project shows what can be achieved, that cardiovascular disease (CVD) rates can be reduced dramatically—and, despite the severe climate, they are continuing to increase their physical activity."

The upshot of much scientific research is that causes of obesity are straightforward, according to Dr Macdonald. Obesity is caused by eating too much and exercising too little. He comments, "It has to be that simple, because the laws of thermodynamics must apply. So, if 'energy in' is greater than 'energy out,' the energy stored will increase. The reality is that it is easier to overconsume high-fat foods, which are not easily detected by the appetite feedback mechanisms. People have obtained the habit of wanting to feel full. Most people in Europe have never experienced starvation. To prevent overeating, people need to be more aware of what they are consuming."

Metabolic Considerations

The Physical Activity Taskforce of the International Association for the Study of Obesity (IASO; see table) estimates that a physical activity level (defined as the total energy expenditure divided by the basal metabolic rate) of 1.65 to 1.75 is required to avoid obesity, compared with the 1.55 achieved with 30 minutes of daily brisk walking, 1.40 for an office worker, and the 1.27 absolute minimum associated with sleeping, washing, dressing, and standing upright.

Dr Macdonald considers current thinking on the physiology of adipose tissue. "It is metabolically very active, secreting large amounts of cytokines, inflammatory mediators and the like, that are released into the circulation and affect insulin sensitivity. Adipose tissue is more like an organ than a tissue and increases the risk of CVD, especially when the adipose tissue is within the abdomen—central adiposity," he says. "The reasons are not known, but we speculate that it is more metabolically active than subcutaneous fat and releases fatty acids, which proceed via the portal vein to the liver, where they increase insulin resistance, leading to increased very-low-density lipid synthesis, though I must emphasise that this is very speculative."

Cardiovascular Implications

Commenting on the effects of the obesity epidemic in Europe on the prevalence of CVD, Dr Macdonald says, "Obesity will have an effect on CVD. Where we currently see rates of myocardial infarction and atherosclerosis-related disease going down, I predict this fall will bottom out and will then start to go up again." He continues, "This is the real worry for cardiologists. We ought to start to be seeing the effects of growing obesity, which has been apparent for 10 to 15 years. But it may be that the beneficial effects of statins and reduced rates of smoking are offsetting the effects,



Cristina Pedrazzini/SPL

The causes of obesity are straightforward, Dr Macdonald believes—eating too much and exercising too little. The laws of thermodynamics must apply.

though life assurance statistics are not encouraging."

Dr Macdonald believes, perhaps controversially, that for the seriously obese, a slight heart attack could be good news. "It's not too late to take effective action after the first myocardial infarction. For some of these patients, surgical measures such as gastric banding or bypass may be indicated. Losing as little as 10% excess weight can significantly reduce lipid levels and normalise a variety of risk factors. If a myocardial infarction is not a motivating factor to lose weight, I don't know what is!"

Obesity Specialists and Training

Dr Macdonald, who is chair of the finance committee of the International Association for the Study of Obesity, advocates improved communication between cardiologists and obesity specialists. He says, "I think there is a lot more room for improving links. One of the problems is that obesity management is not a clinical speciality—it's more a subspeciality of internal medicine. You can't train to be an 'obesiologist' like you can to be a diabetologist or a cardiologist. Most clinicians in this area are endocrinologists, and other specialists who seek their advice see them as part-timers. There is something of a turf war going on, though some Eastern European countries do have clinical obesity specialists. Of course, effective management of obesity touches on a lot of areas—respiratory, locomotor, gastrointestinal, and so on. And the large numbers of patients involved inevitably means that it must be done in a primary care setting. Yet, most general practitioners lack the necessary training in nutrition, behavioural therapy, and suchlike."

Training for physicians in obesity and its management, available at IASO courses and on its Web site, is much used, according to Dr Macdonald. IASO offers training for the Specialist Certificate of Obesity Professional Education, which is earned by accumulating sufficient points at courses held regularly in association with major conferences, together with an online course and an online examination involving

multiple-choice questions. This specialist certification is supported by an educational grant from 3 pharmaceutical companies. Forthcoming courses are being held on April 25, 2007, in association with the Fifteenth European Congress on Obesity in Budapest, Hungary, and on June 27–29, 2007, at a meeting of the UK Association for the Study of Obesity, in Liverpool, United Kingdom.

Government Action

In addition to better training in the medical community, Dr Macdonald advocates major investment by governments and has little faith in the free market. In November 2006, ministers from the 53 member states of the European Region of the World Health Organisation met in Istanbul, Turkey, to adopt the European Charter on Counteracting Obesity, urged on by a coalition of 12 nongovernmental agencies that included the IASO, the European Heart Network, and the Royal College of Physicians of London. In a joint statement aimed at limiting obesity in the rising generation, the agencies said, “Governments must recognise their responsibility to regulate marketing to children, who are increasingly targeted via the Internet as well as via television and through practices such as viral marketing [marketing techniques that use pre-existing social networks to produce increases in brand awareness]. Tackling obesity requires a strong lead from governments and strong action from all sectors if we are to avert one of the biggest public health threats of the 21st Century.”

Giving his prescription to governments, Dr Macdonald says, “We know the clinical health service tools that are effective, such as exercise prescription and cognitive behavioural therapy. We now need governments to take appropriate public health initiatives, such as making it easier to access low-fat foods. UK health economists have shown that obesity costs the country €6 billion a year. I would have thought that a return to more normal levels of obesity could be achieved

The International Association for the Study of Obesity

- ♦ IASO is the umbrella for 51 local obesity organisations representing 55 countries.
- ♦ In 2002 it merged with the International Obesity Taskforce, which is pledged to fight the health problems of excess weight worldwide.
- ♦ In addition to its flagship publication, *International Journal of Obesity*, of which Dr Macdonald is joint editor, IASO publishes a formidable stable of journals, including the *International Journal of Pediatric Obesity*; *Obesity Reviews*; *Diabetes, Obesity and Metabolism*; and *Obesity Research and Clinical Practice*.
- ♦ People with a special knowledge of obesity management may apply for an IASO fellowship. The association started the scheme with about 50 of its Founding Fellows from the countries of Europe and has awarded about 25 fellowships in each of the categories termed European Fellows and National Fellows.
- ♦ Countries of Eastern and Northern Europe have strong representation, whilst others, such as Croatia, Georgia, Finland, Iceland, Republic of Macedonia, Portugal, and Turkey, have none.

with an investment of €6 billion a year for 10 years. It’s a lot of money, but it is graspable.”

Dr Macdonald points out, “Governments commit similar sums of money to major transport works, such as a high-speed rail link, and to the Olympic Games.” A good plan is needed, but the benefits are enormous, in terms of reducing back problems, CVD, diabetes, and depression and of increasing productivity for a greater part of the working life. “And before anyone asks,” adds Dr Macdonald, “I take note of my own advice, by cycling to work, playing golf regularly, and working out at the gym 3 times a week.”

Barry Shurlock is a freelance medical writer.

The opinions expressed in *Circulation: European Perspectives in Cardiology* are not necessarily those of the editors or of the American Heart Association.

Profile of a Young Cardiology Researcher: Eric Morel, PhD

A New Protein Could Hold Clues to Cardiac Hypertrophy

Dr Eric Morel won the poster prize at the Heart Failure Association Research Winter Meeting in Garmisch-Partenkirchen earlier this year for his work in helping to highlight a brand new signalling pathway involved in hypertrophy of the myocardium. He talks to Mark Nicholls about his enthusiasm for cardiological research.

The discovery of a new protein, Epac, could hold clues to cardiac hypertrophy and help provide a treatment against heart failure. The protein is a key part of the investigative work of cardiology researcher Dr Eric Morel, who is 32 years of age. His research is with the Institut National de la Santé et de la Recherche Medical (more commonly known as INSERM), and he works in the U-769 laboratory that takes part in cardiac signalling and physiopathology work (see Figure) directed by Rodolphe Fischmeister, PhD,



and Dr Frank Lezoualc’h, PhD.

Dr Morel says the team is looking at the small guanine nucleotide binding proteins and their role in the field of heart hypertrophy and failure. “We are trying to investigate the implication of the recently discovered protein Epac in cardiac hypertrophy and heart failure,” he comments. Epac activation leads to morphological changes and induces expression of cardiac hypertrophic markers. Dr Morel explains, “We hope to develop a new treatment against

heart failure. This involves several approaches, including the transgenic germ line.”

Dr Morel obtained a postdoctoral position in Dr Fischmeister’s laboratory, later joined the team in a permanent role, and took up his current position of teacher/researcher at the Faculty of Pharmacy of Université Paris-Sud at the end of last summer. He says the teaching has a number of advantages for the progress of his work. “I try to share my time as efficiently as possible between my research work and my work teaching biotechnology to students in their third to fifth year of training as pharmacists.”

The teaching—in the area of cellular and gene therapy—allows him to retain contact with well-known professors and specialists on topics such as human stem cells and virology and to receive the latest updates on research data and clinical trials. He adds, “Teaching allows me to get in touch, to structure my ideas and presentations, and to gain self-assurance. It probably played a role in obtaining the Poster Prize in Garmisch.”

The award was presented at a congress that brought together the best European scientists working on the basic and translational science in the field of heart failure. The prize acknowledged Dr Morel’s work in helping to highlight a brand new signalling pathway from the receptor to the transcription factors leading to cardiac hypertrophy following the discovery of Epac. “Receiving this distinction from mentors was really an honour for me,” he says.

Dr Morel is equally focussed on the attributes others may wish to draw upon to follow a similar route. “Passion, adaptation, courage, patience, a little bit of opportunism, and never give up unless the second option is more interesting. Another important factor is chance, but you could try to influence its probability.”

He says his work is still in developing the Epac subject, looking for all the interrelations and neurohormonal regulations of the protein and for more evidence of the calcium–Epac relationship. Dr Morel explains, “The Epac protein can be activated in parallel to the canonical signalling pathway ‘cAMP/PKA,’ mediating all the cardiac functions of contraction, relaxation, and automaticity.” He continues, “Epac thus has emerged as a novel mediator of a pivotal process in the cardiac system that includes cellular calcium handling, hypertrophy, and heart failure.”

The biochemistry of cardiac hypertrophy has become an area of specific interest for Dr Morel. He says, “You have multiple ‘crosstalks’ between signalling pathways of major importance on a cardiac system which is very dynamic and reactive. Concerning the topic of the target Epac, it’s very stimulating to discover more than a complete pathway, as we probably have a possibility of innovative therapy.”

Dr Morel says that he knew from the beginning of his studies that he wanted to be a scientist, and he was driven by a curiosity to study the fundamental rules of nature through the physical and biological sciences rather than the human sciences. He began his research while working on his thesis in the Institut de Radioprotection et de Sûreté Nucléaire laboratory, studying the effects of ionising



Dr Morel’s research is with INSERM, and he works in the U-769 laboratory that involves cardiac signalling and physiopathology.

radiations on the gastrointestinal tract, first by studying the ionic transport across the colonic epithelium. “I decided then to reorient my thesis subject and focus on the radiation-induced alteration of the signalling pathways. This has probably played a role for my permanent position in my current lab, as I’m still working on these signalling pathways but in a different model—the cardiomyocyte.”

Dr Morel studied biochemistry and biology at Université Paris-Sud 11, Orsay, and specialised in physiology and physiopathology with a focus on cellular biology and nutrition at Université Paris 7. He had a break in his studies for military service, which enabled him to do some research in collaboration with the French army and the US Air Force. The work examined the physiological effects of caffeine and melatonin in individuals with jet lag.

Dr Morel cites an unusual first choice of mentor—the French navigator Eric Tabarly, whom he met at a nautical exhibition. Dr Morel recalls, “His strength of will and eagerness to get over physical and psychological difficulties, his perseverance in the pursuit of perfection for his boats, all that with a real modesty, inspired me. Of course, your career is constructed by the people you meet. But some of them are distinguished by their clever minds and kindness.”

Other areas in which Dr Morel is interested include biotechnology, medicine, and genetic therapy. He is also fascinated by astrophysics and eighteenth- and nineteenth-century history. As for where his future ambition lies, he can envisage competing for a future position as a university professor. However, he may decide to focus strictly on research, with his current team in France or abroad.

Dr Morel is married to Sandrine, who works at the Commissariat à l’Énergie Atomique, and speaks of his 2-year-old daughter Ambre as his proudest achievement.

Mark Nicholls is a freelance medical writer.

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