

History of the Blood Pressure Unit at the Charitable Infirmary and Beaumont Hospital 1978-2006



Professor Eoin O'Brien, Professor of Molecular Pharmacology, Conway Institute of Biomolecular and Biomedical Research, University College Dublin. President of the Irish Heart Foundation.

Humble beginnings

The history of hypertension in Ireland in the last 30 years is mirrored, I believe, in the history of the Blood Pressure Unit that was founded in the Charitable Infirmary in 1978, the only facility dedicated in name and purpose to bringing the most efficient and up-to-date management of this serious risk to the Irish people, while also determined to bring an Irish influence to international hypertension research. The latter endeavour was based on the belief that achievement in medical science could be best achieved through collaborative research – there was no longer a place for the scientist or institution to be an island unto themselves – the age of collaboration had arrived and only by sharing one's skills with others could the cause of science be advanced. This philosophy was shared by Kevin O'Malley, who I approached after he was appointed to the Chair of Clinical Pharmacology in the Royal College of Surgeons in Ireland (RCSI). We both knew that hypertension, particularly in the elderly, a group he had espoused in earlier research, was one of the major risks for stroke and heart attack; we also knew that it was one of the most poorly managed.

We had little going for us – in particular we had no money and there was little hope of financial support. We had, on the other hand, the boldness of belief in ourselves, a desire to reach outside of Ireland and a willingness to work very long hours. We persuaded RCSI and its teaching hospital, the Charitable Infirmary in Jervis Street, to provide a portacabin on the last piece of lawn in the hospital and here we founded the Blood Pressure Unit in 1978. This was the beginning of a unique collaboration between the 'bedside' at the clinical front-line in the Charitable Infirmary and the scientific laboratory 'benches' in the Department of Clinical Pharmacology in RCSI – what is today known as 'translational research'.

Early steps

One of the earliest benefactors was The Irish Heart Foundation, which published a booklet in 1978 entitled *Management of Hypertension* showing that cross-institutional collaboration was at last possible in Ireland – Kevin O'Malley and I were authors

from RCSI and Risteárd Mulcahy and the late Noel Hickey were from UCD. Our earliest significant sponsor was Servier Laboratories, where Jacques Servier and Jacques Thiel took an affectionate interest in our early work, and this company has remained loyal to the Blood Pressure Unit; for the past 20 years, Laurent Perret, President of Research and Development at Servier, has been an enthusiastic supporter of the Irish contribution to hypertension research. It is fair to say that without this support we would have foundered.

From the outset, the Unit concentrated on research into the pharmacology of blood pressure lowering drugs, particularly in the elderly, and on the development of blood pressure measuring techniques, especially techniques of ambulatory blood pressure measurement.

Some early papers enhanced our reputation. A series of no less than seven papers on 'The ABC of Blood Pressure Measurement' in the *British Medical Journal* in 1978, earned us the sobriquet of 'the Gilbert and Sullivan of hypertension'. Publication of 'Management of Hypertension in the Elderly' in the *New England Journal of Medicine* in 1980 was a serious statement of scientific intent. Participation of our Unit as a major centre in the European Working Party on High Blood Pressure in the Elderly (EWPHE) Study was to be the beginning of a long and fruitful collaborative relationship that began in Leuven with the late Anton Amery and endures today with Jan Staessen. How many other lifelong friends we made through this collaboration – too many to mention, but all are reflected in our publications. However, dear Willem Birkenhaeger stands out as a father figure, who gently and wisely curtailed youthful inexperience to guide us through some tempestuous moments.

Measurement of blood pressure

Empiricism was a characteristic that Kevin and I never shied from and we believed that if the premise on which all decisions in hypertension were based, be they in management or research, was flawed, then all that followed was open to question. In many publications, we railed against the reliance of both the practice and research of hypertension taking for granted the

measurement of blood pressure on which all decisions must be based. In particular, we cautioned against conventional measurement in artificial surroundings. The work of Sir George Pickering in Oxford in the seventies on direct intra-arterial ambulatory measurement particularly impressed me and I travelled to California where I was aware that a device had been developed for NASA for measuring blood pressure intermittently in astronauts. And so it was that we performed our first non-invasive ambulatory blood pressure measurement (ABPM) with the Remler monitor in 1980. Since then, the Blood Pressure Unit has performed over 25,000 ABPMs and is one of the leading centres in the world on this technique.

The accuracy of blood pressure measurement, which is so often taken for granted in scientific research, became a major interest of the Blood Pressure Unit and led to the Unit leading international committees to produce protocols to standardise the validation of blood pressure measuring devices. The British Hypertension Society Protocol was followed by the European Society International Protocol and the Unit has validated over 20 devices for the measurement of blood pressures and established a not-for-profit website devoted solely to blood pressure measurement – www.dableducational.org. This website has received 1.2 million visits since its launch in the Embassy of Ireland in Paris in 2004; it now receives an average of 69,867 visits per month and is consulted by 567 organisations in more than 80 countries.

International collaborative research on anti-hypertensive medication

Questions as to the efficacy of anti-hypertensive medication can rarely be answered in small single-centre studies and the Blood Pressure Unit has been a major participant in a number of multicentre international studies that have changed the clinical management of hypertension. The EWPHE Study showed clearly for the first time that blood pressure reduction was beneficial in elderly people with high blood pressure; the Systolic Hypertension in Europe (Syst-Eur) Study showed that lowering isolated systolic hypertension prevented stroke and heart attack; the Ambulatory Blood Pressure and Treatment of Hypertension (APTH) Study showed that treatment based on ambulatory measurement was superior to that based on conventional measurement; the Treatment of Hypertension Based on Home or Office Blood Pressure (THOP) Study likewise demonstrated that self measurement of blood pressure also favourably influenced drug treatment of hypertensive patients; the REASON study showed the superiority of a perindopril-indapamide combination to a β -blocker in lowering blood pressure; the Perindopril Protection Against Recurrent Stroke (PROGRESS) Study went on to show that this combination reduced the risk of secondary stroke by 25%; the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), in which 20,000 patients were recruited from Scandinavian countries, the

UK and Ireland (where 500 patients recruited by the Arterial Disease Assessment Prevention and Treatment [ADAPT] Centre were overseen by Alice Stanton), showed that patients receiving statin treatment had a reduction of 30% in heart attack and 25% in stroke, compared with patients receiving placebo, and in 2004, the Data Monitoring Committee recommended that the blood pressure lowering arm of ASCOT be closed prematurely because of a lower total mortality in the 10,000 patients receiving a calcium-channel blocker and angiotensin-converting enzyme inhibitor combination compared to the 10,000 patients receiving a β -blocker and thiazide combination. These landmark results, which have major implications for the future management of cardiovascular disease, have been published in recent editions of *The Lancet* and analyses of the data in the main study and in more than 20 sub-studies are ongoing. The Unit has also conducted studies on many classes of anti-hypertensive drugs, most recently completing a series of detailed studies on the first new class of anti-hypertensive drug to be introduced for over a decade – the renin inhibitors.

Multiple risk factor control

In keeping with the international trend to manage hypertension within the totality of cardiovascular risk, the ADAPT Clinic was established in collaboration with Professor David Bouchier-Hayes and Professor Desmond Fitzgerald in 1997. The rationale for this unique clinic was based on the concept that disease of the arterial organ was a fundamental denominator in all cardiovascular disease. The ADAPT Clinic was established to ensure that all patients with cardiovascular disease, regardless of the specialty to which they presented, would receive the most comprehensive risk factor assessment, with appropriate lifestyle modification and evidence-based drug treatment directed at the arterial organ.

The ADAPT concept was further developed in 1999 with the establishment of the ADAPT Centre, which became the research facility of the Blood Pressure Unit at Beaumont Hospital. The ADAPT Centre was committed to the emerging role of translational research in bridging the void between the clinical 'bedside' and the laboratory 'bench'. The ADAPT Centre provided outpatient facilities and a cardiovascular laboratory equipped to perform state-of-the-art cardiovascular assessment that included echocardiography, electrocardiography with stress testing, Holter monitoring, applanation tonometry, pulse wave velocity analysis, 24-hour APBM, beat-to-beat non-invasive blood pressure monitoring, 24-hour silent ischaemia monitoring, fundal photography and imaging, and carotid wall (intima-media thickness) imaging. Through its association with the Charitable Infirmary Trust Molecular Medicine Laboratories and the Clinical Research Centre in the RCSI Building at Beaumont Hospital, and with the Department of Clinical Pharmacology, the Centre for Proteomics, SURGEN, and BIOSYS at RCSI, the ADAPT Centre was able to further translational

research into the biochemical and genetic markers of risk, thrombosis and endothelial damage. In June 2006, the authorities at Beaumont Hospital closed the ADAPT Centre at short notice.

The dabl database

The first computerised record of a patient with hypertension attending the Blood Pressure Unit in the Charitable Infirmary was made in 1979 and since then, computerised data have been collected on over 26,000 patients with high blood pressure, using a programme designed specifically to manage cardiovascular disease – the dabl programme, making this the largest single-centre database of its kind in the world. The database permitted the first publication on normal ABPM data when data were collected from 916 normal subjects in the Allied Irish Bank. Known internationally as the AIB Study, this database has been developed not only to provide phenotypic data on normal subjects but also to provide genetic information on this cohort. Recently, a collaborative partnership was established with Jan Staessen in the Catholic University of Leuven to analyse the predictive value of blood pressure parameters in cardiovascular deaths in the Dublin database. Led by Eamon Dolan, this study, known as the Dublin Outcome Study, has shown the superior value of ambulatory blood pressure and particularly nocturnal blood pressure in the prediction of stroke and heart attack, with the results being published in recent editions of *Hypertension*. Another collaborative venture with the Department of Health and Children used the dabl programme to link primary care to permit sharing of information on cardiovascular risk between a specialist hospital clinic and primary care physicians. Known as the Reduction in Heart Attack and Stroke Project (RHASP), this successful pilot project, by bringing best management of cardiovascular disease to primary care, is capable of effecting a 30% reduction in stroke and heart attack with rigorous drug treatment of hypertension and dyslipidaemia. The extension of the RHASP model to cope with the increasing burden of heart failure in Ireland has been approved by the Health Services Executive and is now being established at St Vincent's Hospital.

Publications and communications

The Blood Pressure Unit and ADAPT Centre have published over 600 papers in peer-reviewed journals since their foundation and presentations have been made at international meetings in many countries in all continents of the world.

International and national working parties

Staff from the Blood Pressure Unit have been either members or chairpersons of a number of international and national bodies responsible for the global management of hypertension. These include the Blood Pressure Measurement Working Group of the European Society of Hypertension, the Irish Heart Foundation

Council on High Blood Pressure, EU Standards Committee on Blood Pressure Measurement, the WHO Committee for Blood Pressure Measurement in Low Resource Countries, the British Standards Institute, the Association for the Advancement of Medical Instrumentation in the US, the ASCOT Steering Committee, the ASCOT Sub-study Committee, the ASCOT Genetics Committee and the International Centre for Health and Co-operation at Fordham University. Likewise, the Unit has been represented on the editorial boards of the *Journal of Hypertension*, the *Journal of Human Hypertension*, *Blood Pressure* and *Blood Pressure Monitoring*.

History of hypertension

Over the years the Unit has produced papers and exhibitions on the history of hypertension. The blood pressure measuring devices collected over the life of the Blood Pressure Unit have been shipped to Paris where the O'Brien/Spengler Museum of Blood Pressure Measurement will open in 2007.

Servier Chair

In June 2006, I resigned from the Servier Chair of Cardiovascular Pharmacology at the RCSI and I was appointed to the Servier Chair of Molecular Pharmacology at the Conway Institute of Biomolecular and Biomedical Research, University College Dublin. The ongoing international research being conducted through the network of centres of excellence across the world (listed below) will continue from the new Blood Pressure Unit that is being established in St Michael's Hospital and from the Conway Institute.

Acknowledgements

The research achievements outlined in this brief history of the Blood Pressure Unit have been made possible by the facilities provided by the Charitable Infirmary, Beaumont Hospital and the Royal College of Surgeons. Financial support has been provided by the Irish Heart Foundation, the Health Research Board and many pharmaceutical companies, but the main source of sponsorship in the last 20 years has been the Charitable Infirmary Charitable Trust, which has given valuable and unstinting support to the Blood Pressure Unit and ADAPT Centre. Nothing, however, would have been achieved without the loyalty and diligence of the medical, nursing, secretarial and technical staff, who have served the Unit over nearly 30 years. Space would not permit a complete listing of these individuals and it would be invidious to single out individual names, but all are acknowledged in each of the 21 published Annual Reports of the Blood Pressure Unit and in the scientific communications to which so many contributed.

The future

A ramble down the lanes of history can in itself be a pleasant pastime, but if such peregrinations do not provide a vision for

the way forward, the exercise becomes little more than an egocentric reminiscence. So how can this historical review influence the future management of cardiovascular disease in Ireland?

Hypertension affects from 20-30% of the world's population. In those over the age of 60 years, the prevalence of isolated systolic hypertension at least doubles, with normotension being the exception in the elderly community. In the Republic of Ireland, stroke presently strikes down approximately 10,000 people each year, adding to a residue of some 30,000 survivors who are disabled for the rest of their lifespan. Stroke is the third most common cause of death, accounting for more deaths than breast cancer, lung cancer and bowel cancer combined. Add to this the daunting fact that patients who have had a stroke have a 30% chance of experiencing a recurrent stroke in the next five years, and are at increased risk of myocardial infarction and other vascular events, and the burden of this disabling illness on the community becomes one of the most urgent issues affecting healthcare provision.

Bad though these figures are, they are based on data showing that Ireland presently has the lowest percentage of elderly people among the 25 EU member states – 17% of the total population. However, by 2050, the percentage of over-65s is expected to almost double to make up nearly 30% of the population and unless we take action now, we need not be mathematicians to calculate that the annual rate of new strokes each year will exceed 20,000, which, when taken with the incidence of recurrent stroke, will result in an enormous number of severely incapacitated and disabled elderly people in the Irish community.

However, there is hope because stroke is largely a preventable disease – but we must act now. High blood pressure is the most consistent and powerful predictor of stroke. Smoking, excessive alcohol intake, obesity, dyslipidemia, diabetes mellitus, carotid artery disease, atrial fibrillation, heart failure and other forms of heart disease are treatable risk factors for stroke that must be addressed, as must the acute and long-term management of patients who have experienced a stroke. But, among the modifiable risk indicators, reducing blood pressure is the single most effective way of preventing stroke and we have the means at hand to do so. We must recognise, however, that the rule of halves is applicable to the Irish population: half of the people with high blood pressure are undetected; half of those who are identified are not on treatment and half of those on treatment are not achieving the goal levels of blood pressure control that are needed to reduce stroke.

Moreover, controlling high blood pressure is not simply a matter of writing a prescription. For this reason the American Hypertension Society and the European Society of Hypertension have created the grade of hypertension specialist to facilitate the community control of hypertension and concomitant risk factors as well as fostering research. To take but one aspect of the complexity of hypertension management, we need only look to

one of many lessons from this historical review. As far back as 1988, we reported that an abnormal circadian blood pressure profile with decreased night-time dipping was associated with an extremely high risk of stroke; recently, the results of the Dublin Outcome Study have confirmed that night-time blood pressure predicts outcome more accurately than any other measure of blood pressure: for each 10mmHg rise in mean night-time systolic blood pressure, the mortality risk increases by 21%. So we need to be able to provide patients with access to ABPM in order to identify those with nocturnal elevation of blood pressure.

These daunting statistics should leave us in no doubt that the management of high blood pressure integrated within a strategy of total cardiovascular risk management must be urgently improved in Ireland if an epidemic of stroke in the elderly is to be averted. The Blood Pressure Unit at Beaumont Hospital has proved itself to be an effective model, which is about to be replicated in conjunction with the Heart Failure Unit at St Michael's Hospital in scientific collaboration with the Conway Institute at UCD. It would seem timely for other similar units to be established around the country to provide a nationwide network linked to primary care to ensure that by effectively controlling hypertension we can reduce the present intolerable burden of stroke on the Irish community, and, importantly, prevent an epidemic of this devastating illness in a rapidly ageing population.

International research network

Over the years, the Blood Pressure Unit and the ADAPT Centre established a collaborative network with centres of excellence across the world, from which scientific papers emanate on a regular basis; these include the following centres:

- Roland Asmar, Société Française D'Hypertension Arterielle, FRANCE
- Lawrie Beilin, University of Western Australia, AUSTRALIA
- Gareth Beevers, City Hospital, Birmingham, UK
- Mark Caulfield, St Bartholomew's Hospital, London, UK
- Denis L Clement, Universitair Ziekenhuis, Gent, BELGIUM
- Bjorn Dahlhoff, Sahlgrenska University Hospital, Gotenborg, SWEDEN
- Peter De Leeuw, Academisch Ziekenhuis, P Maastricht, THE NETHERLANDS
- Robert Fagard, Katholieke Universiteit Leuven, BELGIUM
- John Graves, The Mayo Clinic, Rochester, Minnesota, USA
- Tine Willum Hansen, Bispebjerg Hospital, Copenhagen, DENMARK
- Yutaka Imai, Tohoku University Graduate School of Pharmaceutical Science and Medicine, Sendai, JAPAN
- Thomas Kahan, Karolinska Institutet, SWEDEN
- Sverre Kjeldsen, Sykehus Medisinsk Klinik, Oslo, NORWAY
- Tony Lever, Western Infirmary, Glasgow, SCOTLAND
- Gregory Lip, City Hospital, Birmingham, UK
- Jean-Michel Mallion, Centre Hospitalier Universitaire de Grenoble, FRANCE
- Giuseppe Mancia, Universita Degli Studi di Milano-Bicocca, Monza, ITALY
- David B Matchar, Duke Center for Clinical Health Policy Research, Durham,

North Carolina, USA
 Gordon McInnes, Western Infirmary, Glasgow, SCOTLAND
 Jesper Mehlsen, Frederiksberg Hospital, DENMARK
 Shanthi Mendis, Management of Noncommunicable Diseases, WHO, Geneva, SWITZERLAND
 Thomas Mengden, University Clinic Bonn, GERMANY
 Stephan Mieke, Physikalisch-Technische Bundesanstalt, Berlin, GERMANY
 Alan Murray, Freeman Hospital, Newcastle upon Tyne, UK
 Martin G Myers, Sunnybrook Health Sciences Centre, Toronto, CANADA
 Marrku Nieminen, University Central Hospital, Helsinki, FINLAND
 Juerg Nussberger, CHUV, Division of Hypertension, Lausanne, SWITZERLAND
 Ingrid OS, Ullevål Hospital, Oslo, NORWAY
 Paul Padfield, Western General Hospital, Edinburgh, SCOTLAND
 Gianfranco Parati, University of Milano-Bicocca and Ospedale San Luca, Milan, ITALY
 Paolo Palatini, Università di Padova, Padua, ITALY
 Thomas G Pickering, Mount Sinai Medical Center, New York, USA
 Neil Poulter, International Centre for Circulatory Health National Heart & Lung Institute, Imperial College London. UK
 Josep Redon, Hospital Clinico, University of Valencia, Valencia, SPAIN
 John Reid, Western Infirmary, Glasgow, SCOTLAND
 Peter Sever, International Centre for Circulatory Health National Heart & Lung Institute, Imperial College London. UK
 Andrew Shennan, St Thomas' Hospital, London, UK
 Simon Thom, International Centre for Circulatory Health National Heart & Lung Institute, Imperial College London. UK
 Michel Safar, Hôpital Hôtel-Dieu, Paris. FRANCE
 Jan Staessen, Katholieke Universiteit Leuven, BELGIUM
 George Stergiou, Sotiria Hospital, Athens, GREECE
 Gert van Montfrans, Academisch Medisch Centrum, Amsterdam, THE NETHERLANDS
 Paolo Verdecchia, Ospedale R. Silvestrini, Perugia, ITALY
 Bernard Waeber, Centre Hospitalier Universitaire Vaudois, Lausanne, SWITZERLAND
 William White, The University of Connecticut Health Center, Farmington, Connecticut, USA
 Bryan Williams, University of Leicester School of Medicine, UK
 Li Yan, Shanghai Institute of Hypertension, CHINA
 Ji-Guang Wang, Shanghai Institute of Hypertension, CHINA

Selected publications 1978 – 2006

These publications are selected from over 600 papers published in peer-reviewed journals over the past 28 years as being selective of the progress and developments in hypertension research, particularly in the Blood Pressure Unit:

If I had... hypertension. *Br Med J* 1978; 2: 1469-70.
 The ABC of blood pressure measurement. *Br Med J* 1979; 2: 775-6.
 Management of hypertension in the elderly. *New Eng J Med* 1980; 302: 1397-401.

Reporting of blood pressure data in medical journals. *Br Med J* 1980; 4: 1603-4.
 Accuracy of the London School of Hygiene and Remler M 2000 sphygmomanometers. *Clin Sci* 1981; 61: 399S-401S.
 Anti-hypertensive therapy in patients above age sixty. Fifth Interim Report of the European Working Party on High Blood Pressure in the Elderly (EWPHE). *Curr Concepts Hypertens Cardiovasc Disord* 1981; 2: 14-9.
 Inaccuracy of the London School of Hygiene sphygmomanometer. *Br Med J* 1982; 284: 18-9.
 Sphygmomanometers in hospitals and family practice: problems and recommendations. *Br Med J* 1982; 285: 469-71.
 Baroreflex function in elderly hypertensives. *Hypertension* 1983; 5: 763-6.
 Accuracy of indirect blood pressure measurement in the elderly. *Br Med J* 1983; 286: 1545-6.
 The efficacy of indapamide in hypertensive patients failing to respond to a β -blocker alone. *Drugs of Today* 1984; 20: 27-31.
 The role of home and ambulatory blood pressure resording in the management of hypertension. *J Hypertens* 1985; 3 (suppl 1): 35-9.
 Blood pressure measurement: current practice and future trends. *Br Med J* 1985; 290: 729-34.
 Mortality and morbidity from the European Working Party on High Blood Pressure in the Elderly Trial. *Lancet* 1985; i: 1349-54.
 Recommendations on blood pressure measurement. *Br Med J* 1986; 293: 611-5.
 Influence of anti-hypertensive drug treatment on morbidity and mortality in patients over the age of 60 years. EWPHE results: sub-group analysis based on entry stratification. *J Hypertens* 1986; 4 (suppl 6): S642-7.
 Standards for blood pressure measuring devices. *Br Med J* 1987; 244: 1245-6.
 High Blood Pressure: What it means for you and how to control it. 2nd Edition. Optima. Macdonald & Co. London, 1987.
 Dippers and non-dippers. *Lancet* 1988; ii: 397.
 Diuretics - a risk in the long-term treatment of hypertensive patients? *J Hypertens* 1988; 6: 925-30.
 Over-diagnosing hypertension. *Br Med J* 1988; 297: 1211-2.
 Measurement of blood pressure measurement in children. *Br Med J* 1989; 299: 497.
 Relation between mortality and treated blood pressure in elderly patients with hypertension: report of the European Working Party on High Blood Pressure in the Elderly. *Br Med J* 1989; 298: 1552-6.
 Ambulatory blood pressure measurement in the evaluation of blood pressure lowering drugs. *J Hypertens* 1989; 7: 243-7.
 Inaccuracy of the Hawksley random-zero sphygmomanometer. *Lancet* 1990; 336: 1465-8.
 Inaccuracy of seven popular sphygmomanometers for home-measurement of blood pressure. *J Hypertens* 1990; 8: 621-34.
 The British Hypertension Society Protocol for the evaluation of automated and semi-automated blood pressure measuring devices with special reference to ambulatory systems. *J Hypertens* 1990; 8: 607-19.
 Twenty-four-hour ambulatory blood pressure in men and women aged 17 to 80 years: the Allied Irish Bank Study. *J Hypertens* 1991; 9: 355-60.
 Blood Pressure Measurement. Volume 14. Handbook of Hypertension.

- Birkenhager WH, Reid JL. Eds. Elsevier. Amsterdam, 1991.
- The role of twenty-four-hour ambulatory blood pressure measurement in clinical practice. *J Hypertens* 1991; 9 (suppl 8): S63-5.
- Clinical application of ambulatory blood pressure measurement in pregnancy. *J Hypertens* 1991; 9 (suppl 8): S75-7.
- Accuracy of the SpaceLabs 90207, Novacor DIASYS 200, Del Mar Avionics Presurometer IV and Takeda TM-2420 ambulatory systems according to the AAMI and BHS criteria. *J Hypertens* 1991; 9 (suppl 6): S332-3.
- Risks and benefits of the trial of the European Working Party on High Blood Pressure in the Elderly. *J Hypertens* 1991; 9: 225-30.
- Cumulative sums in quantifying circadian blood pressure patterns. *Hypertension* 1992; 19: 93-101.
- The increase in blood pressure with age and body mass index is overestimated by conventional sphygmomanometry. *Am J Epidemiol* 1992; 136: 450-9.
- Effects of ageing and hypertension on plasma angiotensin II and platelet angiotensin II receptor density. *Am J Hypertens* 1992; 5: 687-93.
- Where are the guidelines for treating hypertension in the elderly. *Br Med J* 1992; 305: 845-6.
- The British Hypertension Society Protocol for the evaluation of blood pressure measuring devices. *J Hypertens* 1993; 11 (suppl 2): S43-63.
- Anti-hypertensive therapy and circadian blood pressure profiles: a retrospective analysis utilising cumulative sums. *Blood Pressure* 1993; 2: 289-95.
- Twenty-four hour ambulatory blood pressure measurement in a primigravid population. *J Hypertens* 1993; 11: 869-73.
- Comparative accuracy of six ambulatory devices according to blood pressure levels. *J Hypertens* 1993; 11: 673-5.
- Relationship between blood pressure measured in the clinic and by ambulatory monitoring and left ventricular size as measured by electrocardiogram in elderly patients with isolated systolic hypertension. *J Hypertens* 1993; 11: 269-76.
- The ambulatory blood pressure in normotensive and hypertensive subjects: results from a large international database. *J Hypertens* 1994; 12 (suppl 7): S1-12.
- The history of blood pressure measurement. *J Human Hypertens* 1994; 8: 73-84.
- Clinical trials with ambulatory blood pressure monitoring: fewer patients needed? *Lancet* 1994; 344: 1552-6.
- A method of quantifying retinal microvascular alterations associated with hypertension and age. *J Hypertens* 1995; 13: 41-8.
- A new audio-visual technique for recording blood pressure in research: the sphygmocorder. *J Hypertens* 1995; 13: 1734-7.
- State of the market: a review of ambulatory blood pressure monitoring devices. *Hypertension* 1995; 26: 835-42.
- Ambulatory monitoring uncorrected for placebo overestimates long-term anti-hypertensive action. *Hypertension* 1996; 27 [Part 1]: 414-20.
- Hypotension: a forgotten illness. *Blood Pressure Monit* 1996; 2: 3-14
- Ave atque vale: the centenary of clinical sphygmomanometry. *Lancet* 1996; 348: 1569-70.
- The nocturnal blood pressure fall on ambulatory monitoring in a large international database. *Hypertension* 1997; 29: 30-9.
- Can 24-hour ambulatory blood pressure measurement predict the development of hypertension in primigravidae? *Br J Obstet & Gynaecol* 1997; 104: 356-62.
- Accuracy of the Dinamap Portable Monitor, Model 8100: a review of the evidence for accuracy. *Blood Pressure Monit* 1997; 2: 31-3.
- Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. *Lancet* 1997; 350: 757-64.
- Anti-hypertensive treatment based on conventional or ambulatory blood pressure measurement: a randomised controlled trial. *JAMA* 1997; 278: 1065-72.
- The arterial organ in cardiovascular disease: Arterial Disease Assessment, Prevention, and Treatment (ADAPT Clinic). *Lancet* 1998; 352: 1700-2.
- Quality of life in elderly patients with isolated systolic hypertension: baseline data from the Syst-Eur Trial. *J Hypertens* 1998; 16: 1117-24.
- Calcium channel blockade and cardiovascular prognosis in the European Trial on Isolated Systolic Hypertension. *Hypertension* 1998; 32: 410-6.
- Predicting cardiovascular risk using conventional vs. ambulatory blood pressure in older patients with systolic hypertension. *JAMA* 1999; 282: 539-46.
- Diagnosis of white coat hypertension by ambulatory blood pressure monitoring. *Hypertension* 1999; 34: 267-72.
- Effects of calcium-channel blockade in older patients with diabetes and systolic hypertension. *New Eng J Med* 1999; 340: 677-84.
- Use and interpretation of ambulatory blood pressure monitoring: recommendations of the British Hypertension Society. *Br Med J* 2000; 320: 1128-34.
- Comparison of anti-hypertensive and metabolic effects of losartan and losartan in combination with hydrochlorothiazide: a randomised controlled trial. *J Hypertens* 2000 18: 339-45.
- Arterial hypotension: prevalence of low blood pressure in the general population using ambulatory blood pressure monitoring. *J Human Hypertens* 2000; 14: 243-7.
- Replacing the mercury sphygmomanometer. *Br Med J* 2000; 320: 815-6.
- Blood pressure measuring devices: recommendations of the European Society of Hypertension. *Br Med J* 2001; 322: 531-6.
- Rationale, design, methods and baseline demographic data of participants in the Anglo-Scandinavian Cardiac Outcomes Trial. *J Hypertension* 2001; 19: 1139-47.
- Properly defining white coat hypertension. *Eur Heart J* 2001; 23: 106-9.
- European Society of Hypertension International Protocol for validation of blood pressure measuring devices in adults. *Blood Press Monit* 2002; 7: 3-17.
- Predictive value of clinic and ambulatory heart rate for mortality in elderly subjects with systolic hypertension. *Arch Intern Med* 2002; 162: 2313-21.
- Night-time blood pressure – dipping into the future? *J Hypertens* 2002; 20: 2131-3.
- Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet* 2003; 361: 1149-58.

- Prognostic value of ambulatory blood pressure recordings in patients with treated hypertension. *New Engl J Med* 2003; 348: 207-15.
- Blood pressure lowering in essential hypertension with an oral renin inhibitor, aliskiren. *Hypertension* 2003; 42: 1137-43.
- Systolic blood pressure variability as a risk factor for stroke and cardiovascular mortality in the elderly hypertensive population. *J Hypertens* 2003; 21: 2251-7.
- Ambulatory blood pressure monitoring in the management of hypertension. *Heart* 2003; 89:571-6.
- Anti-hypertensive treatment based on blood pressure measurement at home or in the physician's office. A randomised controlled trial. *JAMA* 2004; 291: 955-64.
- Twenty-four-hour ambulatory blood pressure monitoring efficacy of perindopril/indapamide first-line combination in hypertensive patients. The REASON Study. *Am J Hypertension* 2004; 17: 245-51.
- Effects of immediate versus delayed antihypertensive therapy on outcome in the Systolic Hypertension in Europe Trial. *J Hypertens* 2004; 22: 847-57.
- Regression of left ventricular mass in hypertensive patients treated with perindopril/indapamide as a first-line combination: The REASON echocardiography study. *Am J Hypertension*.2004; 17: 660-7.
- Can improved software facilitate the wider use of ambulatory blood pressure measurement in clinical practice? *Blood Press Monit* 2004; 9: 237-41.
- Self monitoring of blood pressure at home, *Br Med J* 2004; 329: 870-1.
- Clinical review: shared care can help prevent heart disease. *Forum* 2005; 22: 33-5.
- Recommendations for blood pressure measuring devices for office/clinic use in low resource settings. *Blood Press Monit* 2005; 10: 3-10.
- Practice guidelines of the European Society of Hypertension for clinic, ambulatory and self blood pressure measurement. *J Hypertens* 2005; 23: 697-701.
- Superiority of ambulatory over clinic blood pressure measurement in predicting mortality: the Dublin Outcome Study. *Hypertension*. 2005; 46: 156-61.
- Prevention of cardiovascular events with an anti-hypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multi-centre randomised controlled trial. *Lancet* 2005; 366: 895-906.
- Role of blood pressure and other variables in the differential cardiovascular event rates noted in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA) *Lancet* 2005: 366: 907-13.
- Unmasking hypertension. *Hypertension* 2005; 45: 481-2.
- Ambulatory arterial stiffness index derived from 24-hour ambulatory blood pressure monitoring. *Hypertension* 2006; 47: 359-64.
- Ambulatory arterial stiffness index as a predictor of cardiovascular mortality in the Dublin Outcome Study. *Hypertension* 2006; 47: 365-70.
- Ambulatory arterial stiffness index predicts stroke in a general population. *J Hypertens* 2006; 24: 000-000.
- Differential Impact of blood pressure lowering drugs on central aortic pressure and clinical outcomes - Principal results of the Conduit Artery Function Evaluation (CAFE) study. *Circulation* 2006; 113: 1213-25.
- Aliskiren: a renin inhibitor offering a new approach for the treatment of hypertension. *Expert Opin Investigational Drugs* 2006; 15: 1269-77.
- Ambulatory blood pressure measurement: a trove of hidden gems? *Hypertension* 2006; 48: 364-5.