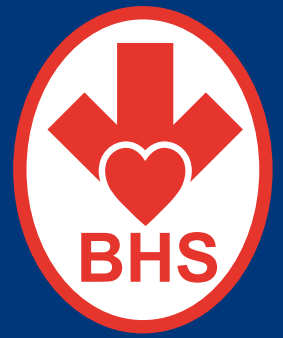




British Hypertension Society



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12th BHS Clinical Education Meeting for Primary Care



A one-day educational meeting for general practitioners, primary care nurses and pharmacists, supplementary and independent prescribers and other primary care healthcare professionals

May be deemed suitable for your CPD programme



Tuesday 25th May 2010

**Institute of Child Health
LONDON**

***Final Programme
and Abstracts***

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WELCOME

Dear Colleague

We are pleased to welcome you to the 12th British Hypertension Society Clinical Education Meeting for Primary Care, being held at the Institute of Child Health, London.

This educational programme is intended to support best practice and successful implementation of evidence-based management and guidelines. Over 1,300 general practitioners, primary care cardiovascular leads, lead pharmacists and nurses have attended BHS Clinical Education meetings and feedback has been highly positive. For this meeting we have constructed a programme based on feedback from previous meetings to consider pragmatic approaches to reducing cardiovascular disease and achieving targets.

To facilitate interaction, please hand in a summary of your difficult cases to the Registration Desk for inclusion in the concluding session of the meeting.

The British Hypertension Society would like to express its gratitude to our sponsors and exhibitors for their support of the meeting, and we should like to invite you to visit the exhibition stands on both floors of the conference centre.

Thank you for taking the opportunity to join us and we look forward to a stimulating meeting.



Professor Mark Caulfield
President
British Hypertension Society



Dr. James McLay
Chairman
BHS Educational Programmes Working Party

MEETING INFORMATION

VENUE: Institute of Child Health (ICH), 30 Guilford Street, London WC1N 1EH.
Telephone: Switchboard 020 7242 9789 (Registration Desk: ext 0718)

CLOAKROOM FACILITIES: Coat racks are located in the foyer of the ICH. Please note that this area is not staffed and delegates leaving belongings do so at their own risk. The Organisers cannot be held liable for personal accidents, loss or damage of personal property during the event.

SECURITY: Name badges must be worn at all times as these serve as the admission pass to sessions and the exhibition.

EXHIBITION, LUNCH AND REFRESHMENTS: The Exhibition is located on the Balcony (Ground Floor) and the Winter Garden (Lower Ground Floor). Lunch and refreshments will also be served on both floors.

CERTIFICATES OF ATTENDANCE: Certificates of Attendance will be available from the Registration Desk at the end of the meeting.

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PROGRAMME

08.30 - 09.30 *REGISTRATION AND COFFEE*

Session 1: **ANTICOAGULATION AND LIPIDS**

Chair: Dr James McLay (Aberdeen)

09.30 - 09.50 1.1 **Aspirin - where are we now?**
Professor Peter Sever
Professor of Clinical Pharmacology, Imperial College London

09.50 - 10.00 Discussion

10.00 - 10.20 1.2 **Lipid lowering - what next?**
Professor Neil Poulter
Professor of Preventive Cardiovascular Medicine, Imperial College London

10.20 - 10.30 Discussion

10.30 - 10.50 1.3 **Atrial fibrillation, stroke and anticoagulation**
Professor Gordon McInnes
Professor of Clinical Pharmacology, Western Infirmary, Glasgow

10.50 - 11.00 Discussion

11.00 - 11.30 *COFFEE*

Session 2: **HYPERTENSION, ASSESSMENT AND PATIENT OUTCOMES**

Chair: Dr Ian Wilkinson (Cambridge)

11.30 - 11.50 2.1 **The primary care management of the patient with heart failure and hypertension**
Dr. Terry McCormack
General Practitioner, Whitby Group Practice

11.50 - 12.00 Discussion

12.00 - 12.20 2.2 **What do ABPM and home blood pressure measurements actually mean?**
Professor John Potter
Professor of Ageing and Stroke Medicine, University of East Anglia, Norwich

12.20 - 12.30 Discussion

12.30 - 12.50 2.3 **Preventing cardiovascular disease in type 2 diabetes mellitus - priorities for optimal intervention**
Professor Neil Poulter
Professor of Preventive Cardiovascular Medicine, Imperial College London

12.50 - 13.00 Discussion

13.00 - 14.00 *LUNCH*

PROGRAMME continued

Session 3: MANAGING SPECIFIC PATIENT GROUPS

Chair: Professor Mark Caulfield (London)

14.00 - 14.20 3.1 **Does elevated blood pressure in childhood equate to increased risk?**
Dr. Ian Wilkinson
Senior Lecturer and Honorary Consultant, Addenbrooke's Hospital, Cambridge

14.20 - 14.30 Discussion

14.30 - 14.50 3.2 **New treatments for diabetes and cardiovascular risk**
Professor Graham Hitman
Professor of Molecular Medicine and Diabetes, Barts and the London School of Medicine and Dentistry, Queen Mary University of London

14.50 - 15.00 Discussion

15.00 - 15.20 3.3 **Hypertension management in anticipation of pregnancy**
Dr. David Williams
Consultant Obstetric Physician, Institute for Women's Health, University College London Hospital

15.20 - 15.30 Discussion

15.30 - 15.45 **TEA**

Session 4: CARDIOVASCULAR RISK CLINIC - CHALLENGING CASES IN PRIMARY CARE

Chair: Professor Mark Caulfield (London)

15.45 - 16.30 To include the following problems:

- ◆ Resistant hypertension
- ◆ Pre-conception hypertension
- ◆ Hypertension during pregnancy
- ◆ Postural hypotension in the uncontrolled hypertensive
- ◆ Uncontrolled hypertension on multiple antihypertensive agents

Panel: Dr. James McLay (*Aberdeen*)
Professor Gordon McInnes (*Glasgow*)
Invited GP from the audience

16.30 **CLOSE OF MEETING**

1.1 Aspirin - where are we now?

Professor Peter Sever

Professor of Clinical Pharmacology, Imperial College London

The use of aspirin to prevent future cardiovascular events in those with a prior history of cardiovascular disease is recommended by all relevant guidelines and is supported by a strong evidence base. However, there has been much publicity and debate resulting from recent reports questioning the benefits of aspirin use in those with no history of prior cardiovascular disease, including those with diabetes^{1,2,3}, particularly in the context of the known increase in risk of gastrointestinal bleeding.

The current BHS Guidelines, published in 2004⁴, recommend that all patients suitable for secondary prevention strategies (those with prior history of cardiovascular disease), including those with type 2 diabetes of greater than 10 years duration, or over 50 years, have a sufficient level of cardiovascular disease risk to benefit from aspirin therapy, and should be considered for low-dose aspirin (75 mg daily) unless they have specific contraindications to aspirin use.

For primary prevention, the balance of benefits vs harm mandate that patients need to be aged over 50 years and have a CVD risk level $\geq 20\%$ over 10 years to shift the balance in favour of benefit. Thus, for primary prevention, low-dose aspirin should only be offered to hypertensive patients aged over 50 years whose blood pressure has been controlled to the audit standard ($<150/90$ mmHg) and who have a baseline CVD risk $\geq 20\%$ over 10 years and no contraindication to aspirin use.

These recommendations were strongly influenced by the assessment of the benefit and harm of low-dose aspirin in well treated hypertensive subjects at different levels of baseline CVD risk⁵. In these analyses the benefit vs harm was neutral at a 10 year CVD risk of about 10%, but favoured benefit at higher levels of risk.

The recently published updated meta-analysis using individual participant data from the original trials of the use of aspirin in primary prevention¹, reported an overall proportional risk reduction in serious vascular events of 12% (0.51% aspirin vs 0.57% control per year, $p=0.0001$) due mainly to a reduction of about one fifth in non-fatal myocardial infarction (0.18% vs 0.23% per year, $p<0.0001$). However, this benefit was offset by an increase in major gastrointestinal and extracranial bleeds (0.10% vs 0.07% per year, $p<0.0001$). Thus the absolute reduction in the risk of vascular events is only about twice as large as the absolute increase in bleeding. As the authors of the meta analysis point out, most of the patients recruited into these primary prevention trials were not taking statins, which would have reduced their absolute risk of vascular events without any increase in harm. Even in those patients at higher risk the number of vascular events was too few to allow any reliable conclusions to be drawn.

In a further report of a meta analysis of trials of aspirin use in the primary prevention of cardiovascular events in people with diabetes² which included three new trials since the last BHS guidelines were published, there was a non-significant trend for benefit on all cardiovascular events (HR 0.90, CI 0.81-1.00), but a significant reduction in the risk of myocardial infarction in men (HR 0.57, CI 0.34-0.94) but not women (HR 1.08, CI 0.71-1.65). The evidence from these trials for harm associated with aspirin was inconsistent.

The most recent trial to report - the AAA Study, published in abstract form only to date³, of low-dose aspirin in the prevention of cardiovascular events and death in subjects with asymptomatic atherosclerosis, demonstrated no benefit of 100 mg aspirin in a placebo-controlled trial in almost 29,000 patients but there was a non-significant excess of major haemorrhage in the aspirin treated group. Further details on this trial are awaited.

Recently the Medicines and Healthcare Products Regulatory Agency (MHRA) have issued a statement that reminds physicians and the public that aspirin is only licensed for the secondary prevention of cardiovascular disease, and that if aspirin is used in primary prevention, the balance of benefits and risks should be considered for each individual, particularly the presence of risk factors for cardiovascular disease and the risk of gastrointestinal bleeding.

On the basis of these findings and reports, and until new information becomes available from ongoing trials, the BHS Working Party reaffirms its earlier recommendations that aspirin use in the prevention of cardiovascular disease in hypertensive people should be restricted to patients with prior history of cardiovascular disease and, in primary prevention (including those with diabetes), to those aged over 50

years with 10 year cardiovascular risk of at least 20%. As advocated by MHRA, physicians should weigh up the benefits and risks of low dose aspirin in all individuals. An accurate quantitative assessment of 10 year cardiovascular risk is essential before prescribing aspirin for the primary prevention of cardiovascular disease.

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1.2 Lipid lowering - what next?

Professor Neil Poulter

Professor of Preventive Cardiovascular Medicine, Imperial College London

Since 1994, with the results of the 4S trial and a succession of further statin trial results, the use of lipid lowering drugs in the UK has change dramatically.¹ The safety and efficacy of statins in terms of preventing cardiovascular morbidity and mortality has been established in the context of primary and secondary prevention, amongst younger and older adults whether male or female².

Some relatively trivial debate remains regarding statin usage - viz. which statins to use (actually a financial and not a scientific debate), at what dose and what treatment thresholds and targets should apply. In general the maxim 'the lower the better' seems to apply to the benefits associated with statin use.

For the vast majority of patients a high dose of an effective statin (e.g. atorvastatin 80mg or rosuvastatin 40mg) will suffice to control lipid levels to current targets, but for financial reasons we are recommended to initiate therapy with simvastatin rising to a dose of 40mg daily. The consensus is that higher doses of simvastatin (i.e. >40mg) should not be used and hence patients need to be switched to other agents in the event of not reaching targets.

One truly contentious issue for practising clinicians is how to get to target if rosuvastatin 40mg is insufficient and/or statin intolerance prohibits the use of statins. The NICE Guidance recommended the combination of simvastatin with ezetimibe for additional lowering of LDL-cholesterol.³ There was no supportive trial-base evidence on cardiovascular benefits associated with ezetimibe on which to base this recommendation. This trial evidence remains absent^{4,5} and it is hard to understand why such a recommendation was made.

More recently the ACCORD trial⁶ has delivered disappointing results regarding the addition of fenofibrate to a statin in the context of high risk diabetic patients.

It may be that the newer formulations of nicotinic acid - which are less likely to cause flushing - may become the favoured add-on to a statin although randomised trial data are invalid.

A second important and outstanding issue regarding the use of lipid lowering agents relates to what agent to use when the major lipid-abnormality is not raised LDL-cholesterol, but rather raised triglycerides and/or low HDL-cholesterol. Expert opinion remains divided but most would recommend statin use as baseline therapy and then, as for achieving lower LDL targets, the optimal add-on drug is not clear!

Fenofibrate has proven disappointing in two major trials and gemfibrozil, although it does have supportive trial evidence as first-time therapy is contra-indicated within a statin.

The first CET-P inhibitor torcetrapib, which generates very large beneficial effects on HDL-cholesterol, was found in the ILLUMINATE trial⁷ to be unsafe, as a result of BP-elevating effects although other agents from the same class may prove not to have this adverse effect and therefore become viable.

Meanwhile trials of the new formulation of nicotinic acid are in progress, as a potential add-on agent for managing a broader spectrum of lipid abnormality. Evidence of the benefit of the use of Omacor (n-3 PUFA) for patients in the post-MI setting and in heart failure is encouraging although the mechanisms for benefit remain controversial.

Meanwhile the optimal agents to achieve additional LDL reduction and the control of low HDL and/or high triglycerides remains uncertain in terms of reducing major cardiovascular events.

¹Primatesta P, Poulter NR. Levels of dyslipidaemia and improvement in its management in England: results from the Health Survey for England 2003. *Clinical Endocrinology* 2006;64:292-298.

²Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statin. *Lancet* 2005; 366: 1267-78

³NICE Clinical Guidance 67. CG67 Lipid modification. May 2008 (reissued March 2010)

⁴ENHANCE trial - *N Engl J Med* 2008; 358: 1431-43

⁵Rossebo AB, Pedersen TR, Boman K, et al. Intensive lipid lowering with simvastatin and ezetimibe in aortic stenosis. *N Engl J Med* 2008; 359: 1343-56.

⁶ACCORD (not yet published, presented ACC: March 2010)

⁷ILLUMINATE; *N Engl J Med*: 2007; 357: 2109-22

1.3 Atrial fibrillation, stroke and anticoagulation

Professor Gordon McInnes

Professor of Clinical Pharmacology, Western Infirmary, Glasgow

Atrial fibrillation (AF) is the commonest sustained cardiac dysrhythmia. Hypertension is the most important causal factor but AF is often associated with coronary heart disease and heart failure¹. Roughly 1 in 3 patients with AF do not have detectable heart disease. The lifetime risk for the development of AF is about 1 in 4 for all people aged 40 years or older^{2,3} and about 1 in 6 for those without structural heart disease. Prevalence of AF rises from 1% at age 55 - 59 years to 18% at 85 years or older³. With an increasingly elderly population, the prevalence of AF is set to risk substantially.

AF is associated with increased cardiovascular morbidity and mortality with stroke, primarily the results of cardioembolism of a fibrin-rich thrombus, being an especially important and potentially devastating complication. The risk of stroke is increased 4 to 5-fold by non-valvular AF; risk is similar in paroxysmal and permanent AF. Asymptomatic cerebrovascular events may contribute to dementia and impaired cognitive function in AF.

Irrespective of aetiology or clinical subtype of AF (paroxysmal, persistent or permanent), rate control or rhythm control, appropriate antithrombotic therapy is mandatory, based on risk factors for stroke⁴. Rhythm control does not necessarily reduce stroke risk⁵ and lifetime anticoagulation is needed if risk of stroke or recurrence of AF is high⁴. Stroke prevention with effective thromboprophylaxis is also central to the management of atrial flutter.

Adjusted-dose warfarin reduces risk of stroke by 2/3 while aspirin reduces stroke risk by 1/5⁶. Therefore aspirin should not be regarded as an adequate substitute for warfarin for stroke prevention. Balance is needed, however, since, compared with aspirin, warfarin doubles the rate of intra cerebral haemorrhage⁶. Clopidogrel added to aspirin is more effective than aspirin alone⁷ but this combination is less effective than warfarin⁸.

Appropriate antithrombotic treatment depends on an individual's risk of stroke. The popular CHADS₂ risk stratification model⁹ incorporates important risk factors (Congestive heart failure, Hypertension, Age > 75 years, Diabetes, Stroke or transient ischaemic attack). NICE⁴ suggests a similar algorithm-based scheme: low-risk patients should be offered aspirin 75 - 300 mg daily; moderate-risk, aspirin or warfarin titrated to INR 2.0 - 3.0; high-risk, warfarin or aspirin if contraindicated.

Bleeding risk must be assessed at the outset of anticoagulation. The focus should be on high-risk categories - elderly, concomitant anti-platelet or non-steroidal anti-inflammatory drugs, polypharmacy, uncontrolled hypertension, history of bleeding (peptic ulcer or intracerebral) or poorly controlled INR¹. In those conditions, anti-platelet therapy may be preferred.

In AF, oral anticoagulation is grossly underused¹ and, when used, anticoagulation control is inadequate¹¹. Contributory factors include physician non-compliance and informed dissent by patients who do not like frequent blood checks, dietary restrictions and risk of bleeding¹.

New antithrombotic agents e.g. direct thrombin inhibitors and oral factor Xa inhibitors show promise. These drugs are free of food/drug interactions and convenient to take without the need for monitoring. In preventing stroke in AF, ximelagatran is similar to warfarin but was withdrawn because of hepatotoxicity¹². Idaraparinux is more effective than warfarin but caused substantially more bleeding¹³.

The direct thrombin inhibitor, dabigatran, at low doses is equivalent to warfarin in stroke prevention and causes less bleeding while, at higher doses, dabigatran is superior to warfarin with a similar bleeding risk². The balance of benefits against risk at the two doses of dabigatran offers the prospect of dose-titration tailored to patient risk characteristics. Although the rate of myocardial infarction was higher on dabigatran, the composite of stroke plus myocardial infarction was numerically less than in those treated with warfarin. A dose-related increased risk of gastrointestinal bleeding with dabigatran may be a consequence of the pharmaceutical formulation.

Further outcome studies with new antithrombotic agents in high-risk AF will report shortly. These include ROCKET AF with rivaroxaban, and ARISTOTLE and AVERROES with apixaban. Warfarin may not remain the gold standard for anticoagulation in AF for much longer.

Primary care physicians need to be aware that AF is a major risk factor for ischaemic stroke. In patients with low stroke risk, antiplatelet therapy is appropriate. However, in moderate to high risk, consideration should be given to warfarin unless absolutely contraindicated, when aspirin plus clopidogrel is probably the best option. Dabigatran or another of the new antithrombotic agents may offer an attractive alternative in the not too distant future.

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2.1 The primary care management of the patient with heart failure and hypertension

Dr. Terry McCormack

General Practitioner, Whitby Group Practice

The prevalence of heart failure (HF) is usually quoted as about 2% in the UK but the Quality Outcomes Framework prevalence is closer to 1%. The prevalence rises to over 10% in the over 80's and therefore most of these patients are very elderly.

In the "developed world" ischaemic heart disease is the commonest cause of HF. Most patients with hypertension and HF have these two conditions as co-morbidities rather than HF caused by hypertension. Prior to modern therapies becoming available, hypertension was a common cause of HF. Hypertensive heart failure is usually associated with either left ventricular hypertrophy or Heart Failure with Preserved Ejection Fraction >45-50% (HFPEF) sometimes referred to as "diastolic heart failure". Patients with left ventricular hypertrophy will often be hypotensive, particularly in the advanced stages of their disease.

The European Society of Cardiology HF Guidelines 2008 recommend that in LV dysfunction the target BP is $\leq 140/90$ and $\leq 130/80$ in diabetics and high risk patients. In hypertensive patients with HFPEF they suggest that aggressive treatment, with several drugs of complimentary mechanisms of action, is used and that ACE inhibitors and ARBs should be first line.

In the Hypertension in the Very Elderly Trial (HYVET) we showed that the group treated with indapamide \pm perindopril had a 64% relative risk reduction of developing HF. A caution needs to be added, however, in that the subjects recruited were generally healthier than those within a general population and the target blood pressure was only 150/80 mmHg.

Drugs of complimentary mechanisms of action should be used in treating those with hypertension and HF. ACE inhibitors or ARBs are the obvious choices with evidence from CONSENSUS, SOLVD, ELITE I&II, Val-HeFT and CHARM. CHARM Preserved did not show a mortality benefit.

Loop diuretics are an evidence free zone in HF but of undoubted benefit. 40% of HF patients have eGFR < 60 and loop diuretics have more influence on BP in CKD. Spironolactone and eplerenone have HF evidence in terms of RALES and EPHEBUS and are known to have marked hypertension benefits in 1^o and 2^o aldosteronism. The beta-blockers bisoprolol, carvedilol, metoprolol and nebivolol have shown benefit in HF trials such as CIBIS II, COPERNICUS, MERIT-HF and SENIOR, despite their negative inotropic actions. Care is required in severe asthma, but they are not contraindicated. Slow titration should be adopted e.g. bisoprolol titrated up 1.25, 2.5, 3.25, 5, 7.5 and 10 mg in weekly steps. Calcium channel blockers are not contraindicated but less value, especially in CKD. Amlodipine has been shown to be safe (Packer M, et al. *NEJM* 1996; 335:1107-14). Alpha antagonists are difficult to use and best avoided.

Standing BP and the patient's weight are the best measurements. There is no benefit shown for the use of statins in HF. An audit of Whitby Group Practice patients with HF and hypertension will be demonstrated in the talk.

2.2 What do ABPM and home blood pressure measurements actually mean?

Professor John Potter

Professor of Ageing and Stroke Medicine, University of East Anglia, Norwich

It is over 100 years since the introduction of the mercury sphygmomanometer into clinical practice made the routine non-invasive measurement of blood pressure (BP) by auscultation possible. Despite the need for accurate BP assessment in the diagnosis and treatment of hypertension, it remains one of the clinical measurements to which little attention is normally paid. It is well-known that BP can vary considerably from beat to beat as well as by the minute, hour, day and season and these natural variations are compounded by the limitations of accurate clinical measurement. Even small errors in BP determination could result in thousands of patients in the UK being misdiagnosed and therefore receiving inappropriate treatment or the level of cardiovascular (CV) risk not being fully appreciated. However clear and precise guidelines for good clinical practice in clinic BP measurements are available¹ and if adhered to will overcome some of the inaccuracy associated with the measurement. Although mean values of clinic/office BP predict CV risk and the benefits of treatment, it is

becoming increasingly evident that other factors such as day/night BP change and variability in BP between recordings may have an equally important prognostic role, these aspects are often difficult to assess using conventional BP recording methods. This has led to the development of alternative forms of BP measurement, e.g. 24 hour ambulatory blood pressure monitoring (ABPM) and self/home monitoring (SBPM) which give more reproducible results.

The benefits of ABPM in more accurately predicting risk than conventional BP recordings were first shown more than 25 years ago. Since then the design and accuracy of ABPM monitors have improved significantly though they remain expensive compared to home BP monitors. ABPM is being increasingly used in primary and secondary care and guidelines from the BHS and European Hypertension Society regarding the indications for use and interpretation of the results have been published^{2,3}. There still remains much debate as to the most appropriate frequency of measurement though consensus views propose daytime measurements (0700 - 2200) should be made every 15 to 20 minutes and night-time measurements every 30 to 60 minutes. The best method of data analysis obtained from a 24-hour recording is also under scrutiny, mean daytime, night-time and 24 hour values are most frequently used, though other methods such as CUSUMS plots, Smoothness index etc may provide further important information. ABPM is useful in the assessment of patients with mild hypertension when treatment would be based solely on BP levels, in excluding whitecoat hypertension and whitecoat effect, in evaluating patients in whom office BP appears resistant to drug therapy, as a guide to determining drug efficiency over 24 hours, assessing unusual clinic BP variability, in identifying nocturnal hypertension and defining "dipper" status as well as picking up episodes of hypertension⁴.

Although SBPM was first described over 80 years ago, it is only over the last decade with the development of cheap, accurate and reliable monitors that the technique has become popular with both physicians and patients alike. As with ABPM, there is a good evidence to show that SBPM levels are a better predictor of the development of CV disease than the clinic measurements and, like ABPM, they can indicate patients with whitecoat or masked hypertension (where home BP values are higher than clinic measurements), a condition associated with increased CV risk. There is no general consensus as to the number and frequency of SBPM recordings for the diagnosis of hypertension although many authorities advocate measurements should be made twice in the AM and PM for 7 days, with the first days recordings being discarded and taking the mean of the resulting 24 recordings⁵. Threshold values for the diagnosis of hypertension have been suggested as >135/85 mmHg, values tending to be between 4-10/2-5 mmHg lower than office measurements⁶. SBPM is also more convenient for patients and better liked than ABPM giving empowerment to patients in terms of their treatment management. However disadvantages include the need for adequate patient training, the potential for reporting bias, unsupervised alteration of treatment and patient anxiety and the inability, compared to ABPM, to assess the night-time BP levels and diurnal change. The clinical role of SBPM has recently been reviewed⁷ highlighting its potential role in the diagnosis and long term monitoring of treatment.

Although few outcome trials have been based solely on ABPM or SBPM values, there are data to suggest these two methods are superior in predicting CV events than standard clinic measurements. There is little doubt that increasing reliance will be put on these two methods of measurement for the accurate assessment of CV risk and treatment effects. Whichever type of monitor is used however it is vital that it has been shown to be accurate and reliable.

Threshold levels of BP for the diagnosis of Hypertension according to measurement method

		SBP (mmHg)	DBP (mmHg)
Office		≥140	≥90
SBPM		>135	>85
ABPM	Day	>135	>85
	Night	>120	>75
	24-hr	>125	>80

SBPM = Self/home BP monitoring

ABPM = Ambulatory/24-hr BP monitoring

1 These figures do not necessarily equate with the need for antihypertensive drug treatment to be started, and therapy must be based on overall CV risk as well as absolute BP levels. Antihypertensive treatment should, however, be initiated in people with sustained office SBP ≥ 160 mmHg or sustained DBP ≥100 mmHg irrespective of other risk factors.

- 2 Lower levels of BP to initiate drug therapy may be considered in some instances, eg, presence of target organ damage eg post-stroke or in diabetes.
- 3 The highest value of SBP or DBP should be used for classification, whichever measurement method is used.

Suggested target blood pressures during antihypertensive treatment. Systolic and diastolic should *both* be attained, eg, <140/85 mmHg means *less than* 140 mmHg systolic and *less than* 85 mmHg diastolic

	Clinic BP (mmHg)		Mean day-time ABPM or home BP (mmHg)	
	No Diabetes	Diabetes	No Diabetes	Diabetes
Optimal BP	<140/85	<130/80	<130/80	<120/75
Audit Standard	<150/90	<140/85	<140/85	<140/80

Audit standard reflects the minimum recommended levels of BP control.

Despite best practice, the Audit Standard will not be achievable in all treated hypertensives.

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2.3 Preventing cardiovascular disease in type 2 diabetes mellitus - priorities for optimal intervention

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Patients with type 2 diabetes (T2DM) are particularly prone to coronary heart disease (CHD) with up to 80% of diabetic patients dying of a cardiovascular (CV) event. One of the key objectives in the management of T2DM is therefore to prevent CV disease.

This preventive process essentially involves providing optimal control of glucose, blood pressure (BP) and lipid levels and stopping smoking. There is no argument about the appropriateness of smoking cessation, although overall, the effectiveness of doing so is less than for the other 3 risk factors because such a relatively small proportion of smoking patients are successful in stopping smoking. One way of addressing all 3 of the other risk factors which need attention is through beneficial changes to diet and lifestyle.

Dietary measures to reduce weight result in improvements in glucose, lipid and BP levels as do increased aerobic exercise output. However, once again the medical profession have tended to be unsuccessful in persuading their patients to lose weight and/or to take up exercise.

More effective ways of lowering glucose, BP and lipid levels are the use of oral hypoglycaemic, antihypertensive and lipid-lowering agents respectively. Furthermore, compliance with these medications - although far from optimal - is better than with achieving diet and lifestyle changes. Therefore whilst the vast majority of T2DM is due to overweight and lack of exercise and optimal prevention of T2DM requires revolutionary changes in the

typical Western diet and lifestyle, pragmatism demands that pharmacological intervention is needed to treat T2DM.

Evidence for the benefits of lowering blood glucose or HbA1C are clear but in the short to medium term the benefits largely relate to microvascular events, particularly renal events, with possibly deferred benefits on major CV events.

By contrast the benefits of BP-lowering on both microvascular and macrovascular CV events have been apparent for many years. Furthermore the Blood Pressure Lowering Treatment Trialists Collaboration (BPLTTC) have provided compelling analyses that suggest that more versus less BP lowering - irrespective of starting BP level - is effective in preventing major CV events. Current UK guidance recommends treating any patient with T2DM and either a systolic BP ≥ 140 mmHg or a diastolic BP ≥ 90 mmHg. The recommended choice of agent is less consistent in guidelines but the majority of patients need ≥ 2 agents to reach current targets ($< 130/80$ mmHg) and the BHS recommendation to include a RAS blocker (ACE-inhibitor or ARB) as part of the cocktail of agents needed, seems reasonable. Beta-blockers and to a lesser extent diuretics are less logical agents to use for patients with T2DM.

The evidence for the use of statin therapy for patients with T2DM is perhaps strongest of all. Major benefits in CV events associated with the use of statins have been shown in patients with T2DM whether in the context of primary prevention (e.g. CARDS) or secondary prevention (e.g. HPS) and the size of the benefit is substantial and consistent. Whilst to consider those with T2DM as "coronary equivalents" is strictly inaccurate it does seem reasonable to treat all patients with T2DM with a statin except possibly newly diagnosed, young (< 40 years) patients.

The question of whether to use aspirin for all or some patients with T2DM has recently been questioned. Pending currently ongoing trial evidence it seems reasonable to recommend aspirin for all those with T2DM who have established CVD or are at high estimated CV risk (e.g. $\geq 20\%$ 10 year risk).

In summary the best evidence for preventing CV disease in patients with T2DM supports the use of a statin, BP-lowering agents, and oral hypoglycaemic agents - in that order, with aspirin as a possible add-on.

3.1 Does elevated blood pressure in childhood equate to increased risk?

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The prevalence of essential hypertension in teenagers has increased significantly over the last 20 years. Recent data from the USA and Europe suggest that $\sim 5\%$ of teenagers meet the current BHS diagnostic criteria for hypertension. The reasons for this dramatic rise are incompletely understood, but increasing levels of childhood obesity, reduced physical activity and higher salt intake in young people are probably all important. The prevalence of secondary hypertension appears more static, with renal parenchymal disease accounting for the majority of cases. However, careful screening for secondary hypertension in all hypertensive teenagers is important, particularly if they have marked elevation of blood pressure, or present at a particularly young age.

Hypertensive teenagers typically present with labile blood pressure, which may lead to confusion over diagnosis. The usual pattern of blood pressure elevation is isolated systolic hypertension. Physiologically this appears to be driven mainly by an excessive cardiac output and failure to adapt to this by reducing peripheral vascular resistance. However, aortic stiffening may also be important in some individuals. It is likely that this will transform into mixed systolic/diastolic hypertension over time as the cardiac output declines and peripheral vascular resistance increases, for reasons that remain incompletely understood. As such, young hypertensives provide an ideal group to investigate the potential underlying causes of essential hypertension. There are no outcome studies in young hypertensives, and the current treatment strategies and targets extrapolate from data in older subjects. Interestingly, there is some evidence that beta-blockers may be more effective in younger people, but current recommendations are to start with an ACE inhibitor, unless contra-indicated.

Traditionally, essential hypertension has been viewed as incurable. Indeed the results of the TROPHY study in the USA recently confirmed this in a cohort of largely overweight middle-aged men. However, whether life style or pharmacological intervention will arrest the development of fixed hypertension in much younger people remains to be fully tested.

3.2 New treatments for diabetes and cardiovascular risk

Professor Graham Hitman

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There is currently a world-wide epidemic of diabetes with the epicenter being in the South East Asian sub-continent; this is also reflected in ethnic minorities living in the UK. Seventy-five percent of all people with diabetes will die of cardiovascular disease (CVD) and at presentation of type 2 diabetes, 50% will already have some evidence of vascular disease. It is therefore clear that the priorities are to implement strategies to prevent diabetes but more importantly its cardiovascular consequences and to aggressively treat CVD risk factors in people with established diabetes. In type 2 diabetes, the UKPDS established that the most important risk factors for myocardial infarction were in rank order: LDL cholesterol, HDL cholesterol, HbA1c, systolic blood pressure and smoking. Evidence base medicine also indicates that the most cost effective measures to prevent cardiovascular disease in type 2 diabetes is to reduce the cholesterol and blood pressure and if appropriate smoking cessation. Strategies to reduce CVD by lowering glucose are not as successful as with cholesterol and blood pressure. Nonetheless in established diabetes lowering glucose has a major impact on reducing the microvascular complications of diabetes.

Why is it that reducing glucose has not lived up to its potential to prevent cardiovascular disease in diabetes and what are the implications for clinical practice - evidence from random clinical controlled trials are providing the clues? Firstly, in contrast to therapies directed to lowering cholesterol and blood pressure, glucose lowering therapies take longer for the effect to be found and are more effective in the earlier stages of the disease. The most effective and safest strategy to delay the onset of diabetes and potentially cardiovascular disease is lifestyle modification. The use of pharmacotherapy in otherwise well individuals at risk of diabetes is less certain apart from the use of metformin. Metformin is one of the few drugs that have been shown to have cardiovascular benefits in patients with type 2 diabetes who are overweight, and for this reason all international guidelines recommend the use of metformin as the first line treatment for type 2 diabetes after a trial of lifestyle intervention. The early use of sulphonylureas and insulin in UKPDS (type 2 diabetes) and insulin in the DCCT (type 1 diabetes) have also translated to CVD benefits but only in the long term. In people with established diabetes the use of insulin to achieve tight glycaemic control in a RCT setting has been controversial with one of the 3 studies terminated early because of an increased risk of death from cardiovascular causes (ACCORD compared to ADVANCE and VADT). A clue to the disbenefit may come from the two-fold risk of hypoglycaemia in these trials.

The current licensed glitazones (rosiglitazone and pioglitazone) were launched many years ago with the great promise that because their main effect was on insulin resistance, they would not only treat diabetes effectively but would reduce cardiovascular disease. This class of drugs also illustrate the pitfalls of making such assumptions, since it soon became apparent that side effects included heart failure, weight gain, a change in lipids and anaemia. Furthermore, in the long term at best the glitazones are neutral for cardiovascular disease and for rosiglitazone there may be disbenefit. Lastly, it has also become apparent that this class of drugs increases the risk of small limb fracture.

There are many new drugs on the market and several in the pipeline to treat type 2 diabetes; again with great promise. Currently we have the DPP4 inhibitors (sitagliptin and vildagliptin) and GLP-1 agonists (exenatide and liraglutide), however, as yet we have no long term data on cardiovascular safety. In the wings we have inhaled insulin, sodium glucose transporter 2 blockers, selective PPAR γ modulators and glucokinase activators.

The FDA, NICE and other licensing authorities recognise the benefits of glucose lowering in those who cannot achieve adequate glycaemic control and have issued guidelines for a stepwise approach to the treatment of diabetes using established drugs including the glitazones. The newer drugs should be considered in specific patient groups and as an alternative to the established drugs if they are not tolerated or fail to achieve glycaemic control. Once we have data on hard end points relevant to cardiovascular disease then these guidelines can be relaxed.

Suggested reading

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3.3 Hypertension management in anticipation of pregnancy

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Management of hypertension in women who are at a fertile age must consider the possibility of pregnancy and in this regard, three issues are important;

1. Has a secondary cause for hypertension been excluded?
 2. Is the blood pressure under control?
 3. Is the anti-hypertensive medicine safe in pregnancy?
1. Secondary causes of hypertension are associated with recurring poor pregnancy outcome. Identifying and correcting secondary hypertension before pregnancy often eliminates the need for treatment, improves pregnancy outcome and avoids management decisions that are much more difficult during pregnancy. Even pre-pregnancy bariatric surgery has been shown to reduce the risk of hypertensive disorders of pregnancy and improve pregnancy outcome.
 2. Women with labile and severe hypertension in early pregnancy have a worse pregnancy outcome compared with women who have controlled hypertension. Approximately 20% of women with chronic hypertension develop pre-eclampsia, a multi-system syndrome of the second half of pregnancy characterized by a rise in blood pressure and proteinuria. Conversely, blood pressure targets in pregnancy are more liberal than for the chronic management of hypertension outside of pregnancy. Over-treatment and relative hypotension reduce perfusion pressure in the utero-placental circulation and impair fetal growth. A pragmatic target range for blood pressure control in women with chronic hypertension has been suggested by the forthcoming (as yet unpublished) NICE guideline as 130/80 to 150/100mmHg. Prospective studies are testing tight versus less-tight BP control on pregnancy outcome.
 3. Anti-hypertensive drugs that inhibit the renin-angiotensin pathway are teratogenic in the first trimester and impair renal and cardiac development in later pregnancy. It is preferable, therefore, to use an effective alternative in anticipation of pregnancy. However, some women may be denied the benefits of ACE-inhibitors or angiotensin II receptor blockers in a prolonged attempt to conceive. If a woman has regular periods and is aware enough to identify pregnancy within a few days of missing a period, then stopping these drugs at that time will prevent the early pregnancy anomalies. Interference with embryonic development is recognized after 6 weeks of pregnancy.

Calcium channel blockers, especially long acting nifedipine preparations, but also amlodipine have been safely used throughout pregnancy without adverse outcome. Labetolol is also widely and safely used, but it is not as effective as atenolol at lowering blood pressure. Atenolol has, however, been associated with fetal growth restriction in high doses. Judicious use of atenolol is a good choice for hypertensive women with an insulin resistant phenotype and a hyperdynamic circulation. Diuretics are not indicated for anti-hypertensive use in pregnancy, as they attenuate plasma volume expansion and cause fetal growth restriction. Methyldopa is then relegated to its place outside of pregnancy as a third or fourth line antihypertensive with unpleasant side-effects.

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