

Special report on South African Cardiovascular Risk Management Symposium

A recent update meeting, held in major centres in South Africa and sponsored by Bayer HealthCare, provided useful data and practical advice from South African experts on improving cardiovascular and diabetes risk management in daily practise.

High-risk hypertensives – at the end of a continuum

‘I don’t believe hypertension itself is a disease’, says Prof James Ker of the University of Pretoria. ‘There is no level below which we do not see resultant disease, except of course 0/0 mmHg, which is death! Rather, it is the target-organ damage caused by high blood pressure, along with other conditions like the metabolic syndrome, that kills.’

Epidemiological data based on 61-million patient years show that risk increases in a continuous line with increasing blood pressure. ‘Factor in target-organ damage or cardiovascular disease and the line becomes a parabola’, says Prof Ker. ‘The more abnormalities a patient presents with, the higher the risk’. Blood pressure is a component of cardiovascular risk and this can be well illustrated in a simple visual concept (Fig. 1).

Blood pressure-related disease in patients is often under-treated. Even a normotensive with other risk factors could also be on antihypertensive treatment if the absolute cardiovascular risk is high. Blood pressure lowering has benefits, regardless, and it’s important to identify sub-clinical organ damage and diagnose conditions like type 2



Professor James Ker, Department of Medicine, University of Pretoria

diabetes mellitus. If a patient is at a high absolute cardiovascular risk, his/her blood pressure is too high, regardless of what the actual measurement is. So give medication and apply stringent target levels. ‘There is also a need for rapid control of blood pressure and a week or two can make a difference to overall risk of CV events in high-risk patients’, says Prof Ker.

Prof Ker has a different opinion of guidelines. ‘A guideline represents the minimum therapy you should give. Realistically, two to four drugs are needed to achieve a stringent target, and

Take-home messages in the treatment of high-risk hypertensives

- Blood pressure must be rapidly controlled. Prescribe drug therapy even in high-risk normotensives. Combine drugs – most are safe and effective – and treat towards a target. Be sure to give a drug that reduces central aortic pressure.
- Focus on end-organ protection. Assess any organ damage and treat.
- Reduce the atherosclerotic burden – give a statin.
- When everything is under control, remember the value of low-dose aspirin.

compliance and cost factors need to be taken into account. This concept has led to the “polypill idea”.

Proper treatment and control of blood pressure can virtually eliminate the predicted blood pressure-related stroke risk, even though coronary artery disease may not be reduced to the same extent. ‘It therefore makes sense to combine a calcium channel blocker

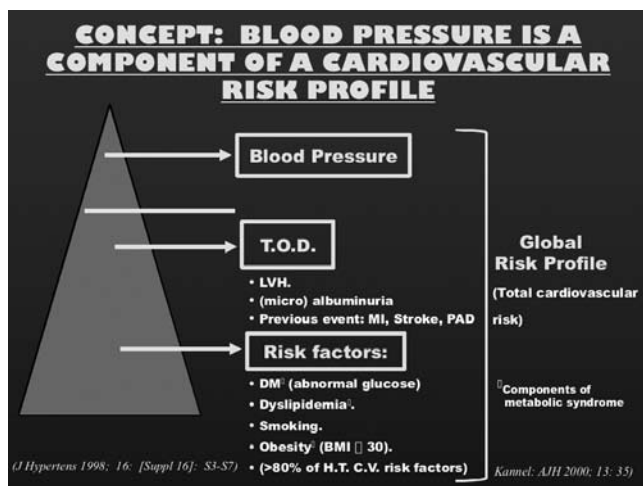


Fig. 1. Blood pressure is a component of a cardiovascular risk profile.

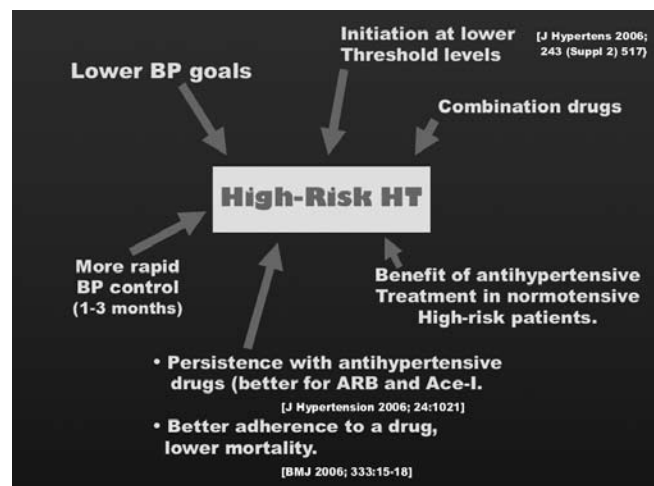


Fig. 2. Treat to prevent MI or stroke, or both.

(CCB) to reduce stroke together with an ACE inhibitor to lower total mortality and cardiovascular disease. There's no clinical test that can predict whether a patient will suffer a stroke, MI or both. So treat to prevent both (Fig. 2). The drugs currently available are effective and safe'.

It has been well documented that even treated hypertensives have an increased risk of cardiovascular complications relative to normotensives. There are numerous reasons for this, including modifiable risk factors like target-organ damage, dyslipidaemia and poorly controlled systolic blood pressure, and non-modifiable risk factors such as a family history of cardiovascular disease.

'The lipid-lowering arm of the ASCOT trial showed the value of statins in hypertensives because they reduce coronary events (fatal and non-fatal).' Prof Ker cautions, however, that older beta-blockers – and specifically atenolol in high doses – have no place in preventative therapy because of their metabolic side-effect profile and lack of cardiovascular protection.

'New-onset type 2 diabetes consequent on drug treatment carries the same excess risk as diabetes at baseline. Angiotensin receptor blockers (ARBs), ACE inhibitors and CCBs, by contrast, show a reduction in new-onset diabetes. We're still unclear as to the exact mechanisms involved, but there's no doubt that it is happening. So this is

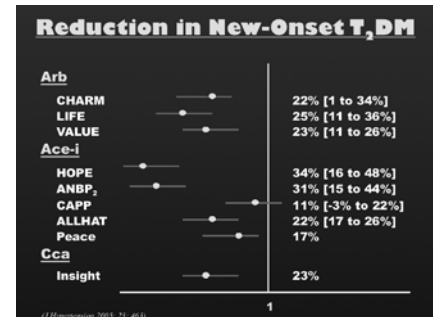


Fig. 3. Reduction in new-onset T₂DM.

yet another argument in favour of using these drugs' (Fig. 3). 'And remember', concludes Prof Ker, 'that it's pointless to reduce blood pressure without also addressing myocardial infarction, renal failure, stroke and dyslipidaemia.'

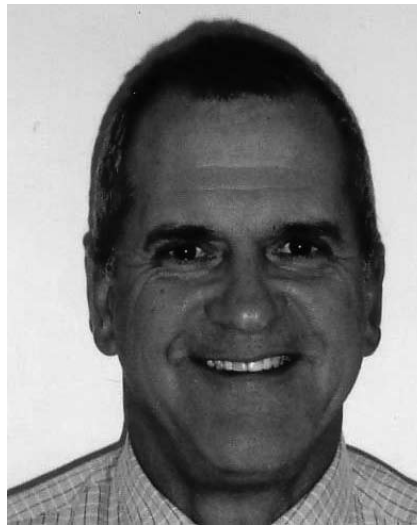
Hypertension guidelines in clinical practice

Dr Adi Horak noted that in his view, clinical guidelines can play an important role in disease management because they represent an accessible and comprehensive consensus of potentially conflicting opinions. 'They're evidence based, tailor made for a disease and a population, and ensure a consistent standard of care and realistic expectations.'

When it comes to hypertension specifically, while he acknowledges the important role played by the JNC-7 guidelines, and those of the European Societies of Hypertension and Cardiology, respectively, he is of the opinion that the new South African Hypertension Guideline, published earlier this year, is currently the most appropriate guide for South African physicians. The guidelines cover all aspects of the disease management process: diagnosis, risk assessment and stratification, investigations, clinical implications and treatment.

Diagnosis and risk assessment

'Use an approved measurement device and be sure to measure both arms at the first consultation. Repeat the measurements on three separate occasions within two months of the first consultation. Twenty-four-hour blood



Dr Adi Horak, cardiologist (private practice), Cape Town

pressure monitoring is not routine, but is indicated in certain patient such as the elderly and diabetics.'

'When it comes to risk assessment, established risk factors are age, smoking, dyslipidaemia, a family history of hypertension, and central obesity.' Dr Horak points out that as yet there is no consensus on the importance of the metabolic syndrome but that the newest data indicate that it does indeed increase the risk, as it is an inflammatory condition, raising the blood levels of C-reactive protein (CRP), which is a

marker of inflammation. 'High blood levels of CRP correlate with the risk of cardiovascular disease and death', he says. Target-organ damage is also a key consideration when assessing hypertensive patients. In this regard, an ECG is necessary to assess left ventricular hypertrophy. Patients should be investigated for arterial wall thickening, microalbuminuria and increased levels of serum creatinine (Table 1).

The range of investigations in the South African Guidelines are subdivided into 'routine', 'recommended', and 'extended', and the decision on how far to go should be guided by the findings of the early tests. 'The extended investigations comprise complex tests of cardiac, cerebral and renal function', says Dr Horak, 'as well as the search for secondary hypertension.'

'The responsible physician's judgment remains paramount. I wish we could get that across to the funders', says Dr Horak.

Once diagnosed

'Once blood levels and overall risk have been established, the physician needs to determine when to initiate therapy and what that should comprise. Lifestyle modification should be initiated first, although this is often easier said than

Table 1. Stratification of risk to quantify prognosis (*Based on the European Society of Hypertension/European Society of Cardiology guidelines)

BP (mmHg)					
Other risk factors and disease history	Normal SBP 120-129 Or DBP 80-84	High-normal SBP 130-139 Or DBP 85-89	Stage 1 Mild Hypertension SBP 140-159 Or DBP 90-99	Stage 2 Moderate hypertension SBP 160-179 Or DBP 100-109	Stage 3 Severe Hypertension SBP >180 Or DBP >110
No other major risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 major risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
≥ 3 major risk factors Or target-organ damage Or diabetes mellitus	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Associated clinical conditions	High added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

done, and requires weight loss, reduction in salt and alcohol intake, regular exercise and no smoking. With regard

to drug therapy, bear in mind the limits of trial data. Clinical trials usually involve high-risk patients in artificial

conditions different from those of real-world medical practice. Compliance is usually higher, the trials are not powered for secondary endpoints and, very importantly, they last for a number of years – regular patients may be lost to follow-up much sooner in a real-world setting’.

Dr Horak cautions that the targets in guidelines are not always easy to achieve in high-risk patients. ‘A systolic blood pressure under 140 mmHg is difficult to achieve; it’s also important to factor in pulse pressure, as well as the variance between systolic and diastolic pressures. Bear in mind, too, that blood pressure-lowering drugs are beneficial, even in patients without hypertension who have coronary heart disease.’

When it comes to drug therapies, the new South African Guidelines spotlight three drug classes – thiazides, ARBs/ACE inhibitors and CCBs. The latter are recommended for stroke, ACEIs

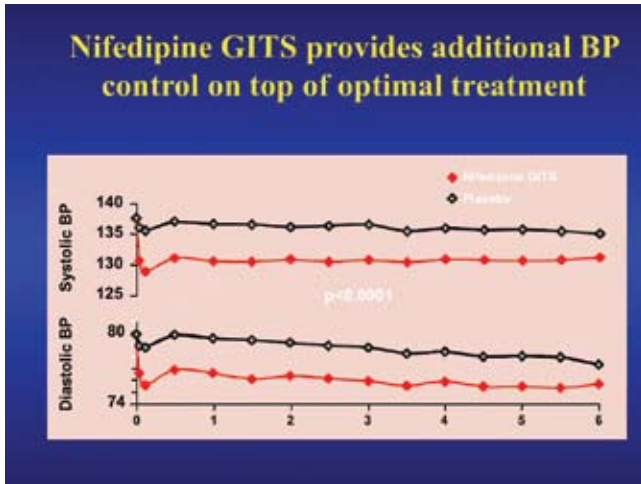


Fig. 4. Nifedipine GITS – additional BP treatment.

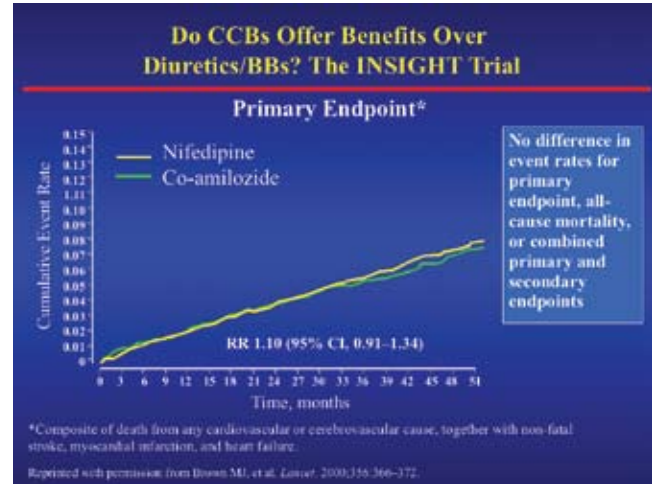


Fig. 5. Do CCBs offer benefits over diuretics/BBs?

and ARBs for renal protection, while ACEIs should also be first choice in patients who've suffered a myocardial infarction. Beta-blockers are no longer recommended because they've been shown not to reduce the cardiovascular morbidity and mortality associated

with hypertension. Most recently, the ASCOT trial showed convincingly that a combination of CCB/ACEI is by far the best overall option for lowering blood pressure. The ACTION and INSIGHT studies have provided further important data (Figs 4, 5).

'The key message', Dr Horak concluded, 'is that most hypertensive patients require more than one drug to reach goal, and the doctor needs to keep in mind that different drugs have different synergies. Where appropriate, use a fixed-dose combination.'

The complex cluster

Defining and treating the metabolic syndrome

Addressing the issue of the metabolic syndrome, Prof Lionel Opie asked the following questions: 'What is it? Can it be simplified? What can we do about it?'

'It's just not clear cut', he noted, pointing out that it is difficult to define the metabolic syndrome precisely, given that the risk-factor definitions differ from country to country. Waist measurements, for example, are arbitrary cut-offs. 'But the definitions are not really that important. What is important is that there is no doubt that the metabolic syndrome consists of five components and leads to type 2 diabetes mellitus and increased cardiovascular disease. The risk factors are linear and have a tendency to cluster. The more of them that are present, the greater the risk. Also, the mechanisms whereby each of the risks act are clear, which means this is a *bona fide* syndrome and not just an arbitrary group of risk factors.'

Currently any three of the following five risk factors need to be present for a diagnosis (Fig. 6):

- blood pressure above 130/85 mmHg
- abdominal obesity (most conservatively above 102 cm in men, above 88 cm in women; lower values are given by the International Diabetes Federation)
- fasting plasma glucose levels of 5.6 mmol/l or higher
- blood triglyceride levels of 1.7 mmol/l or higher
- blood HDL levels lower than 1.1 mmol/l in men or 1.3 mmol/l in women.

'The most essential piece of equip-

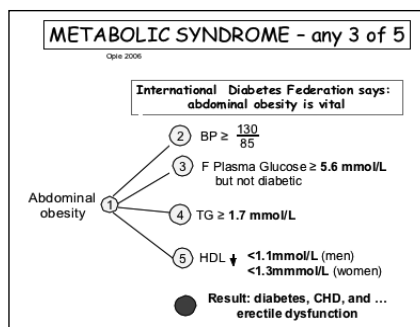


Fig. 6. Metabolic syndrome.



Professor Lionel Opie, director of the Hatter Institute for Cardiovascular Research and the Cape Heart Centre, Cape Town

ment when assessing patients is a simple tape measure to measure the waist. We now know that adipose tissue is not just a benign lump of fat, but rather something that is hormonally very active. Dietary hyperphagia leads to the formation of adipose tissue. Abdominal obesity, in its turn, precipitates higher levels of free fatty acids (FFAs), which initiate the chain of reduced glucose uptake and its consequences.'

The most sensitive indices are an early enlarged waist circumference, which reflects the amount of lipids around the internal organs, and an early increase in blood triglyceride levels. Indeed, the combination of these two gives as accurate a prediction of future adverse events as does the conventional three or more of five criteria (*Circulation* 2006; 111: 1883). 'And remember that neither of these is mentioned in the Framingham risk calculations', says Prof Opie. 'Free fatty acids and glucose come together in the liver to make triglycerides, which combine with HDL to create triglyceride-rich HDL, which in turn is broken down into small, dense HDL. This means, in short, that when triglycerides go up, HDL comes down.'

Therapeutic strategies in dealing with the metabolic syndrome

Lifestyle modification is imperative

when there is insulin resistance and should be the initial area of focus. 'Patients need to eat less and exercise more', says Prof Opie, acknowledging nonetheless that this can be easier said than done and that doctors need to be realistic about what they can persuade patients to do. When it comes to pharmacological treatments, he is optimistic that cannabinoid receptor blockers like rimonabant, which decrease appetite, will be an important part of the answer. (Glitazones also help in non-diabetics, as does metformin.) Studies have shown that rimonabant impacts positively on all risk factors, and that even modest weight loss – 5% of total body mass – was of benefit, significantly reducing the risk of new-onset diabetes.

Prof Opie noted that there are five healthy habits patients need to follow and that following all five can prevent 62% of coronary events. Exercise for 30 minutes daily; eat lots of fruit and vegetables; drink alcohol moderately; don't smoke; and be 'waist and weight' conscious. 'Men need to emulate women in the latter regard, as they are generally far more conscious of this than men.'

The role of erectile dysfunction

Prof Opie also underscored the important of erectile dysfunction (ED) when evaluating male patients for the metabolic syndrome. 'Incidence of ED is 50% higher in those with the syndrome, and these patients should be questioned about ED. It starts with the endothelium, which is protective against atherosclerosis until it becomes damaged. ED is a consequence of endothelial dysfunction.'

Eating a Mediterranean diet has been shown to improve ED in patients with the metabolic syndrome, resulting in improved endothelial function and reduced C-reactive protein levels. In addition to such lifestyle measures, PDE5 inhibitors are important, as is the treatment of associated hypertension and dyslipidaemia. 'But bear in mind that PDE5s interact adversely with nitrates in patients with established heart disease', says Prof Opie.

In summary, Prof Opie noted once again that the metabolic syndrome

begins with abdominal fat, which gives rise to four other features (of which high LDL cholesterol is, however, not

one). Each of the five factors is a graded cardiovascular risk, and doctors need to do a lipogram, and measure sugar

levels, blood pressure and abdominal girth. Lifestyle modification should precede drug therapy.

**It takes three: regaining the couple's satisfaction
Focusing on sexual problems**

'Make it your new resolution to screen patients for sexual problems', says Dr Esther Sapire. 'Talking about sex is not easy, as there are still taboos associated with the subject. Studies have shown that doctors are reluctant to ask about sexual dysfunction, yet eight out of 10 patients who have concerns in this regard would like the doctor to raise the issue. And often when doctors do ask, and receive an affirmative answer, they don't know how to respond, as it is very difficult to find the appropriate language and terminology, and in some cases they do not feel competent about managing sexual problems.'

Sexual dysfunction is common and 50% of divorces are associated with sexual problems. Erectile dysfunction specifically affects 30 million men in the USA and is severely under-treated, in that fewer than two out of 10 men receive help. Many misconceptions about ED persist, notably that it is an inevitable consequence of aging, that the causes are mainly psychological, that treatment options are limited and may be risky and that it isn't especially important, anyway (Fig. 7).

'But', continues Dr Sapire, 'it's very important to deal with ED, especially because of its association with various other forms of morbidity, such as depression, hypertension and diabetes. Further investigations may uncover other issues, such as non-compliance with medication, and increasingly ED is



Dr KE Sapire, general practitioner/sexologist, Cape Town

also being recognised as an early symptom of cardiovascular disease, given that both share common risk factors. It is essential that these co-morbid conditions be uncovered and treated. ED is a vascular disease and can be considered a precursor to systemic vascular disease. It is associated with age but is not an inevitable consequence of aging', she says.

'It's also noteworthy that the depression, frustration and consequent avoidance of sexual situations associated with ED impact on the partners of these men', says Dr Sapire, who talks about the importance of the treatment triad when it comes to addressing sexual dysfunction, namely patient, partner and physician. 'It is important to restore satisfactory sex, not just the erection, and partner involvement is a must, especially if the partner has adjusted to being non-sexual. Menopause affects

sexual function in women and if this is the case, we need to recognise that many symptoms such as dry vagina and dyspareunia can be relieved by hormone replacement therapy.'

'Various treatments exist for ED, but first choice should be oral PDE5 inhibitors. The patient must be informed about the medications available and he will often choose the one that suits him best. They're convenient, reliable, well tolerated, effective and "natural" in that they work only in response to stimulation'. The latter is another key issue in that older men, even those without ED, need direct tactile stimulation and no longer respond automatically to visual stimuli (Fig. 8).

Addressing false expectations and communication barriers

Too often patients meet doctors with closed ears. Some of this can be ascribed to embarrassment and lack of knowledge, and time constraints. 'But', says Dr Sapire, 'it is our responsibility as doctors to let patients know that we're willing to discuss their sexual problems and to provide help, or refer if necessary. Ask open-ended questions in the course of a consultation, thus opening the door so that patients feel comfortable asking for help. And when they do, we need to look at such crucial issues as relationships, false expectations, self-

Take-home messages

- ED is a marker of other medical conditions.
- Look for these co-morbidities and treat them if found.
- PDES inhibitors are the first-line treatment for ED and are effective and safe.
- Control both the patient and his partner to ensure the restoration of intimacy and sexual satisfaction, and not just an erection.

Why Ask About ED?

ED may be an indicator of an undetected physical or psychological disease

The treatment of ED improves

- Quality of life
- The patient's level of satisfaction
- Relationship between the doctor and patient
- Self-esteem
- Symptoms of depression if these are causally related to ED

Fig. 7. Why ask about ED?

Treatment Strategies

- Address risk factors and co-morbidities
 - Obesity
 - Diabetes control
 - Smoking, alcohol
 - Exercise
- Prescription and non-prescription drug use
- Hormone replacement therapy
- Counselling
- Education
- Medical treatment for ED
- Follow up

Fig. 8. Treatment strategies.

worth issues and communication problems.’

‘The whole objective in cases of sexual dysfunction is to restore physical and emotional intimacy, and sometimes all that is required is a change of attitude. We need to focus on the importance of a “sensate journey” that doesn’t necessarily always lead to intercourse. Even if a physical impairment has made intercourse difficult or impossible, couples should still be able to make love, by focusing on caressing, kissing, touching and fantasy, as making love is not only about penile penetration.’ She notes too that performance anxiety affects many men, along with concerns about penis size. ‘Smaller penises are equally functional and size makes no difference to a woman’s enjoyment. Over many years of treating sexual problems, I’ve never heard a woman say her partner’s penis was too small.’

Quotable quotes

Dr Etienne Kok, principal medical officer/senior lecturer, Andrology Unit, Department of Urology, Pretoria Academic Hospital and University of Pretoria Faculty of Health Sciences and head of the Sexual Dysfunction Clinic

Dr Kok presented ‘signposts’ that can assist the primary care practitioner to talk more easily to his/her patients about the common misunderstandings of sexual attitudes between partners. Some of these pointers are underlined in these expressive quotes.

‘Good sex begins with “good morning”!’

‘Men find women in front of stoves irresistible, but women do not feel sexy in the kitchen.’

‘Romance, romance, romance – is the number one sexual stimulus for a woman!’

‘When it comes to sex, men are destination orientated and women are journey orientated.’

‘The key to successful intimacy is to take each other on a journey of mutual discovery. And it’s important to have traveled that road before – alone or with others.’