MANAGEMENT OF BLOOD PRESSURE CONTROL: AT THE CUTTING EDGE

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MEETING SUMMARY

Prof Williams opened the symposium by discussing the current state of blood pressure (BP) control in Europe and the key barriers to improving BP control rates. Prof Weiss presented the 'Low BP in Vienna' initiative that has been initiated in Austria in order to improve BP control. Prof Mourad discussed the ongoing campaign to improve BP control rates in France, and Prof Volpe presented a case study of an elderly patient with hypertension and chronic kidney disease (CKD). Prof Parati concluded the symposium by commenting on the improvements in technology with respect to BP control.

The meeting objectives were to review the current achievement of BP goals in Europe since 2008; to evaluate the 70% BP goal initiatives in France and Italy; to use practical examples to assess the use of single-pill fixed-dose combinations (FDCs); and to assess the impact of technological advances on BP control.

Chairperson's Introduction: What Are the Key Barriers That Are Holding Back Improvements in Blood Pressure Control in 2015?

Professor Bryan Williams

Rates of BP control (BP <140/90 mmHg) are suboptimal in the majority of countries across Europe, with many countries having a control rate <50%.[1-3] Barriers to achieving optimal BP control, identified in the 2013 guidelines from the European Society of Hypertension (ESH) and European Society of Cardiology (ESC), include therapeutic or physician inertia; low patient adherence to therapy; and deficiencies within the healthcare systems that do not encourage or allow for a system-wide approach to improving treatment.[4] Achieving good BP control will result in significant savings to the healthcare economy, despite the costs of therapy. In the USA, 56,000 fewer cardiovascular events and 13,000 fewer deaths would occur each year if previously untreated patients were treated according to the guidelines.[5,6]

Non-adherence to treatment is a significant issue and may have significant consequences in this high-risk illness. A study of 367 patients with uncontrolled hypertension, including 108 with treatment-resistant hypertension, showed that, of the patients with uncontrolled BP (n=76) on ≥4 drugs, half (53%) were non-adherent, of whom 30% demonstrated complete non-adherence to treatment when blood drug levels were tested.[7] A direct relationship has been demonstrated between the number of drugs that a patient is prescribed and the likelihood of the patient being adherent, with patients on more medications being less likely to adhere to therapy (Figure 1).[8]

A simplified treatment approach, such as the Simplified Therapeutic Intervention to Control Hypertension (STITCH)-care algorithm used in Canada, may be a potential solution to non-adherence. A study has demonstrated significantly improved levels of BP control using the STITCH-care algorithm, in which patients were started on treatment with a combination of two treatments with subsequent up-titration of dose and addition of further diuretics in a step-wise approach, compared with the usual standard of care.[9] Similarly, a study in which patients were allowed to self-monitor their BP and up-titrate their own medication according to an algorithm found highly significant improvements in BP control compared with patients being managed by their regular physician.[10,11]

Non-adherence	New referrals	Follow-up	Referral renal denervation
% complete	8.8	9.1	23.5
% partial	9.6	28.8	0
Any	18.4	37.9	23.5

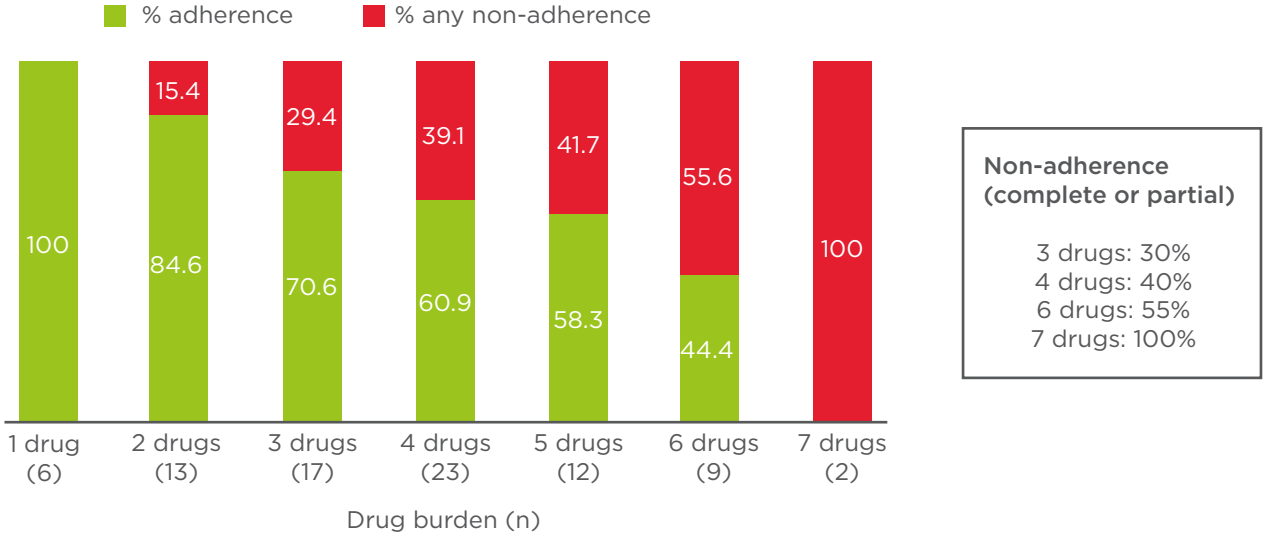

Figure 1: Blood drug-detection levels and adherence.[8]

Although efficacy of available medications has been demonstrated, two important questions remain: how can we encourage patients to take the medications, and how do we encourage the physicians to prescribe them?[12]

Blood Pressure Parameters Today: Has There Been Any Change Since 2008?

Professor Thomas Weiss

A white paper was published in 2008 in response to the suboptimal rates of BP control across Europe,[13] and which encouraged physicians to drive awareness of the dangers of hypertension, increase patient education, encourage patients to be more accountable for their health, and to simplify treatment. In comparison with European rates of BP control that range from 17–46%,[14-16] Canada has demonstrated superiority with 65% of patients achieving optimal control.[17] However, implementation of disease management programmes has improved rates of BP control in several European countries.[1-3]

In Austria, a prospective registry that includes approximately 10,000 patients has commenced in collaboration with the Pharmacists College Vienna (urban) and Lower Austria (rural). All patients with a prescription for an antihypertensive drug are included. Information collected includes BP, socioeconomic data, comorbidities, and comedications. These data will be used to obtain information on the types of antihypertensive medications that are prescribed and the percentages of patients with controlled BP, and will permit various comparisons such as BP control in rural versus urban areas.

In parallel with the registry, a hypertension management programme, 'Low BP in Vienna',[18] is being developed that aims to: enhance BP control in primary care; raise general practitioner (GP) awareness of BP control; introduce GPs to standardised and simplified titration measures with single-pill FDCs; provide data on BP control in primary care in Vienna; and identify patients with treatment-resistant hypertension.

The study is based on two concepts. Firstly, it aims to use an effective intervention in the general population as per the Canadian STITCH study. According to the STITCH algorithm,[9] a patient with uncontrolled hypertension starts on an angiotensin-converting enzyme (ACE) inhibitor and diuretic, or an angiotensin receptor blocker (ARB) and diuretic.

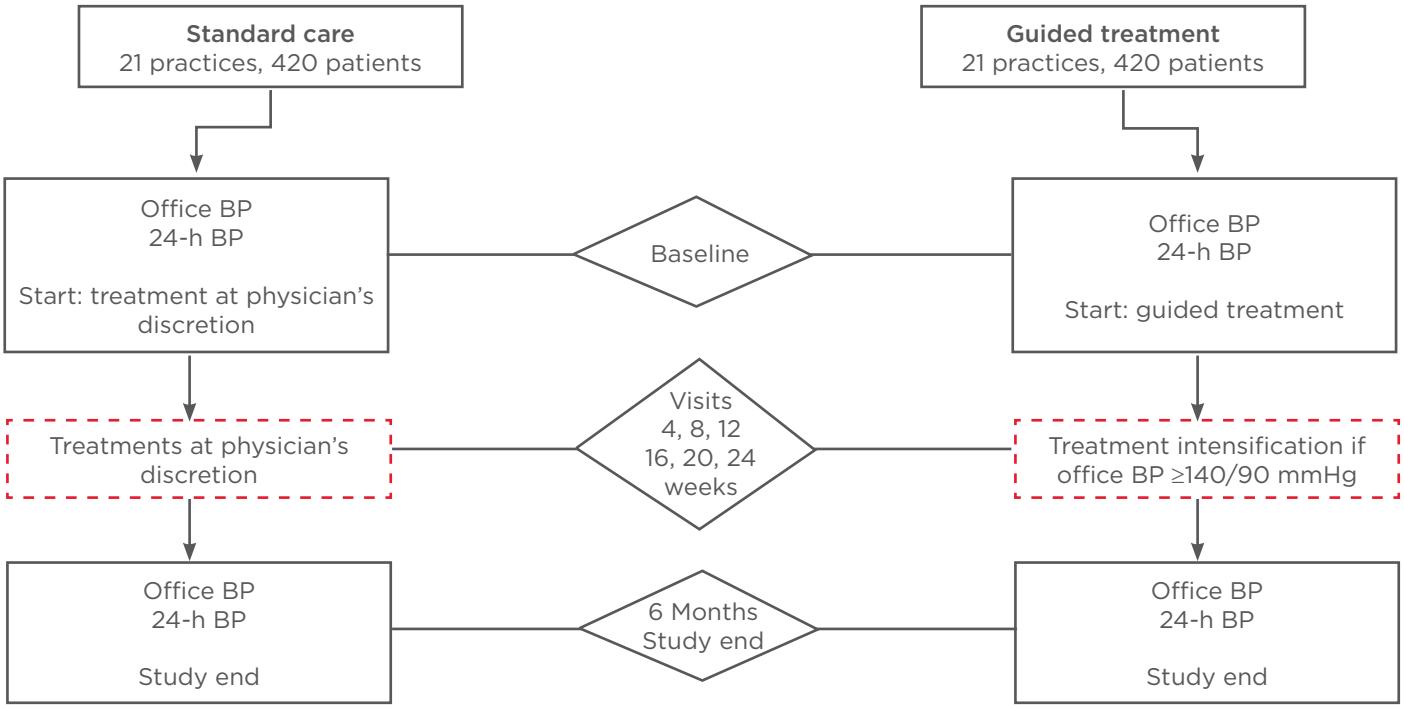

Figure 2: Low BP in Vienna study design.
BP: blood pressure.

If BP is not controlled, the medications are up-titrated to the highest dose. A calcium channel blocker (CCB) may be added and up-titrated, followed by an alpha or beta-blocker or spironolactone, if treatment remains unsuccessful. The second concept involves the use of a simple treatment regimen that is easy for the doctor and for the patient. The BP Control in all Subgroups with Hypertension (BP-CRUSH) trial evaluated olmesartan and amlodipine, prescribed at the lowest dose, using single-pill FDCs throughout the treatment regimen, resulting in maximum doses of olmesartan, amlodipine, and hydrochlorothiazide of 40 mg, 10 mg, and 25 mg, respectively.[19] The high level of BP control (90%) achieved in this trial may not be achievable in a real-world setting. However, even a smaller improvement will still be very important.

In the Low BP in Vienna trial, 840 patients from 42 practices have currently been included and results are expected in approximately 1 year. Physicians are randomised 1:1 to provide standard of care or the guided treatment protocol (Figure 2).

For standard of care, the treatment regimen is at the physician's discretion. Monthly visits are recommended but not protocol-mandated. In the guided treatment arm, treatment intensification is conducted as per the study's algorithm, based upon the BP-CRUSH algorithm[19] if office BP is above 140/90 mmHg. Patients begin with the lowest possible single-pill FDC of olmesartan and amlodipine, which is then up-titrated to the maximum dose of the triple therapy comprising olmesartan, amlodipine, and hydrochlorothiazide using single-pill FDCs throughout. Patients already taking antihypertensive medications start at different points in the algorithm, depending on their medical history. The primary endpoint is the proportion of patients with an office BP under 140/90 mmHg after 6 months; the secondary endpoint is improvement in 24-hour BP profile after 6 months.

Although there has been much improvement since 2008, 100% BP control has not yet been achieved. The 2008 white paper is currently being updated, with a focus on: achieving the BP target of <140/90 mmHg; reducing inertia to treatment intensification; simplifying treatment, e.g. through the use of FDCs; improving patient empowerment; and involving other stakeholders in the control of BP.

How Have Initiatives Implemented in France and Italy to Achieve 70% Blood Pressure Control Among Treated Hypertensives Changed the Situation?

Professor Jean-Jacques Mourad

The French Ministry of Health began a campaign against stroke in 2012, the objective of which was to achieve BP control rates of 70% by 2015.[20] Although the rate of BP control (45%) was good in comparison with some other countries, it was felt that the newer recommendations were not making any further improvements in BP control in France. The campaign aimed to focus on the two main barriers to improvement in terms of BP control rates: inertia with regards to treatment intensification and non-adherence to current therapies. The campaign's guidelines stated that patients' BP should be controlled within a 6-month period after initiation of antihypertensive therapy. If this was not possible, patients were to be referred to a specialist. It was recommended that GPs should switch to combination therapy after initial failure with monotherapy, preferably using an FDC. In addition, it was highlighted that at least one-third of patients require triple therapy, and it was recommended that triple therapy should be proposed if the patient was not controlled by two different combination therapies at different dosages. The campaign's seven key points were included in a booklet that was released in 2012.[20]

In a survey conducted in the general French population in 2006, the global BP control rates in patients aged 18–74 years were around 50%, with generally more female patients being controlled from age 45 years onwards.[21] The survey also identified an over-reliance on monotherapy, with 36% of patients treated with just one drug, of which only 35% were uncontrolled.

Surveys conducted in GPs' offices in 1994 and 1999 showed that almost one in two patients entering GP offices in France were hypertensive and that only 32% of patients were achieving the target of hypertension treatment in 1999.[22] A similar survey conducted in 2014 involved 1,000 GPs working in France (the PASSAGE Survey).[23] The GPs were requested to include the first consecutive 20 hypertensive patients that entered their offices from autumn to winter 2013/2014. The definition of BP control was set as BP <140/90 mmHg for all patients, excluding patients aged >80 years in

whom systolic BP should be <150 mmHg. BP control rates were comparable with results from recent surveys conducted in the general population. The majority of elderly hypertensive patients in France were on target, likely due to the increased threshold for BP control in this group. Interestingly, the number of antihypertensive treatments used seemed to be the only modifiable factor that was positively associated with BP control.

A similar initiative in Italy that aims to achieve BP control in 70% of treated patients recommends more extensive use of dual or triple combination therapy, and advocates for the use of single-pill combinations to improve adherence and maintain optimal BP control.[24]

Has the Introduction of Single-Pill Fixed-Dose Combinations Affected Blood Pressure Management? Presentation of a Patient Case: The Elderly Patient with Chronic Kidney Disease

Professor Massimo Volpe

Prof Volpe presented the case of an elderly patient with hypertension and CKD. The patient was male, 74 years old, and of normal height, weight, and body mass index. He was a former smoker with a relatively high cardiovascular risk profile, including hypercholesterolaemia treated with atorvastatin, and carotid atherosclerosis treated with aspirin. There was mild renal impairment. The patient had a 20-year history of hypertension, which had been treated mostly with a beta-blocker, diuretic, and dihydropyridinic CCB. Home BP control was poor and the patient had fatigue. The referring physician added an ACE inhibitor (low-dose ramipril) and titrated the dosage of the CCB to twice daily (BID). The patient stopped treatment as he felt no improvement in BP control and thought there were too many pills to take.

Upon referral, the electrocardiogram findings indicated that the patient was likely to have future atrial fibrillation or heart failure. Renal artery ultrasound was relatively normal and carotid artery ultrasound showed a mild increase of the intima–media thickness, without haemodynamic effects. The creatinine level was 1.5 mg/dL, with an estimated glomerular filtration rate of 49 mL/min/1.73 m^2. Cholesterol was well controlled and the patient had mild albuminuria and microalbuminuria of 37 mg/24 hours.

Home BP was 160/80 mmHg and office BP was 168/88 mmHg. The patient had a heart rate (HR) of 64 beats per minute (bpm). Daytime (159/81 mmHg) and night-time (136/74 mmHg) 24-hour BPs were abnormal. The patient was taking atenolol 50 mg as half a pill BID, chlorthalidone 25 mg, nifedipine slow release 30 mg BID, aspirin, atorvastatin, and a proton-pump inhibitor. The patient was determined as high-risk, with predominantly systolic hypertension resistant to multiple drug combination therapies, and mild CKD.

Use of ACE inhibitor-based therapy in the Hypertension in the Very Elderly Trial (HYVET) reduced the risk of death and stroke,[25] while data from the Losartan Intervention for Endpoint Reduction (LIFE) trial showed that, in a cohort of patients with isolated systolic hypertension, ARB therapy resulted in a significant reduction in the composite primary endpoint (cardiovascular death, stroke, or myocardial infarction) and total mortality.[26] A recent meta-analysis showed that use of renin–angiotensin system (RAS) blockers is one of the most effective BP-lowering strategies to provide renal protection.[27] ARBs were shown to provide significant protection against the development of end-stage renal disease, and also promote regression of albuminuria; this effect was even stronger with a combination of ARBs and CCBs.[27]

A practical, individualised platform has been developed to identify antihypertensive strategies using a single-pill, ARB-based combination therapy.[28] Based on this strategy, the current case of an elderly patient with isolated systolic hypertension could benefit from a combination of an ARB with hydrochlorothiazide. With respect to the microalbuminuria and nephropathy observed in this patient, the patient may also benefit from a combination of an ARB and CCB. Triple therapy may also be useful if control is not achieved on dual therapy. ARBs have been shown to be efficacious in elderly patients. The Efficacy and Safety in elderly Patients with Olmesartan medoxomil versus Ramipril Treatment (ESPORT) trial found a significant improvement in 24-hour BP control with olmesartan compared with ramipril in elderly patients.[29]

The fatigue experienced by the current patient could have been related to his treatment with

beta-blockers. Therefore, chlorthalidone and nifedipine were discontinued and single-pill FDC therapy with olmesartan 20 mg and amlodipine 5 mg was commenced. At 1-month follow-up, there were no relevant side effects or adverse reactions, home BP was 150/70 mmHg, office BP was 152/82 mmHg, HR was 64 bpm, and creatinine level was more or less unchanged. Olmesartan and amlodipine were titrated to 40 mg and 5 mg, respectively. At 6-month follow-up, the patient reported fatigue as having a major impact on his quality of life and wished to take fewer pills. The beta-blocker was discontinued and a thiazide diuretic was directly combined with the ARB and CCB in a single pill as a triple therapy.

After 9 months of treatment, home BP and office BP had improved. Creatinine remained similar and 24-hour BP was satisfactory. This study highlighted the potential utility of ARB-based therapy for poorly controlled hypertension in elderly patients with CKD, and also the importance of single-pill FDCs in non-adherent patients. The practical platform[28] used in this case may be a companion for treatment of most cases of hypertension, even when the patients appear to be treatment-resistant.

The Impact of New Technology Like Home Blood Pressure Monitoring and Smartphone Apps on Blood Pressure Control

Professor Gianfranco Parati

A recent study has shown that only 13% of physicians are proactively utilising strategies to improve poor BP control, such as increasing dose and adding or switching to another drug.[30] Home BP monitoring with the use of new technologies, telemonitoring, and the recent progress in smartphone apps and patients' management software may help to improve BP control. Studies have shown that increases in home BP are more likely to predict increased risk of cardiovascular death compared with office BP,[31] while a recent meta-analysis has shown that home BP monitoring improves BP control.[32] In addition, the improved BP control achieved with home BP monitoring may be associated with improved patient adherence to treatment.[33]

It is often not possible to go through patient logs of BP values in detail during the short consultation times available. Telemonitoring may be a useful adjunct to home BP monitoring: data are collected, organised, analysed, and sent to the GP by email before each visit. The TeleBPCare study found that telemonitoring resulted in an important and significant increase in control of ambulatory BP compared with regular care, and also resulted in improved adherence.[34]

There are many smartphone apps available for healthcare, lifestyle, and wellbeing. Software is available to analyse the data on the physician's computer, in order to facilitate data interpretation and inform subsequent therapy decisions. The widespread availability of smartphones may provide potential for better care. There are a variety of different apps that permit measurement of HR, oxygenation, blood flow, and BP. However, few apps are validated and almost none are supported by the relevant scientific societies. Combining apps with a BP-monitoring device results in the formation of a medical device that requires legal regulation.[35]

The ESH has developed a specific, validated, and supported app for smartphones as part of the EUROHYPERTENSION project, with the aim of improving interaction between patients and physicians. This app allows collection of BP data and monitoring of changes over time, which can be easily sent directly to the patient's physician. In addition, users can obtain a simple summary of the ESH/ESC guidelines and information on hypertensive centres throughout Europe, thereby allowing the user to find and get in touch with experts for management of their hypertension. This app may be combined with the dedicated software that is in development for use by physicians to collect the data. This app may facilitate the achievement of BP control and a reduction in major cardiovascular risk factors, such as smoking, hypercholesterolaemia, and glycaemia.

In summary, the rate of BP control in Europe is still unacceptably low, especially considering the number of medications available and the progress in technology. Improvements in patient adherence to treatment and physician inertia to treatment intensification may help to improve BP control rates. It is important to consider the reasons behind patients' non-achievement of goals, e.g. due to side effects, difficulties in obtaining the prescription, and poor local healthcare system support, and therapies should be selected by matching with the individual patient's needs.Simplification of the therapeutic contact system is essential; single-pill

FDCs may help in improving adherence. Information technology has a role in improving BP control through better use of home BP monitoring with telemedicine and smartphone apps.

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