


Personalised Single-Pill Combination Therapy in Hypertensive Patients: An Update of a Practical Treatment Platform

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Abstract Despite the improvements in the management of hypertension during the last three decades, it continues to be one of the leading causes of cardiovascular morbidity and mortality worldwide. Effective and sustained reductions in blood pressure (BP) reduce the incidence of myocardial infarction, stroke, congestive heart failure and cardiovascular death. However, the proportion of patients who achieve the recommended BP goal (< 140/90 mmHg) is persistently low, worldwide. Poor adherence to therapy, complex therapeutic regimens, clinical inertia, drug-related adverse events and multiple risk factors or comorbidities contribute to the disparity between the potential and actual BP control rate. Previously we published a practical therapeutic platform for the treatment of hypertension based on clinical evidence, guidelines, best practice and clinical experience. This platform provides a personalised treatment approach and can be used to improve BP control and

simplify treatment. It uses long-acting, effective and well-tolerated angiotensin receptor blocker (ARB) olmesartan, in combination with a calcium channel blocker amlodipine, and/or a thiazide diuretic hydrochlorothiazide. These drugs were selected based on the availability in most European Countries of single-pill, fixed formulations in a wide range of doses for both dual- and triple-drug combinations. The platform approach could be applied to other ARBs or angiotensin-converting enzyme inhibitors available in single-pill, fixed-dose combinations. Here, we present an update, which takes into account the results of the recently published studies and extends the applicability of the platform to common conditions that are often neglected or poorly considered in clinical practice guidelines.

Keywords Antihypertensive therapy · Angiotensin receptor blockers · Angiotensin-converting enzyme inhibitors · Calcium channel blockers · Hypertension · Olmesartan medoxomil

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1 Introduction

Hypertension is the most frequent cardiovascular risk factor and strongly contributes to the development and progression of major cardiovascular and cerebrovascular events. Elevated blood pressure (BP) is associated with an increased risk of myocardial infarction, stroke, congestive heart failure and cardiovascular death, independently of age, gender and comorbidities [1]. A meta-analysis of randomised clinical trials has convincingly demonstrated the beneficial effects of lowering BP below 140/90 mmHg [2]. Achievement of this target reduces risk of developing hypertension-related complications and cardiovascular death. At present, a large number of antihypertensive drugs from different classes are available and detailed clinical practice guidelines for the treatment of hypertension are published regularly. Nevertheless, in many patients, hypertension is not satisfactorily controlled [3].

Several explanations of this discrepancy are possible, including poor adherence to prescribed therapy, complex therapeutic regimens (heavy pill burden), reluctance to intensify therapy (clinical inertia), drug-related adverse events (discontinuations) and presence of multiple risk factors and comorbidities. In addition, many hypertensive patients are treated with a single-drug regimen, despite the fact that less than one third of patients on monotherapy achieve BP control, and most require a combination of at least two antihypertensive drugs [4]. Another cause of poor adherence is the failure to achieve treatment benefits rapidly. This is often the result of adopting the same or similar therapeutic strategy in different patients. However, as many physicians who deal with it would attest, in hypertension, as in many other clinical conditions, the “one size fits all” approach does not work.

International clinical practice guidelines for the treatment of hypertension recommend that patients who are at high cardiovascular risk, as well as those who require a reduction of more than 20 mmHg in systolic BP and more than 10 mmHg in diastolic BP in order to meet the target level of 140/90 mmHg, may benefit from initiating treatment with a two-drug combination therapy [5]. This strategy is emphasized in other international guidelines, especially those produced in the US [6] and Canada [7, 8]. According to this approach, failure to achieve BP control with a two-drug combination at full dose may require switching to a different two-drug combination or the addition of a third drug [5–10]. When compared with the traditional method, the approach that aimed to achieve high rates of BP control (more than 70% of patients) resulted in reduction in the number of deaths from myocardial infarction and stroke in over 500,000 patients [11].

2 Background

In order to help physicians for achieving the following results in their clinical practice: (1) simplify therapy; (2) overcome therapeutic inertia; and (3) promote the achievement of the recommended BP targets, we recently proposed a platform for prescribing single-pill, dual- or triple-drug, fixed-dose combination therapies that takes into account the presence of various risk factors, markers of organ damage and comorbidities, as well as the grade of hypertension [12].

In designing this platform, we took into account the fact that the only triple therapy combination recommended by clinical practice guidelines for the treatment of hypertension consists of a renin-angiotensin system (RAS) blocking agent, a calcium channel blocker (CCB) and a thiazide diuretic. In particular, we selected a strategy based on the angiotensin receptor blockers (ARBs) on the basis of their excellent tolerability profile and high rates of adherence [13–15]. Furthermore, ARBs are equivalent to angiotensin-converting enzyme (ACE) inhibitors in terms of their efficacy [16, 17] and cardioprotective properties [18]. We designed the platform around an ARB olmesartan (OLM), because at the time we proposed the first treatment platform, it was available in multiple single-pill, fixed-dose, triple-therapy combinations with amlodipine (AML) and hydrochlorothiazide (HCTZ) [19]. These combinations have a long-lasting effect on BP and a good tolerability profile, with a low incidence of drug-related adverse events and discontinuations [20, 21]. These effects have been demonstrated in numerous clinical trials performed in hypertensive outpatients at different cardiovascular risk profile. The fact that each individual component is available in a wide variety of doses provides flexibility for up- or down-titration. The same approach could be used with other ARBs that are available for the management of hypertension, as well as for ACE inhibitors that are effective over a 24-h period, to allow for once-a-daily, single-pill administration [22–24].

Effective management of hypertension remains a pressing concern due to the continually rising prevalence of this condition in the general population and the growing number of patients with cardiovascular and non-cardiovascular comorbidities. For these reasons, we have produced an update to the treatment platform for the management of hypertension, which takes into account the results of the recently published randomised clinical trials. The update also extends the applicability of the platform to conditions that are common in the clinical practice, but often neglected or poorly considered in guidelines.

3 Platform organisation

The method that were used to create the platform has been described previously [12]. Briefly, the platform is neither an algorithm nor a guideline, but an attempt to apply evidence-based medicine, when available, to the management of hypertension in routine clinical practice [12]. The platform also proposes best practice solutions for the types of patients who are poorly represented in randomised clinical trials, or for whom no clinical practice guidelines recommendations are available. This approach is not intended to replace ongoing therapy for clinical conditions and comorbidities that require specific drug treatments. Furthermore, effective therapy that allows the patient to achieve the recommended BP targets should not be replaced. Instead, the platform represents an attempt to help physicians better control hypertension, and should be considered as an educational advice or a “secondo opinion” [25–29]. Therefore, it is important to consider compatibility with existing therapy for underlying conditions. The referring physician must determine the appropriate therapy and dosage for individual hypertensive patients, as recommended by current guidelines [5]. In addition, the platform is organised to match the intensity of therapy (defined as the recommended dosage range and type of combination) with the appropriate grade of hypertension and the global cardiovascular risk profile of an individual patient. For example, the need to achieve BP control is more urgent in patients with higher cardiovascular risk. Therefore, such patients may benefit from higher doses and/or combination therapy, potentially as the first-line treatment [5].

The first version of the platform was organised in two sections. The first section addressed patients with specific concomitant risk factors and organ damage (electronic Table 1, available online), while the second section referred to patients with associated clinical conditions that match frequent comorbidities (electronic Table 2, available online) [12]. In order to help physicians in choosing the most appropriate therapeutic regimen, we decided to maintain this approach in this update and propose two additional tables, addressing patients with uncontrolled hypertension (Table 1) and those who belong to special populations or have comorbidities (Table 2).

The structure of the tables is similar to that used in a clinical practice guideline for the management of hypertension [5]. The appropriate intensity of therapy can be determined based on the BP levels, as well as the assessment of risk factors, subclinical organ damage or clinical conditions. In the tables, the intensity of antihypertensive treatment increases from left to right, according to increasing hypertension grade [12]. Hypertensive patients with additional non-conventional risk factors may benefit from more intensive therapy and a lower threshold for

further intensification [12]. The effectiveness of the selected antihypertensive therapy should be assessed after 4 to 6 weeks.

4 Specific forms of hypertension

The therapeutic platform proposed for a number of specific forms of hypertension is presented in Table 1.

4.1 White-coat hypertension

White-coat hypertension is a clinical condition characterized by above-normal BP during clinical consultations and normal BP during the 24-h ambulatory BP monitoring [30]. Clinical studies have demonstrated that, although time-limited, BP elevations recorded in this condition are associated with an increased risk of development and progression of hypertension-related organ damage, as well as with cardiovascular events [31–33]. Therefore, it is important to detect this clinical condition early, at the asymptomatic stage, if possible. Whether patients with white-coat hypertension should receive pharmacological treatment depends on individual circumstances, particularly on the level of office BP and global cardiovascular risk.

Clinical studies of OLM-based therapy have demonstrated that therapy with OLM provides effective and sustained systolic and diastolic BP reductions over the 24-h period, both as monotherapy [34, 35] and in combination with AML [36]. The results of a relatively large randomised clinical study have shown that the OLM/AML combination produces a greater reduction in 24-h and central BP compared with combination therapy based on an ACE inhibitor and AML [37]. In addition to the immediate vasodilatory effect, long-term administration of OLM causes remodelling of the arterial system, reducing the stiffness of large arteries and leading to further reductions in systolic BP and pulse pressure [38].

4.2 Pseudo-resistant hypertension due to poor adherence

Pseudo-resistant hypertension is a clinical condition in which the recommended BP targets can be achieved by addressing non-adherence to prescribed therapy and optimizing and simplifying the treatment regimen. Several diagnostic algorithms have been proposed for identifying pseudo-resistant hypertension [39–42], and several studies have demonstrated that, after excluding secondary forms of hypertension, BP can be effectively and safely lowered to targets in this group of patients [43].

Table 1 (a) Personalized single-pill combination therapy based on an angiotensin receptor blocker combined with either a thiazide diuretic or a calcium-channel blocker (or both) in patients with specific forms of hypertension according to individual global cardiovascular risk stratification and (b) personalized single-pill combination therapy

based on an angiotensin receptor blocker combined with either a thiazide diuretic or a calcium-channel blocker (or both) in patients over 50 years old with hypertension and high cardiovascular risk (SPRINT eligible patients), according to individual global cardiovascular risk stratification

(a)

Clinical condition	Grade 1 HT (SBP 140–159 mmHg or DBP 90–99 mmHg)	Grade 2 HT (SBP 160–179 mmHg or DBP 100–109 mmHg)	Grade 3 HT (SBP \geq 180 mmHg or DBP \geq 110 mmHg)
White-coat HT ^a	OLM 20–40 mg If not at target, →	OLM/AML 20–40/5 mg If not at target, →	OLM/AML 40/10 mg
Persistent HT due to poor adherence	OLM/AML 20/5 mg If not at target, →	OLM/AML 40/5 mg If not at target, →	OLM/AML 40/10 mg
LV diastolic dysfunction	OLM/HCTZ 20/12.5 mg If not at target, →	OLM/HCTZ 40/12.5–25 mg If not at target, →	OLM/AML/HCTZ 40/10/25 mg
Elevated heart rate	OLM 20–40 mg If not at target, →	OLM/HCTZ 20–40/12.5 mg If not at target, →	OLM/HCTZ 40/25 mg

(b)

Clinical condition	High-normal BP (SBP 130–139 mmHg or DBP 85–89 mmHg)	Grade 1 HT (SBP 140–159 mmHg or DBP 90–99 mmHg)
Patients over 50 years old with hypertension and high cardiovascular risk (SPRINT eligible patients)	OLM/HCTZ 10–20/12.5 mg If not at target, →	OLM/HCTZ 20–40/12.5 mg

^a Before prescribing treatment, consider individual circumstances and the overall cardiovascular risk. *ACE* angiotensin-converting enzyme, *AML* amlodipine, *BB* beta-blocker, *COPD* chronic obstructive pulmonary disease, *DBP* diastolic blood pressure, *HCTZ* hydrochlorothiazide, *HT* hypertension, *LV* left ventricle, *SBP* systolic blood pressure, *OLM* olmesartan, *BP* blood pressure, *HCTZ* hydrochlorothiazide

Table 2 Personalized single-pill combination therapy based on an angiotensin receptor blocker combined with either a thiazide diuretic or a calcium-channel blocker (or both) in special populations of

patients with hypertension or hypertension caused by other conditions, according to individual global cardiovascular risk stratification

Clinical condition	Grade 1 HT (SBP 140–159 mmHg or DBP 90–99 mmHg)	Grade 2 HT (SBP 160–179 mmHg or DBP 100–109 mmHg)	Grade 3 HT (SBP \geq 180 mmHg or DBP \geq 110 mmHg)
Children and adolescents	OLM 10–20 mg If not at target, →	OLM 20–40 mg If not at target, →	OLM/AML 40/5–10 mg
Chronic obstructive pulmonary disease	OLM 20–40 mg If not at target, →	OLM/HCTZ 20–40/12.5 mg If not at target, →	OLM/HCTZ 40/25 mg
Low weight/hypovolemia	OLM 10–20 mg If not at target, →	OLM/AML 20–40/5 mg If not at target, →	OLM/AML 40/10 mg
Obesity/peripheral venous insufficiency or oedema	OLM/HCTZ 20/12.5 mg If not at target, →	OLM/HCTZ 20–40/12.5 mg If not at target, →	OLM/HCTZ 40/25 mg
Rheumatic or immunological diseases, treatment with NSAIDs	OLM/AML 10–20/5 mg If not at target, →	OLM/AML 20–40/5 mg If not at target, →	OLM/AML 40/10 mg
Rheumatic or immunological diseases, treatment with glucocorticoids	OLM/HCTZ 10–20/12.5 mg If not at target, →	OLM/HCTZ 20–40/12.5 mg If not at target, →	OLM/HCTZ 40/25 mg

AML amlodipine, *DBP* diastolic blood pressure, *HCTZ* hydrochlorothiazide, *HT* hypertension, *LV* left ventricular, *NSAIDs* non-steroidal anti-inflammatory drugs, *OLM* olmesartan, *SBP* systolic blood pressure

Treatment with antihypertensive drugs is often interrupted early and spontaneously [44, 45]. The use of single-pill combination therapy has the potential to reduce the frequency of treatment discontinuation, particularly if the components of the pill are effective throughout the day. For these reasons, the choice of an effective, well-tolerated and convenient first-line therapy is a key factor in ensuring adherence to prescribed medications.

Studies of OLM, both as monotherapy and, to a greater extent, as a component of combination therapies, have consistently demonstrated that it has a better tolerability profile than placebo and that the risk of drug-related adverse events is at least comparable to that with other ARBs and lower than with any other antihypertensive drug class, including diuretics [46–49]. Of note, the incidence of drug-related adverse events was largely independent of dose titration and was, in fact, lower when the drug was used in fixed-dose combination therapies with HCTZ, AML or both [46–49]. In addition, a recent randomised, double-blind, controlled clinical study demonstrated the non-inferiority of the fixed-dose combination of OLM and AML to the combination of perindopril and AML in reducing diastolic BP after 24 weeks of treatment and after a missed dose (– 11.7 and – 10.5 mmHg, respectively) [50, 51].

4.3 Left ventricular diastolic dysfunction

Left ventricular (LV) diastolic dysfunction is a common condition in hypertensive patients, with or without evidence of structural cardiac organ damage, such as LV hypertrophy. Although this condition has not been recognised in the current guidelines as a marker of hypertension-related organ damage [5], some studies have demonstrated its association with the risk of developing mitral regurgitation, atrial fibrillation, pulmonary oedema and congestive heart failure [52, 53].

Antihypertensive therapies based on RAS blockers, CCBs and diuretics have been shown to reduce the incidence of new-onset heart failure in different clinical settings across the cardiovascular continuum, proving that effective BP control is the cornerstone of any preventive strategy aimed at reducing the occurrence of such complication [54–56]. In hypertensive patients who are at high cardiovascular risk, diuretics are the most effective class of drugs for preventing heart failure, followed by RAS inhibitors [57]. Therefore, we suggest that early use of single-pill combination therapy with HCTZ should be considered in patients with grade 2 hypertension and early electrocardiographic or echocardiographic markers of diastolic dysfunction.

4.4 Elevated heart rate

Physicians frequently encounter patients with an elevated heart rate in routine clinical practice. This condition is often the result of sympathetic over-activity and, in hypertensive patients, it has been associated with a high risk of complications [58, 59]. Elevated heart rate is often successfully managed with the use of beta-blockers. The combination with thiazide diuretics is preferred in patients with uncontrolled hypertension who require combination therapy, but are intolerant of beta-blockers, or for whom they are contraindicated, because vasodilating drugs, including CCBs, may cause reflex activation of the sympathetic nervous system and tachycardia.

4.5 Patients over 50 years old with hypertension and high cardiovascular risk (SPRINT eligible)

The Systolic Blood Pressure Intervention Trial (SPRINT) was a large, randomised, controlled clinical study that was performed in the US under the auspices of the National Institutes of Health (NIH). The aim of the study was to explore the effects of lowering systolic BP to less than 120 mmHg (intensive treatment arm) on the risk of major cardiovascular events compared with the conventional systolic BP target of less than 140 mmHg (conventional treatment arm) [60]. The study included hypertensive patients aged more than 50 years, with no history of diabetes or stroke, but who had a high cardiovascular risk, defined as one or more of the following items: clinical or subclinical cardiovascular disease other than stroke, chronic kidney disease with an estimated glomerular filtration rate of between 20 and 60 ml/min/1.73 m² and a $\geq 15\%$ 10-year risk of cardiovascular disease, as measured by the Framingham risk score [61]. In order to achieve early and sustained reductions in BP, patients in the intensive treatment arm were systematically treated with additional diuretics. At the end of the observational period, the frequency of major cardiovascular events, (heart failure and cardiovascular and non-cardiovascular death) was significantly lower in patients in the intensive treatment arm compared with those in the conventional treatment arm [60]. However, the generalizability of the results of the SPRINT study is undermined by the criticisms that have been levelled against its methods, in particular, the way BP was measured, which has been characterised as imprecise.

It has been estimated that hypertensive patients over 50 years old, who have a high risk of cardiovascular complications, comprise approximately 20–30% of the entire population of people with hypertension [62]. A pharmacological strategy based on OLM may be effective in managing hypertension in this cohort because of its

pharmacodynamic characteristics (i. e. high affinity and strong binding to the AT1 subtype of angiotensin II receptors, and the greater reductions in systolic BP that can be obtained after dose titration, with or without diuretics) [62].

5 Hypertension in special populations or caused by other conditions

The therapeutic platform proposed for these patient populations is presented in Table 2.

5.1 Children and adolescents

Observational studies and epidemiological surveys have shown that the incidence of hypertension in children and adolescents has increased over the last several decades, and that hypertension now affects a higher proportion of individuals under 18 years old, primarily in Western and industrialised countries. Several factors are believed to be implicated in this phenomenon, including genetic predisposition (family history of hypertension), high salt intake, poor diet and limited physical activity. Early reduction of elevated BP may be an effective therapeutic approach in this population and may help to reduce the burden of hypertension-related cardiovascular disease in the future.

In the past, due to the absence of prospective, long-term, randomised, controlled clinical trials in young individuals with hypertension, lifestyle changes were often considered to be the only strategy for reducing high BP [63]. More recently, clinical data on the efficacy and safety of the five major classes of antihypertensive drugs have become available. In particular, a clinical study has demonstrated the efficacy and safety of OLM in children and adolescents with hypertension [64]. On the other hand, long-term use of diuretics in this group of patients may lead to deterioration of renal function and is, therefore, not recommended.

5.2 Chronic obstructive pulmonary disease

Co-occurrence of hypertension and chronic obstructive pulmonary disease (COPD) is relatively common [65]. In this subset of hypertensive patients, the presence of cardiac adaptations, primarily hypertrophy and/or dysfunction of both ventricles, may promote the development and progression of effort dyspnoea, hypoxxygenation, pulmonary congestion and congestive heart failure.

Descriptions of therapeutic goals and BP targets for patients with hypertension and COPD are currently lacking. The only exception is a newsletter of the European Society of Hypertension (ESH) published in 2012 [66]. This document proposes that the therapeutic goals in

hypertensive patients with COPD should be reduction of long-term pulmonary function decline, prevention and treatment of exacerbations, reduction of hospitalisations and mortality, relief of disabling dyspnoea and improvement of exercise tolerance and health-related quality of life [66]. The proposed goals of antihypertensive treatment include normalisation of BP, prevention of cardiovascular morbidity and mortality, extension of lifespan and improvement of the quality of life [66]. The fact that the majority of antihypertensive drugs can affect airway function complicates the treatment of hypertension in patients with COPD. RAS inhibitors, including ACE inhibitors and ARBs, are preferred, despite the fact that only limited data are available [67–69]. Depending on the haemodynamic profile and the presence of tachycardia and/or pulmonary hypertension, as well as the tendency to develop right-heart failure, a combination therapy with thiazide diuretics may be useful.

5.3 Low weight/hypovolemia

While the high prevalence of overweight or obesity are frequent in clinical studies of patients with hypertension, and the impact of these conditions on BP is recognized, the potential effect of low body weight or hypovolemia has often been neglected or insufficiently considered. There are subgroups of high-risk patients with hypertension, such as individuals of advanced age (e.g. octogenarians), those with neurological (e.g. severe cognitive impairment or Alzheimer's disease) or psychiatric disorders (e.g. anorexia) or those with end-stage chronic illness (e.g. cachexia, solid tumours or cancers), in which high peripheral vascular resistance and accelerated atherosclerotic disease of large arteries may lead to the development of hypertension in the presence of hypovolemic status. This may increase the risk of symptomatic hypotension, renal failure, neurological deterioration and syncope. For this reason, it may be useful to adopt a therapeutic regimen characterized by sustained and consistent antihypertensive efficacy over the period of 24 hours, thus avoiding abnormal BP variations and reducing the risk of complications due to hypotension. Therefore, combination therapies with CCBs are recommended, while diuretics should be avoided.

5.4 Obesity/peripheral venous insufficiency

Central or visceral obesity is frequently associated with essential hypertension and markedly increases the risk of developing metabolic syndrome, dyslipidaemia, new-onset diabetes and cardiovascular disease. This risk is further increased by concomitant use of some beta-blockers in combination with medium-to-high dose diuretics [70–72].

In addition, dihydropyridinic CCBs, including AML, promote lower-limb oedema, mostly in female patients with venous insufficiency and obesity. Therefore, a predisposition to venous insufficiency or lower-limb oedema, is a contra-indication for the use of CCBs, including in combination therapy. On the other hand, combination therapy with an ARB or an ACE inhibitor with low-dose HCTZ is the recommended treatment in such patients.

5.5 Rheumatic and immunological diseases

Patients with rheumatic diseases have been systematically excluded from randomised, controlled clinical trials conducted in hypertension, as well as other cardiovascular conditions, and, therefore, definitive evidence of the therapeutic efficacy and safety of many antihypertensive treatments in this high-risk population is lacking. Rheumatic and immunological diseases are characterised by life-long symptoms and increased levels of systemic and local inflammation. This may promote rapid and aggressive atherosclerotic and arteriosclerotic disease, as well as lead to pro-coagulative status and increased peripheral vascular resistance and arterial stiffness [73–75]. For these reasons, the incidence of cardiovascular complications, primarily atrial fibrillation and other arrhythmias, coronary artery disease, myocardial infarction, ischemic stroke and congestive heart failure, is relatively high in patients with rheumatic and immunological conditions. The use of non-steroidal anti-inflammatory drugs or glucocorticoids may necessitate the use of CCB and diuretic combination therapies to control blood pressure [76]. Because the therapeutic regimens necessary to treat rheumatic and immunological conditions are often complex, a fixed combination therapy, administered once daily and consisting of a combination of a long-lasting ARB and AML, may be well suited for reducing the risk of cardiovascular complications. In patients exposed to long-term treatment with non-steroidal anti-inflammatory drugs, who are more susceptible to developing renal dysfunction or chronic renal failure, the use of diuretics may exacerbate renal impairment and is, therefore, not recommended. In contrast, in patients undergoing long-term treatment with steroids, a combination with thiazide diuretics is preferable.

In chronic conditions which require complex long-term treatment regimens, several reports described hypertension due to the use of anti-neoplastic or anti-vascular growth factor monoclonal antibodies. These drugs have been shown to induce vessel rarefaction and increased peripheral vascular resistance. In such conditions, the use of use of single-pill combination therapies based on CCBs is recommended.

6 Conclusions

Effective and well-tolerated single-pill, dual- or triple-drug, fixed dose combination therapies have the potential to greatly improve BP control and close the gap between the promising results of interventional trials and the often disappointing data from routine clinical practice. An approach aiming to determine the appropriate therapeutic intensity based on concomitant conditions may help physicians design personalised treatment strategies. When applied as part of a comprehensive approach that includes regular follow-up and timely therapy intensification, it may also increase the proportion of patients with hypertension who achieve the recommended BP targets, thus reducing the burden of hypertension-related cardiovascular, cerebrovascular and renal diseases.

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Compliance with ethical standards

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Ethical approval This article does not contain data derived from studies with human participants performed by any of the authors. The clinical studies referred in the text received relevant ethical approval.

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