




New perspectives for hypertension management: progress in methodological and technological developments

Gianfranco Parati ^{1,2*}, Alexandra Goncalves³, David Soergel⁴, Rosa Maria Bruno⁵, Enrico Gianluca Caiani⁶, Eva Gerdts ⁷, Felix Mahfoud ⁸, Lorenzo Mantovani⁹, Richard J. McManus¹⁰, Paola Santalucia¹¹, and Thomas Kahan^{12,13}

¹Department of Cardiovascular, Neural and Metabolic Sciences, Istituto Auxologico Italiano IRCCS, Ospedale San Luca, Piazzale Brescia 20, 20149 Milano, Italy; ²Department of Medicine and Surgery, University of Milano-Bicocca, Via Cadore 48, 20900 Monza (MB), Italy; ³Strategy & Partnerships, Philips, Cambridge, MA 02141, USA; ⁴Cardiovascular, Renal, and Metabolic Drug Development, Novartis, Basel, CH 4056, Switzerland; ⁵Paris Cardiovascular Research Centre (PARCC-INSERM U970) & Université de Paris, Paris 75015, France; ⁶Politecnico di Milano, Electronics, Information and Bioengineering Department, Institute of Electronics, Computer and Telecommunication Engineering (IEIT), National Research Council of Italy (CNR), Milan 20133 & 24-10129, Italy; ⁷Department of Clinical Science, University of Bergen, Bergen NO-5020, Norway; ⁸Department of Internal Medicine III, Cardiology, Angiology, Intensive Care Medicine, Saarland University Hospital, Homburg 66123, Germany; ⁹Value-based Healthcare Unit, IRCCS MultiMedica Research Hospital, University of Milan, Milan, Italy; ¹⁰Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford OX2 6HD, UK; ¹¹Italian Association Against Thrombosis and Cardiovascular Diseases (ALT Onlus), Milan 20123, Italy; ¹²Division of Cardiovascular Medicine, Department of Clinical Sciences, Danderyd Hospital, Karolinska Institutet, Stockholm SE 182 88, Sweden; and ¹³Department of Cardiology, Danderyd University Hospital Corp, Stockholm SE 182 88, Sweden

Received 21 April 2022; revised 21 July 2022; accepted 5 September 2022; online publish-ahead-of-print 8 September 2022

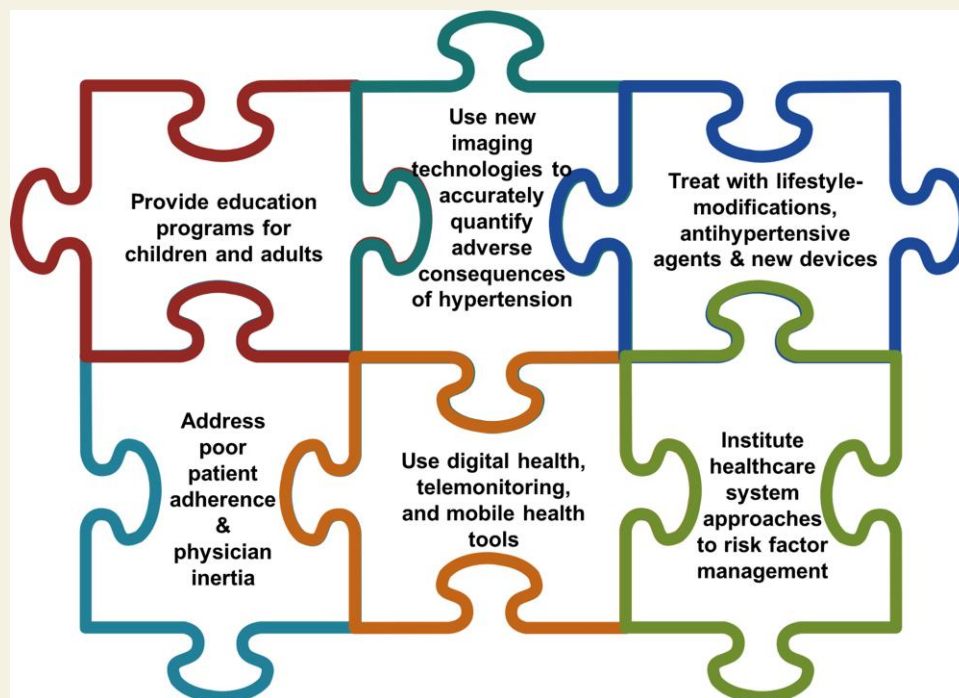
See the editorial comment for this article ‘Managing hypertension in the future: a multifactorial approach’, by N. Pagonas *et al.*, <https://doi.org/10.1093/eurjpc/zwac238>.

Hypertension is the most common and preventable risk factor for cardiovascular disease (CVD), accounting for 20% of deaths worldwide. However, 2/3 of people with hypertension are undiagnosed, untreated, or under treated. A multi-pronged approach is needed to improve hypertension management. Elevated blood pressure (BP) in childhood is a predictor of hypertension and CVD in adulthood; therefore, screening and education programmes should start early and continue throughout the lifespan. Home BP monitoring can be used to engage patients and improve BP control rates. Progress in imaging technology allows for the detection of preclinical disease, which may help identify patients who are at greatest risk of CV events. There is a need to optimize the use of current BP control strategies including lifestyle modifications, antihypertensive agents, and devices. Reducing the complexity of pharmacological therapy using single-pill combinations can improve patient adherence and BP control and may reduce physician inertia. Other strategies that can improve patient adherence include education and reassurance to address misconceptions, engaging patients in management decisions, and using digital tools. Strategies to improve physician therapeutic inertia, such as reminders, education, physician–peer visits, and task-sharing may improve BP control rates. Digital health technologies, such as telemonitoring, wearables, and other mobile health platforms, are becoming frequently adopted tools in hypertension management, particularly those that have undergone regulatory approval. Finally, to fight the consequences of hypertension on a global scale, healthcare system approaches to cardiovascular risk factor management are needed. Government policies should promote routine BP screening, salt-, sugar-, and alcohol reduction programmes, encourage physical activity, and target obesity control.

* Corresponding author. Tel: +39 02 619112890, Email: gianfranco.parati@unimib.it

© The Author(s) 2022. Published by Oxford University Press on behalf of the European Society of Cardiology. All rights reserved. For permissions, please email: journals.permissions@oup.com.

Graphical Abstract



Combined strategies to reduce hypertension-related cardiovascular risk

Keywords

Screening • Education • Lifestyle • Inertia • Adherence • Control

Introduction

Hypertension is the single most common risk factor for cardiovascular disease (CVD) burden and mortality worldwide. In 2019, hypertension was reported as the number 1 cause of death in women, and the number 2 cause of death in men, accounting for almost 20% of deaths (~11 million) globally.¹ There is robust evidence that treatment of hypertension can substantially lower blood pressure (BP) and reduce premature morbidity and mortality.² Despite this, and recommendations from national and international guidelines, approximately 2/3 of people with hypertension are undiagnosed, untreated, or under treated,³ and hypertension remains the major preventable cause of CVD and mortality.²

This document is the product of in-depth discussions among hypertension experts involved in clinical medicine or in technological development, during a Cardiovascular Round Table workshop supported by the European Society of Cardiology (ESC), with the aim of developing new solutions for better hypertension control. The goal of this paper is to discuss current perspectives to improve hypertension management using new technologies and methodologies. In particular, this work focuses on (i) education programmes for children and adults, (ii) progress in imaging technology for more accurate quantification of adverse consequences of hypertension, (iii) progress in hypertension treatment with lifestyle modifications, antihypertensive agents, and new devices, (iv) tools for addressing poor patient adherence and physician inertia, (v) digital health, telemonitoring, and mobile health approaches, and (vi) healthcare system approaches to CV risk factor management.

Preventing hypertension: early BP screening and the importance of education at younger ages

Elevated BP in childhood predicts hypertension in adulthood.⁴ In a meta-analysis of 50 studies in diverse populations the correlation increased with age, from infancy through adolescence. Childhood BP elevations are associated with long-term increased risks of coronary heart disease, acute myocardial infarction, ischaemic or haemorrhagic stroke, and CVD mortality in adulthood.^{5–7} These findings suggest that diagnosing and controlling high BP in children and adolescents may be an effective primary prevention strategy for adult CVD. Thus, systematic screening and management of elevated BP is recommended in children and adolescents, beginning as early as age 3 years.⁸ An overview of strategies to prevent hypertension and its complications are shown in *Figure 1*.⁹

The risk factor landscape is changing, and hypertension awareness programmes will need to adapt (*Table 1*).^{10,11} Obesity, fuelled by poor nutritional habits and physical inactivity, is a major risk factor for hypertension, diabetes, dyslipidaemia, and metabolic syndrome, and its prevention and treatment can be targeted by education and public health policies.^{10,11}

A report from the National Heart, Lung, and Blood Institute (NHLBI) suggested two main strategies targeted to young adults to help maintain CV health, which they called primordial and primary prevention.¹² Many of these are appropriate for targeting paediatric

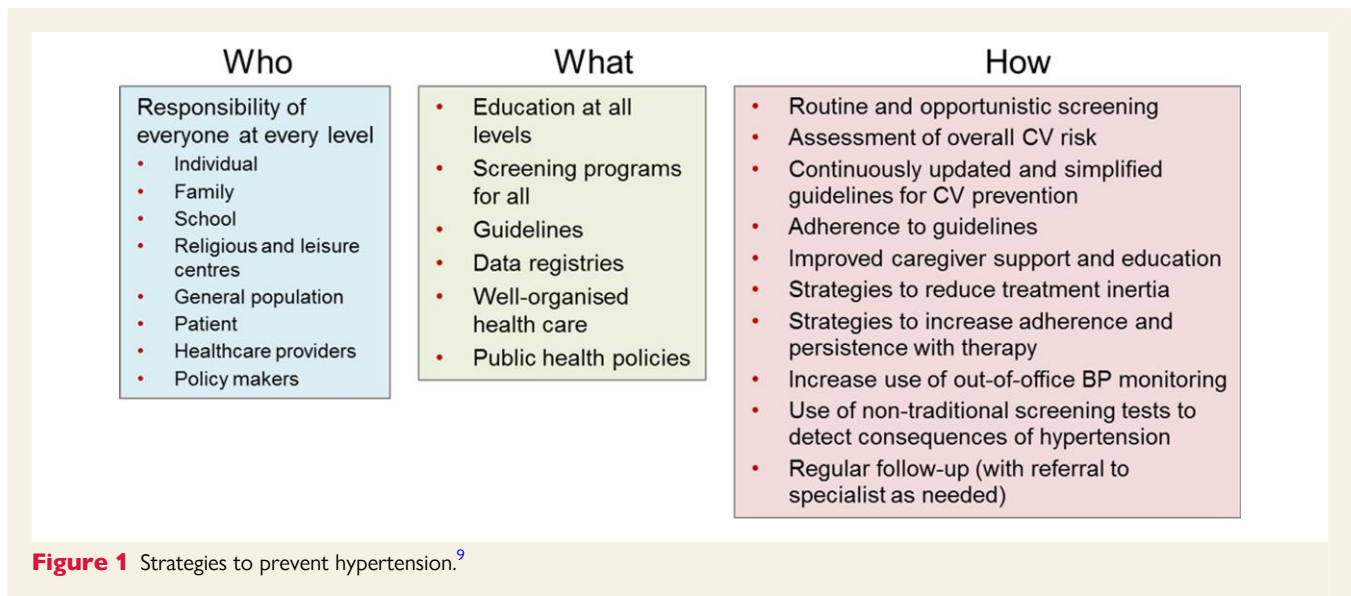


Table 1 The changing risk factor landscape^{10,11}

- Food habits
- Obesity
- Physical activity/inactivity
- Tobacco and recreational drug use
- Blood pressure trends (SBP vs. DBP)
- Educational systems, public health issues
- Care providing organisations

DBP, diastolic blood pressure; SBP, systolic blood pressure

populations as well. Primordial prevention includes population-based strategies to prevent the development of risk factors, such as governmental policies (laws, taxes, and subsidies), making neighbourhoods more walkable, promoting healthier food choices and more regular physical activity, media campaigns, and screening programmes. Primary prevention strategies include screening and managing BP, lipid, and glucose abnormalities. It is essential that primordial and primary prevention initiatives be practical and realistic, particularly from early life. For example, young adults may prefer more flexible care such as telemedicine, increased use of social media and websites, and other digital health apps. Many good educational initiatives are available online. See the section on 'technology platforms' below for more information on these programmes.

Accurate screening and diagnosis in adults

Because hypertension is generally an asymptomatic condition, the 2018 European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) joint guidelines recommend population-based screening programmes and opportunistic measurement of BP.^{2,13} All adults should have their BP measured at regular intervals and should be aware of their measurements. Physician visits for other reasons can provide good opportunities to screen for hypertension.

Office BP measurement using sphygmomanometers has been the cornerstone of hypertension assessment for over 100 years.¹⁴ It is inexpensive, widely available, and has a demonstrated impact on outcomes. However, office BP measurements are prone to measurement errors, and they may not reflect a patient's BP in their daily lives (e.g. white-coat hypertension, i.e. elevated office BP values and normal out-of-office BP, and masked hypertension, i.e. normal or high normal office BP values associated with elevated out-of-office BP), which occur in as many as 10–25% of patients.^{15,16}

Because of these limitations, guidelines are increasingly recommending combined use of office and out-of-office BP monitoring [e.g. home BP monitoring (HBPM) and ambulatory BP monitoring (ABPM) over 24 h] to improve hypertension diagnosis.^{2,13,17,18} *Table 2* summarizes some of the advantages and disadvantages of office, HBPM, and ABPM.^{2,16–20}

HBPM, when combined with education, lifestyle counselling, mHealth tools, or telemonitoring is becoming increasingly important in improving hypertension control and thereby reducing organ damage and improving CV outcomes.^{21–23} Studies have shown that patients are able to use HBPM to successfully titrate their antihypertensive medication, and this translates into improved BP control rates.¹⁴ HBPM may also reduce physicians' therapeutic inertia; in a meta-analysis, physicians were more likely to change medications when HBPs were elevated.²⁴

The increased availability of more affordable, automated electronic devices for HBPM makes this a viable strategy to improve BP control for many patients. Regardless of the type of device, accuracy is essential.^{17,25} Standardized protocols are available to assess the clinical validation of electronic BP monitors. STRIDE BP is an international organization affiliated with the ESH, the International Society of Hypertension, and the World Hypertension League, which is dedicated to improving the accuracy of BP measurement and hypertension diagnosis. The STRIDE BP group conducted a systematic review of 419 validation studies, and of the 260 included devices, 83% were approved as accurate for OBP, ABPM, or HBPM.^{25,26} Updated lists of validated BP monitors are available online from www.stridebp.org, as well as from scientific organizations

Table 2 Advantages and disadvantages of office blood pressure, ambulatory and home BP monitoring^{2,16–20}

	Advantages	Disadvantages
OBP	<ul style="list-style-type: none"> • Readily available • Strong data link to CVD. Used in most hypertension outcome trials 	<ul style="list-style-type: none"> • Poor standardization can lead to overestimation of BP • Inadequate reproducibility (single-visit OBP has low diagnostic accuracy) • Issues of WCH^a and MH^b
ABPM	<ul style="list-style-type: none"> • Identification of WCH^a and MH^b • Reproducible average 24-h, day and night-time values • Large number of readings in daily environment • Assessment of nocturnal BP • Useful to assess response to antihypertensive therapy (poor control or excessive BP lowering) • Good prognostic evidence (CV morbidity and mortality) 	<ul style="list-style-type: none"> • Costly • Limited availability in primary care settings • May cause discomfort, particularly at night • Patients may be reluctant to use it
HBPM	<ul style="list-style-type: none"> • Generally inexpensive; widely available • Identification of WCH^a and MH^b • Useful for long-term monitoring • Useful to assess response to antihypertensive therapy (poor control or excessive BP lowering) • Patient engagement may improve adherence • Can be used with telemonitoring 	<ul style="list-style-type: none"> • Potential for measurement errors • Static BP readings only • No work-place readings • Limited evidence on new devices also yielding nocturnal measurements. • Possible patient 'obsessional' behaviour and anxiety • Possible unsupervised treatment changes • Potential for digital exclusion

ABPM, ambulatory BP monitoring; HBPM, home BP monitoring; MH, masked hypertension; OBP, office blood pressure; WCH, white-coat hypertension.

^aWCH: elevated office BP values and normal out-of-office BP.

^bMH: elevated out-of-office BP with normal office BP values

from many other countries.¹⁷ Notably, of the estimated 4000 devices being marketed worldwide, fewer than 10% have been adequately validated.¹⁷

Progress in imaging technology to improve hypertension control

Progress in imaging technology has provided the means for earlier detection, and more accurate quantification, of the adverse

consequences of hypertension. While identification of conventional risk factors is useful in CV risk assessment, the detection of preclinical disease may help identify those patients with hypertension who are likely to progress to functional disease and CV events.²⁷ It is possible to non-invasively detect preclinical disease in asymptomatic patients, including left ventricular hypertrophy, systemic atherosclerosis, large artery stiffness and renal dysfunction.²⁷ Arterial stiffness is an independent predictor of hypertension and CV risk in adults,²⁸ and in adolescents, arterial stiffness was associated with an elevated risk of hypertension and adiposity in adulthood.²⁹ These preclinical findings predict CV risk better than traditional risk factors and can improve risk stratification and outcomes.^{27–31} In the SCOT-HEART (Scottish COmputed Tomography of the HEART Trial), detection of preclinical disease based on computed tomography (CT) angiography was shown to lead to changes in preventive treatment and subsequent improvements in outcomes.³²

Beyond traditional basic screening, echocardiography, carotid ultrasound, pulse wave velocity, ankle-brachial index, cognitive function testing, measurements of arterial stiffness, and brain imaging can also be used to detect adverse consequences of hypertension.^{2,13,28} For example, the severity of white matter hyperintensities, which are associated with cognitive decline, have been shown to progress with age and BP levels, even in patients aged younger than 50 years.³³ These findings suggest that early treatment of elevated BP may be warranted. However, while some tests identify target organ damage where treatment can modify prognosis, for other measures of hypertension damage it is not yet known whether treatment will modify the damage, as in the case of cognitive tests and brain imaging.

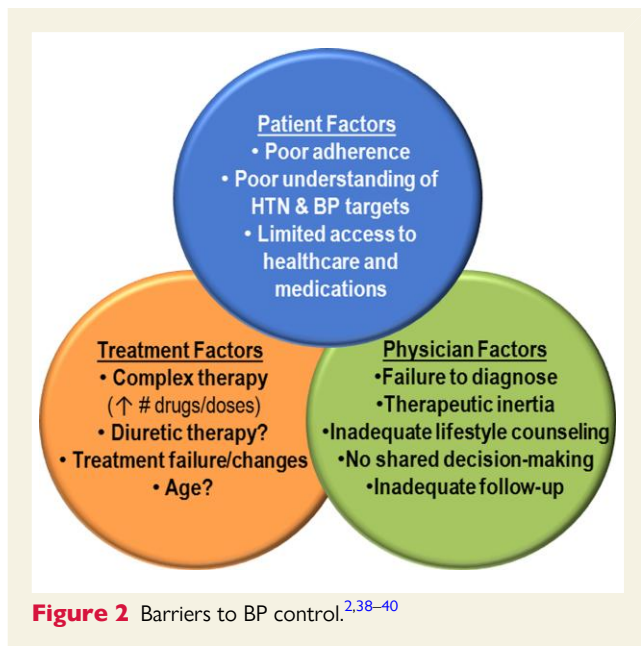
Optimal use of current treatments to improve hypertension control

Lifestyle modifications

Lifestyle interventions and antihypertensive drug therapy are well-established strategies to lower BP.^{2,13,34} Lifestyle modifications have demonstrated efficacy for prevention and adjuvant treatment of hypertension, although adherence and long-term persistence is often poor.^{2,34,35} Recommended lifestyle modifications include: increased physical exercise, body weight normalization and healthy eating habits (salt restriction; moderation of alcohol consumption; high consumption of vegetables and fruits).^{2,13,34} Obesity prevention and treatment should be a priority to lower the burden of hypertension and related conditions.³⁴

Antihypertensive agents

A large meta-analysis included data on 348 854 individuals from 48 clinical trials of antihypertensive medications over an average of 4 years follow-up.³⁶ Results showed that each 5 mm Hg reduction in systolic BP (SBP) obtained through this approach was associated with a 10% reduction in the relative risk of major CV events (including stroke, ischaemic heart disease, heart failure, and CV death). Neither the presence of prior CVD nor baseline BP modified the effect of treatment.



The renin–angiotensinaldosterone system (RAAS) is an important target for antihypertensive treatments such as angiotensin converting enzyme inhibitors and angiotensin II Type 1 receptor blockers (ARBs). Novel agents targeting RAAS have recently been made available or are under investigation including atrial natriuretic peptide inhibitors, non-steroidal mineralocorticoid receptor antagonists, and angiotensin II Type 2 (AT2) agonists.³⁷

Despite the well-proven efficacy of lifestyle and medication, uncontrolled BP remains a major problem worldwide. Three important barriers to BP control that can be targeted by current and new technologies are (i) poor patient adherence to management, (ii) physician inertia in monitoring BP and escalating therapy, and (iii) complexity of treatment (Figure 2).^{2,13,38–40}

Device-based strategies

It is important to differentiate between uncontrolled BP due to non-adherence, and treatment-resistant hypertension. The latter is diagnosed if BP remains uncontrolled despite optimal therapy (with at least three antihypertensive drugs of different classes including a diuretic, all at maximally tolerated doses).^{2,13} On the other hand, studies show that 23–66% of patients with apparent treatment-resistant hypertension are poorly adherent to drug treatment.^{41,42}

Device-based therapies for patients with severe hypertension, including renal denervation, baroreflex activation therapy, and pacemaker-mediated hypertension treatment are actively under investigation.^{2,43–45} The most studied of these approaches is renal sympathetic denervation.^{44,46} Randomized, sham-controlled trials, making use of both office and ambulatory BP monitoring, have proven its BP-lowering efficacy in patients with and without concomitant antihypertensive medication.⁴⁴ However, most patients will continue to require drug therapy.⁴³

Guidelines do not currently recommend routine use of device-based therapies outside of clinical trials.^{2,47} However, European guidelines were written before the most recent evidence became available.² For this reason, a recent position paper from the ESH suggested that renal denervation may play a role in difficult-to-treat

hypertensive patients who are selected based on BP values and current treatment, high lifetime CV risk, poor drug adherence, intolerance to multiple BP-lowering drugs, the underlying pathophysiology, and patient preferences where shared decision-making is essential.⁴⁸

Strategies to improve hypertension control

Reducing complexity of therapy

Each additional antihypertensive drug has been associated with 2–3 times the risk of non-adherence.^{38,49} A meta-analysis of 16 studies including 62 481 patients with hypertension found a 15% improvement in medication adherence with single-pill combination vs. free-equivalent combination therapies, and an almost doubling of the rate of persistence.⁵⁰ A single-pill combination can also significantly improve both systolic BP (mean difference, -3.99 mm Hg, $P = 0.05$) and diastolic BP (-1.54 mm Hg, $P = 0.0076$) at week 12.⁵¹ International guidelines emphasize the importance of using single-pill combination therapy.¹⁸ Diuretics have been associated with lower rates of adherence than other antihypertensive drugs.^{38,49} This fact may be related to pharmacokinetics, pharmacodynamics, or side effects, as well as to their frequent use in free-equivalent combination regimens.³⁸ Simplified treatment regimens through single-pill combinations can improve patient adherence and may simplify therapy for physicians.

Improving patient adherence

Adherence with pharmacotherapy for hypertension one year after initiation is typically reported as up to 50%, however, an estimated 2/3 of patients take only some of their medication.^{40,49} This emphasizes the need to engage with patients and assess their reasons for non-adherence.

Poor adherence can be intentional, related to disease or treatment misperceptions; or unintentional, related to forgetfulness or difficulty accessing healthcare and healthy food.³ Contributing factors include complexity of therapy, patient beliefs about hypertension and antihypertensive drugs, and the physician–patient relationship (Table 3).^{38,40,49} Approaches to address patient non-adherence to hypertension management are shown in Table 3.^{18,40,49–58} However, the first step toward addressing patient non-adherence is to identify it; among the possible approaches, chemical adherence testing has become increasingly available and used, especially in apparently treatment-resistant patients. Physician–patient discussion of therapeutic drug monitoring results is a fundamental step towards improvement of patient adherence.⁵⁸

Patient misconceptions about hypertension and antihypertensive treatments are important factors in intentional non-adherence, including beliefs and fears about stress, symptoms, and dependence on medication, as well as dislike of medications.³ In a survey of 711 patients, adherent patients were more likely to believe that hypertension was a chronic condition, and that treatments are beneficial to reduce BP and for the prevention of CVD compared with non-adherent patients. They did not believe that doctors overuse drugs, but rather that the medications were necessary to maximize their health.⁵⁹

Table 3 Common barriers to patient adherence and proposed strategies to overcome them

Barrier	Proposed strategies	Digital/technological solutions that can help
Complexity of therapy	<ul style="list-style-type: none"> Use single-pill combinations^{50,51} Use simplified regimens and once-daily dosing¹⁸ Monitor adherence as warranted, provide patients with feedback on adherence⁵⁸ Review all concomitant prescriptions, aim to reduce complexity of therapy⁵³ 	<ul style="list-style-type: none"> Reminder apps (cue-dosing) Telemonitoring Smart pills^{40,52} Smart dispensers, or caps Educational websites and apps Interactive Apps to increase patient engagement Telemonitoring Educational websites and apps
Diuretic therapy	<ul style="list-style-type: none"> Avoid diuretics when appropriate^{38,49} Consider closer monitoring, and dosage adjustments as needed 	<ul style="list-style-type: none"> Devices that monitor BP with apps that provide feedback on risk levels, or provide results electronically to physicians Educational websites and apps Interactive apps to increase patient engagement Interactive exercise and dietary modification apps
Patient beliefs/attitudes about hypertension and medication (health literacy)	<ul style="list-style-type: none"> Acknowledge and address patient beliefs/fears about stress, symptoms^{3,59} Provide an accurate description of the benefits and adverse effects of treatment³ Use patient-centred approaches, particularly those that are nurse- or pharmacist-led^{40,55,56} Provide accessible information for schoolchildren and adults, (esp. diet, exercise from a young age) Suggest easy to adopt lifestyle modification 	<ul style="list-style-type: none"> Technology is a matter of patient preference and accessibility. Do not assume that age is a reason not to suggest websites or apps
Age and gender	<ul style="list-style-type: none"> Age and gender have not consistently been identified as risk factors for non-adherence, but strategies should address age or gender specific needs and concerns^{49,54} Younger: Tailor education to personal risk, beliefs, and attitudes.^{55,57} Older: Consider a review of cognitive abilities and digital literacy of patients, their family and caregivers, regular reminder systems, and easy-to-manage pill containers⁵³ 	<ul style="list-style-type: none"> Technology is a matter of patient preference and accessibility. Do not assume that age is a reason not to suggest websites or apps
Physician–patient relationship	<ul style="list-style-type: none"> Cultivate a strong physician–patient relationship, customized to the patient's needs and lifestyle Listen to patients and gain their trust Use a collaborative communication style rather than an inquisition style^{40,55} Discuss patients' sociodemographic circumstances as well as their hypertension medications⁵⁶ Engage patients in decisions and agree on tasks and goals⁴⁰ 	<ul style="list-style-type: none"> Telemonitoring HBPM to monitor BP linked to apps that provide feedback on risk levels, or provide results electronically to physicians Interactive apps to increase patient–physician interactions and patient engagement

Clinicians should acknowledge patients' concerns, and educational initiatives must directly target patients attitudes.³ Patients engaged in decisions about their treatment are more adherent than patients who are not.⁴⁰ Interactions that include discussions of the patient's sociodemographic circumstances (living situation, relationship with partner), in addition to their medication can positively impact adherence.⁵⁶

Digital tools such as websites can be useful, but it is important for physicians to be aware of trustworthy websites, and advocacy groups that they can direct their patients to. Digital tools such as smartphone reminder app, can also be useful when adherence is unintentional due to forgetfulness. See the section on 'technology platforms' below for more on these tools.

Reducing therapeutic (physician) inertia

Therapeutic inertia, or clinical inertia, defined as a failure of clinicians to initiate or intensify treatment in accordance with current guidelines⁶⁰ is a pervasive problem in hypertension management.⁶¹ For example, although combination antihypertensive therapy has been shown to be associated with a lower risk of CV events, and better adherence than monotherapy,^{2,13,47,62} a study found that up to 3/4 of patients were initiated on monotherapy and, among these, 2/3 remained on one drug during the 3-year follow-up.⁶²

Provider factors that contribute to therapeutic inertia include lack of knowledge about appropriate therapeutic goals, high patient volume, and time constraints,^{60,61} patients with multiple comorbidities (esp., psychiatric conditions or diabetes) and patient being 'near' or at

Table 4 Strategies to target therapeutic inertia⁶⁰

Proposed strategies	Digital/technological solutions that can help
<ul style="list-style-type: none"> Physician and patient reminders ABPM Physician and patient education Physician peer visits Task-sharing 	<ul style="list-style-type: none"> Risk calculators, and automated prompts for intensification integrated into EHR systems Automatic uploads of HBPM and other patient-generated data into EHR Websites for physician–patient interaction and personalization of treatment strategy

ABMP, ambulatory blood pressure monitoring, EHRs, electronic health records

‘acceptable’ targets.^{60,61} Strategies to target physician inertia have been associated with increased rates of BP control (Table 4).⁶⁰ Patient education may also help improve therapeutic inertia, patient non-adherence and patient preference have been cited by physicians as a reason not to intensify therapy when warranted.⁶³

Physicians and patients should be aware of the importance of treating hypertension in the context of CV risk. A large meta-analysis showed that reductions in BP were associated with reductions in the risk of major CV events regardless of prior diagnosis and even at normal or only mildly elevated BPs.³⁶ This can help when physicians are discussing with patients the need for antihypertensive treatment to reduce CV risk rather than focusing on BP alone.

Physician time constraints, exacerbated by complex patients, and high patient volume, can contribute to not intensifying therapy. Strategies that can help are ‘task-sharing’ interventions, remote monitoring programmes that integrate into current workflows, and adequate reimbursement. A meta-analysis including 31 studies found that task-sharing with nurses, pharmacists, dieticians, and community health workers led to significant decreases in BP.⁶⁴ An update, including 43 studies, found that sharing tasks including administrative, basic, or advanced clinical tasks resulted in improvements in SBP control.⁶⁵ When used as part of a multi-component strategy this approach has demonstrated efficacy and cost-effectiveness especially in low- and middle-income countries.^{64,66}

The use of remote monitoring was rapidly accelerated by the COVID-19 pandemic.⁶⁷ The pandemic resulted in improved infrastructure (including video consultations, website portals for interactions), increased integration into electronic health records, and reimbursement for telemedicine in many countries.⁶⁸ Incorporating HBPM and other patient-generated health data into electronic health records has been shown to improve BP control rates when used by physicians and pharmacists to support clinical management.^{69–71} The success of remote monitoring tools may be largely due to the improved link between the patient and the physician.⁷² For clinicians, integrating digital solutions into practice can be a challenge.⁶⁹ In a survey of primary care providers there were concerns around how to use the HBPM data, the ability to individualize the frequency of patient measurements, the frequency of physician viewing of data, and the alert parameters.⁶⁹ Some of these tools are described in more detail in the section on technology platforms below.

Technology platforms to engage patients and improve BP control: digital health approaches

Digital health involves the use of information and communication technologies (ICT) to improve health.^{73,74} It is sometimes divided in two categories, mHealth and telemedicine, but many programmes include both. mHealth strategies encompass smartphones and wearable technologies for health services, while telemedicine refers to delivery of remote care (patient data transmitted to physician, with telephone or website-based patient–physician interaction).^{73,74}

Most digital tools aim to target behavioural changes such as adherence (dosing reminders) and lifestyle modifications (e.g. diet, exercise).^{75,76} These generally provide feedback to patients, and some include educational information. Other tools are designed to monitor BP (and adherence), such as HBP telemonitoring, wearables, or smart pills linked to apps to capture information, transfer it to the healthcare team, and provide feedback to the patient. There is also increasing interest in the development of cuff-less BP measuring devices.^{75,77}

Digital health solutions are based on hardware or software and should be classified as medical devices, which means they must undergo extensive development, validation, and approval processes.^{68,75} This is particularly important for devices that measure BP. However, many health apps are not adequately tested for efficacy, usability, and acceptability but rather are labelled as ‘wellness or fitness’ products to avoid regulations.⁶⁸

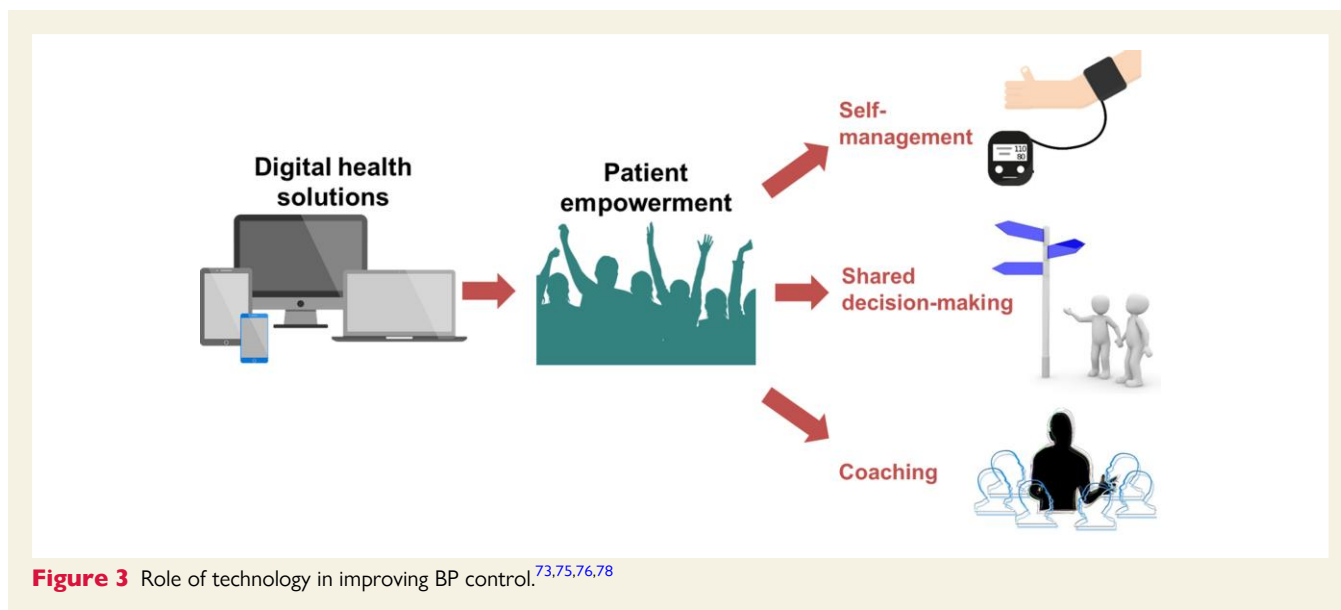
Of the 1000 s of mHealth apps, few have undergone regulatory approval.⁷⁶ This makes it difficult to identify apps that are trustworthy and have demonstrated clinical utility. In addition, standards for approval of apps varies widely from country to country.⁷⁶ Attempts to highlight trustworthy apps through assessment schemes have been implemented: for example, in the UK, the NHS has outlined digital technology assessment criteria (<https://www.nhs.uk/key-tools-and-info/digital-technology-assessment-criteria-dtac/>).

Few digital tools have been studied with long enough follow-up to demonstrate reductions in CVD risk. Nevertheless, evidence to date suggests that mHealth strategies can improve patient health, empower patients to manage their personal health, and improve patient–physician shared decision-making (Figure 3).^{73,75,76,78} In 2019, the ESC e-Cardiology Working Group published a position paper on the use of digital health in CV medicine.⁷³ They concluded that digital healthcare delivery has the potential to improve CV care.

mHealth (mobile apps and websites)

A European Heart Network review of mHealth or ICT for CV patients included over 40 studies assessing various web- or mobile phone-based tools, with or without HBPM and remote or telemonitoring.⁷⁴ The review concluded that smartphone mHealth apps have potential in remote monitoring and improving patient adherence, but there is insufficient evidence to confirm benefits over existing strategies.⁷⁴

A scoping review published in 2021 assessed 15 studies (including 10 RCTs) of web-based dietary and physical activity intervention programmes for patients with hypertension that were published between 2011 and 2020.⁷⁸ Most web-based tools demonstrated



benefits, especially improved communication between clinicians and patients. Clinicians also reported some improvement in patient adherence to medication and appointment schedules. Patients showed improved health with use of the website in addition to their regular schedule, and were empowered to manage their personal health. Studies that have assessed acceptability and the suitability of websites report that they must be highly accessible, and must include many multimedia and interactive features.⁷⁸

One example of a digital programme that has undertaken a rigorous approach to development and validation is the ESH CARE programme. ESH CARE is a BP management app that was developed by a scientific society, and has been adopted by the ESH.⁷² ESH CARE is a multi-component tool that allows users to send stored BP readings to a dedicated website where they can be evaluated by the healthcare team, allowing more precise and continuous patient management. The app includes educational information and is designed to empower patients to actively participate in their BP management.⁷² A pilot study found that a combination of HBPM, the ESH CARE app, and a dedicated website (a programme called POST, Patient Optimal Strategy of Treatment) improved BP control at the 6-month follow-up (72.3% vs. 40.0% in the usual care group).⁷⁹ Additional large, long-term studies are planned to further evaluate the POST-strategy, and its effects on BP control, as well as on CV morbidity and mortality.⁷²

mHealth strategies that were more interactive, were more likely to demonstrate significant benefits, and were more likely to keep patients engaged for a longer period of time.^{3,80} Interactive features can include interactive prompts, transmission of patient measurements, treatment plan/goals, and patient–physician communication.⁸⁰

Telemedicine

BP telemonitoring combines a telemedicine strategy with patients' HBPM, with values being transmitted to the healthcare team, usually via the internet.⁷⁷ The COVID-19 pandemic increased the availability and use of telemedicine around the world.⁶⁸ Data show that patients can accurately measure their vital signs including systolic and diastolic BP, heart rate, peripheral oxygen saturation, body temperature, and

Table 5 Elements of a successful telemedicine programme in hypertension management⁶⁸

- Remote monitoring and transmission of vital signs (e.g. blood pressure)
- Telephone or website communication (with optional video consultation)
- Support for adherence to medication and other management strategies
- Education on lifestyle and risk factors
- Both an automated feedback strategy and a multidisciplinary supervisory team (physician, nurse, or pharmacist)

respiratory rates. In one study, patients learned how to use the devices within 10 min, and measurements were rapidly available to physicians.⁸¹ Importantly, home BP telemonitoring has been shown to result in greater reductions in both office and 24-h ambulatory BP as compared with usual care.^{24,68,82–85} A meta-analysis of 11 RCTs found a mean reduction in BP of 3.9/2.2 mmHg after 12 months in studies using various combinations of HBPM with telephone calls, email, phone messages, or websites compared with usual care.⁸⁵

A European Heart Network review concluded that telemonitoring may be effective, but studies are needed to demonstrate whether it will provide added benefit over HBPM alone, and whether it is cost-effective.⁷⁴ An international expert position paper on the use of BP telemonitoring in hypertension management found that a multi-component strategy is likely to be the best strategy (*Table 5*).⁶⁸

Wearables (e.g. wrist devices)

An increasing number of affordable, cuff-less BP devices, including smartphone, wearable, and 'tricorder' technologies, have become available. A review of some of the commercially available devices concluded that early data suggest promise but many lack proper

validation.⁷⁷ Use in practice of these technologies is limited by motion artefacts, a lack of adequate software and data transfer, difficulties in calibration, and a lack of reimbursement models.⁷⁷ Several watch-type wearables have demonstrated accuracy according to the standards used for cuff-type BP monitors,^{86,87} but these devices should be validated using protocols customized for the specific sensors or other features of the wearable, including their ability to reliably track BP changes over time.¹⁷

As of December 2021, 53 wrist devices, based on the oscillometric BP measurement technology, have passed the STRIDE BP acceptable validation procedures (updated lists available at <https://stridebp.org/bp-monitors>); however, these devices may be less accurate in actual practice, in part due to issues related to incorrect use (wrist at heart level without flexion or extension).¹⁷

Notably, wristband wearables and other cuff-less devices, which are currently still based on immature BP measurement technologies, were not recommended for HBPM in the 2021 European Society of Hypertension guidelines for office and out-of-office BP measurements.¹⁷

Academic and industry partnerships to improve BP control

To improve the validity and utility of technological solutions, and reduce the global impact of hypertension, collaborations between industry and academic institutions is essential.⁸⁴ The digital health systems need more standardization, proof of accuracy and privacy, and evidence for long-term benefits on hard outcomes like CV events. Work should continue on developing unobtrusive, cuff-less, accurate and reliable self BPM-devices. Clinicians and patients, but also experts in behavioural medicine, should be involved from the beginning in the development of all tools to ensure they are truly useful for both patients and physicians.⁸⁴

The ideal academic/industry co-development programme would focus on validating 2–3 multi-component tools, which would include education, a digital app, home self-care and monitoring, automatic transmission of data, and telemedicine. RCTs with longer-term follow-up should be conducted, and the tool itself should be designed to capture outcome metrics on an ongoing basis and to provide feedback to both patients and physicians. However, validation of such digital health tools can be difficult, as they are not constituted by a single 'ingredient', but rather implement a multi-dimensional approach, for which it could be difficult to define a 'placebo' for the control group. The use of new randomized controlled trial frameworks (Multiphase Optimization Strategy) to test simultaneously multiple interventions, or N-of-1 studies should be explored.⁸⁸ Both academic and industry members should advocate for regulatory and reimbursement standards. Finally, there should be plans in place to fund and integrate digital tools seamlessly into primary care physicians' clinical practice and a strategy to facilitate updating the programme as needed.

Strategies to improve the adoption and utility of digital health tools are shown in [Figure 4](#).^{68,73,74,76} From a patient perspective, governments should invest in infrastructure to increase access to digital tools for everyone, and in education to improve digital and health literacy from a young age. From the healthcare perspectives, tools should be designed from the outset to be fully integrated with

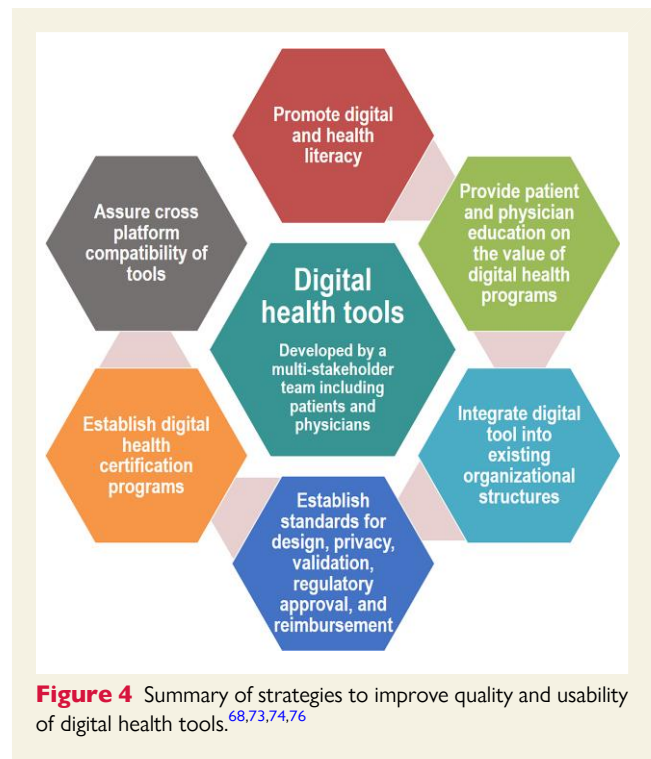


Figure 4 Summary of strategies to improve quality and usability of digital health tools.^{68,73,74,76}

existing organizational structure to ensure they decrease and not increase the workload. This would include a clear pathway for who will view patient data and how the information will be used. More large, long-term trials are needed to provide definitive evidence for physicians, regulatory and reimbursement organization that a certain tool is effective and will improve patient outcomes. Like patients, many healthcare workers also require training in digital health, and this should be integrated into current teaching programmes. Both physicians and patients need reimbursement for the necessary hardware or software to use the tool, and healthcare professionals must also be reimbursed for their time. In addition, patient privacy must be ensured. Therefore, regulatory and reimbursement standards should be developed, and companies should be rewarded for pursuing the more rigorous development pathway.

Healthcare system approaches to risk factor management

Government and healthcare systems approaches are needed to counteract the negative impact of hypertension on a global scale, particularly in light of the fact that CVD mortality rates are often high in rural areas in low-income and middle-income countries where health systems may be weak.^{66,89} Government policies can impact risk factor management including unhealthy diets (high salt, low fruit and vegetable intake), physical inactivity, tobacco and alcohol use, and obesity.¹² Hypertension programmes are often underfunded, especially in low- and middle-income countries, where hypertension funding does not rank in proportion to its resulting disease burden compared with other conditions.⁹⁰

Improved BP control starts with awareness and education. The World Health Organization (WHO) has a detailed education

package (WHO HEARTS) that should be widely implemented on a global scale. Government policies should aim to promote healthy environments including salt, sugar, and alcohol reduction programmes, as well as obesity control including use of laws, taxes, and subsidies. For example, sodium reduction interventions, such as package labelling, and mass media campaigns can decrease intake at the population level and have been found to be highly cost-effective.^{91,92} Obesity control should be a commitment at all ages through education, diet, and exercise. Physical activity can be promoted by providing safe environments and incentives for exercise. Collaborating with the food industry, educational and private institution can be used to help improve nutritional value and make healthy food available at homes, schools, and at work.

Routine BP screening should be performed at all healthcare encounters, and programmemes should be undertaken at pharmacies, markets, religious and social events, vaccinations, elections, and so on, which should be promoted through mass and social media awareness campaigns. Self BP programmes should be encouraged and regulations introduced to improve access to validated BP measurement devices.

Access to healthcare can be improved through task-sharing programmes, including increasing resources for community works, which can cost-effectively improve the diagnosis and treatment of hypertension.⁶⁶ Remote healthcare delivery through mHealth and telehealth programmes can also facilitate access. Hypertension medicines recommended by national guidelines should be on national essential medicines lists and be available free of charge or at affordable cost at all health facilities. Centralized volume buying can be used to help decrease the cost of medications.⁹³ Low cost single-pill treatments can improve control of BP.⁵¹

It should be emphasized that these strategies apply also to hypertension management in low- and mid-income countries, in particular in Africa. As described in a 2022 World Hypertension League Call to Action to improve hypertension management in Africa, the hypertension epidemic is currently responsible for a dramatic increase in CV events and CV mortality, which emphasizes the need for urgent implementation of appropriate strategies for hypertension diagnosis, control, and prevention.⁹⁴

Author contributions

All CRT members that were included as authors contributed to design of the CRT meeting and to selection of the topics; G.P. drafted the initial manuscript. All authors critically revised the manuscript, gave final approval, and agreed to be accountable for all aspects of work ensuring integrity and accuracy.

Acknowledgements

This article was generated from discussions during an online Cardiovascular Round Table (CRT) workshop organised in February 2021 by the European Society of Cardiology (ESC). The ESC CRT is a strategic forum for high-level dialogue between 20 industry companies (pharmaceutical, devices, and diagnostics) and the ESC leadership to identify and discuss key strategic issues for the future of cardiovascular health in Europe. The authors would like to thank Pauline Lavigne and

Steven Portelance (unaffiliated, supported by the ESC) for their contributions to writing and editing the manuscript.

Conflict of interest: G.P.: honoraria for lectures from Omron, Servier, Merck, and Bayer; A.G. Employee of Philips; D.S.: Employee of Novartis; R.S.B.: grants for InSiDe (Integrated Silicon photonics for Cardiovascular Disease monitoring; H2020-ICT-871547); E.G.C.: consulting fees from Medtronic and Summeet Srl; honoraria from Novartis Farma SpA, Havas PR Milan Srl, Servier, and Aim Italy Srl; support for meeting attendance from the European Society of Cardiology (ESC); advisory board participation for Medtronic; and positions on the ESC Advocacy, Regulatory Affairs, and Digital Health Committees; F.M.: support from Deutsche Gesellschaft für Kardiologie (DGK) and Deutsche Forschungsgemeinschaft (SFB TRR219); scientific support and speaker honoraria from Bayer, Boehringer Ingelheim, Medtronic, and ReCor Medical; R.J.M.: Programme grants and funding from the NIH; institutional licensing fees from Omron and Sensyne; and institutional consulting fees from Omron; P.S.: Leadership role (President-elect) of the Italian Stroke Association-ISA; T.K.: Institutional research contracts from Medtronic and ReCor. The other others report no conflict of interest.

Data availability

No new data were generated or analysed in support of this manuscript.

References

1. GBD Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. *Lancet* 2020;**396**:1223–1249.
2. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I, ESC Scientific Document Group. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J* 2018;**39**:3021–3104.
3. Marshall JJ, Wolfe CD, McKeivitt C. Lay perspectives on hypertension and drug adherence: systematic review of qualitative research. *BMJ* 2012;**345**:e3953.
4. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation* 2008;**117**:3171–3180.
5. Yano Y, Reis JP, Colangelo LA, Shimbo D, Viera AJ, Allen NB, Gidding SS, Bress AP, Greenland P, Muntner P, Lloyd-Jones DM. Association of blood pressure classification in young adults using the 2017 American college of cardiology/American heart association blood pressure guideline with cardiovascular events later in life. *JAMA* 2018;**320**:1774–1782.
6. Sundstrom J, Neovius M, Tynelius P, Rasmussen F. Association of blood pressure in late adolescence with subsequent mortality: cohort study of Swedish male conscripts. *BMJ* 2011;**342**:d643.
7. Luo D, Cheng Y, Zhang H, Ba M, Chen P, Li H, Chen K, Sha W, Zhang C, Chen H. Association between high blood pressure and long term cardiovascular events in young adults: systematic review and meta-analysis. *BMJ* 2020;**370**:m3222.
8. Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirsh A, Invitti C, Litwin M, Mancia G, Pall D, Rascher W, Redon J, Schaefer F, Seeman T, Sinha M, Stabouli S, Webb NJ, Wuhl E, Zanchetti A. 2016 European society of hypertension guidelines for the management of high blood pressure in children and adolescents. *J Hypertens* 2016;**34**:1887–1920.
9. Kahan T. Guest editorial challenges in resistant hypertension. *Eur Cardiol* 2016;**11**:18–19.
10. Nguyen NT, Magno CP, Lane KT, Hinojosa MW, Lane JS. Association of hypertension, diabetes, dyslipidemia, and metabolic syndrome with obesity: findings from the national health and nutrition examination survey, 1999 to 2004. *J Am Coll Surg* 2008;**207**:928–934.
11. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, Elkind MSV, Evenson KR, Ferguson JF, Gupta DK, Khan SS, Kissela BM, Knutson KL, Lee CD, Lewis TT, Liu J, Loop MS, Lutsey PL, Ma J, Mackey J, Martin SS, Matchar DB, Mussolino ME, Navaneethan

- SD, Perak AM, Roth GA, Samad Z, Satou GM, Schroeder EB, Shah SH, Shay CM, Stokes A, VanWagner LB, Wang NY, Tsao CW, American Heart Association Council On Epidemiology, Prevention Statistics Committee, Stroke Statistics Subcommittee. Heart disease and stroke statistics-2021 update: a report from the American heart association. *Circulation* 2021;**143**:e254–e743.
12. Gooding HC, Gidding SS, Moran AE, Redmond N, Allen NB, Bacha F, Burns TL, Catov JM, Grandner MA, Harris KM, Johnson HM, Kiernan M, Lewis TT, Matthews KA, Monaghan M, Robinson JG, Tate D, Bibbins-Domingo K, Spring B. Challenges and opportunities for the prevention and treatment of cardiovascular disease among young adults: report from a national heart, lung, and blood institute working group. *J Am Heart Assoc* 2020;**9**:e016115.
 13. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Back M, Benetos A, Biffi A, Boavida JM, Capodanno D, Cosyns B, Crawford C, Davos CH, Desormais I, Di Angelantonio E, Franco OH, Halvorsen S, Hobbs FDR, Hollander M, Jankowska EA, Michal M, Sacco S, Sattar N, Tokgozoglul L, Tonstad S, Tsioufis KP, van Dis I, van Gelder IC, Wannier C, Williams B, Group ESCSD. 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. *Eur J Prev Cardiol* 2022;**29**: 5–115.
 14. Parati G, Stergiou GS, Bilo G, Kollias A, Pengo M, Ochoa JE, Agarwal R, Asayama K, Asmar R, Burnier M, De La Sierra A, Giannattasio C, Gosse P, Head G, Hoshide S, Imai Y, Kario K, Li Y, Manios E, Mant J, McManus RJ, Mengden T, Mihailidou AS, Muntner P, Myers M, Niranani T, Ntineri A, O'Brien E, Octavio JA, Ohkubo T, Omboni S, Padfield P, Palatini P, Pellegrini D, Postel-Vinay N, Ramirez AJ, Sharman JE, Shennan A, Silva E, Topouchian J, Torlasco C, Wang JG, Weber MA, Whelton PK, White WB, Mancia G, Working Group on Blood Pressure Monitoring, Cardiovascular Variability of the European Society of Hypertension. Home blood pressure monitoring: methodology, clinical relevance and practical application: a 2021 position paper by the working group on blood pressure monitoring and cardiovascular variability of the European society of hypertension. *J Hypertens* 2021;**39**:1742–1767.
 15. Parati G, Ochoa JE, Bilo G. Moving beyond office blood pressure to achieve a personalized and more precise hypertension management: which way to go? *Hypertension* 2017;**70**:e20–e31.
 16. Parati G, Lombardi C, Pengo M, Bilo G, Ochoa JE. Current challenges for hypertension management: from better hypertension diagnosis to improved patients' adherence and blood pressure control. *Int J Cardiol* 2021;**331**:262–269.
 17. Stergiou GS, Palatini P, Parati G, O'Brien E, Januszewicz A, Lurbe E, Persu A, Mancia G, Kreutz R. European Society of hypertension council the European society of hypertension working group on blood pressure monitoring cardiovascular variability. 2021 European society of hypertension practice guidelines for office and out-of-office blood pressure measurement. *J Hypertens* 2021;**39**:1293–1302.
 18. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, Ramirez A, Schlaich M, Stergiou GS, Tomaszewski M, Wainford RD, Williams B, Schutte AE. 2020 International society of hypertension global hypertension practice guidelines. *Hypertension* 2020;**75**:1334–1357.
 19. Parati G, Stergiou G, O'Brien E, Asmar R, Beilin L, Bilo G, Clement D, de la Sierra A, de Leeuw P, Dolan E, Fagard R, Graves J, Head GA, Imai Y, Kario K, Lurbe E, Mallion JM, Mancia G, Mengden T, Myers M, Ogedegbe G, Ohkubo T, Omboni S, Palatini P, Redon J, Ruilope LM, Shennan A, Staessen JA, vanMontfrans G, Verdecchia P, Waerber B, Wang J, Zanchetti A, Zhang Y, European Society of Hypertension Working Group on Blood Pressure Monitoring, Cardiovascular Variability. European Society of hypertension practice guidelines for ambulatory blood pressure monitoring. *J Hypertens* 2014;**32**:1359–1366.
 20. Bilo G, Dolan E, O'Brien E, Facchetti R, Soranna D, Zambon A, Mancia G, Parati G. The impact of systolic and diastolic blood pressure variability on mortality is age dependent: data from the Dublin outcome study. *Eur J Prev Cardiol* 2020;**27**:355–364.
 21. Piper MA, Evans CV, Burda BU, Margolis KL, O'Connor E, Whitlock EP. Diagnostic and predictive accuracy of blood pressure screening methods with consideration of rescreening intervals: a systematic review for the U.S. Preventive services task force. *Ann Intern Med* 2015;**162**:192–204.
 22. Ward AM, Takahashi O, Stevens R, Heneghan C. Home measurement of blood pressure and cardiovascular disease: systematic review and meta-analysis of prospective studies. *J Hypertens* 2012;**30**:449–456.
 23. Bliiziotis IA, Destounis A, Stergiou GS. Home versus ambulatory and office blood pressure in predicting target organ damage in hypertension: a systematic review and meta-analysis. *J Hypertens* 2012;**30**:1289–1299.
 24. Agarwal R, Bills JE, Hecht TJ, Light RP. Role of home blood pressure monitoring in overcoming therapeutic inertia and improving hypertension control: a systematic review and meta-analysis. *Hypertension* 2011;**57**:29–38.
 25. Stergiou GS, O'Brien E, Myers M, Palatini P, Parati G, Kollias A, Birmpas D, Kyriakoulis K, Bountzoua I, Stambolliu E, Anagnostopoulos I, Karpettas N, Menti A, STRIDE BP Scientific Advisory Board. STRIDE BP international initiative for accurate blood pressure measurement: systematic review of published validation studies of blood pressure measuring devices. *J Clin Hypertens (Greenwich)* 2019; **21**: 1616–1622.
 26. Stergiou GS, Palatini P, Asmar R, Ioannidis JP, Kollias A, Lacy P, McManus RJ, Myers MG, Parati G, Shennan A, Wang J, O'Brien E, European Society of Hypertension Working Group on Blood Pressure Monitoring. Recommendations and practical guidance for performing and reporting validation studies according to the universal standard for the validation of blood pressure measuring devices by the association for the advancement of medical instrumentation/European society of hypertension/international organization for standardization (AAMI/ESH/ISO). *J Hypertens* 2019;**37**:459–466.
 27. Devereux RB, Alderman MH. Role of preclinical cardiovascular disease in the evolution from risk factor exposure to development of morbid events. *Circulation* 1993; **88**:1444–1455.
 28. Boutouyrie P, Chowienczyk P, Humphrey JD, Mitchell GF. Arterial stiffness and cardiovascular risk in hypertension. *Circ Res* 2021;**128**:864–886.
 29. Agbaje AO, Barker AR, Tuomainen TP. Effects of arterial stiffness and carotid intima-media thickness progression on the risk of overweight/obesity and elevated blood pressure/hypertension: A cross-lagged cohort study. *Hypertension* 2022;**79**: 159–169.
 30. Sehestedt T, Jeppesen J, Hansen TW, Wachtell K, Ibsen H, Torp-Pedersen C, Hildebrandt P, Olsen MH. Risk prediction is improved by adding markers of subclinical organ damage to SCORE. *Eur Heart J* 2010;**31**:883–891.
 31. Ben-Shlomo Y, Spears M, Boustred C, May M, Anderson SG, Benjamin EJ, Boutouyrie P, Cameron J, Chen CH, Cruickshank JK, Hwang SJ, Lakatta EG, Laurent S, Maldonado J, Mitchell GF, Najjar SS, Newman AB, Ohishi M, Pannier B, Pereira T, Vasan RS, Shokawa T, Sutton-Tyrell K, Verbeke F, Wang KL, Webb DJ, Willum Hansen T, Zoungas S, McEnery CM, Cockcroft JR, Wilkinson IB. Aortic pulse wave velocity improves cardiovascular event prediction: an individual participant meta-analysis of prospective observational data from 17,635 subjects. *J Am Coll Cardiol* 2014;**63**:636–646.
 32. Adamson PD, Williams MC, Dweck MR, Mills NL, Boon NA, Daghm M, Bing R, Moss AJ, Mangion K, Flather M, Forbes J, Hunter A, Norrie J, Shah ASV, Timmis AD, van Beek EJR, Ahmadi AA, Leipsic J, Narula J, Newby DE, Roditi G, McAllister DA, Berry C, Investigators S-H. Guiding therapy by coronary CT angiography improves outcomes in patients with stable chest pain. *J Am Coll Cardiol* 2019;**74**: 2058–2070.
 33. Wartolowska KA, Webb AJS. Midlife blood pressure is associated with the severity of white matter hyperintensities: analysis of the UK biobank cohort study. *Eur Heart J* 2021;**42**:750–757.
 34. Hall ME, Cohen JB, Ard JD, Egan BM, Hall JE, Lavie CJ, Ma J, Ndumele CE, Schauer PR, Shimbo D, American Heart Association Council on Hypertension, Council on Arteriosclerosis, Thrombosis and Vascular Biology, Council on Lifestyle and Cardiometabolic Health, Stroke Council. Weight-loss strategies for prevention and treatment of hypertension: a scientific statement from the American heart association. *Hypertension* 2021;**78**:e38–e50.
 35. Valenzuela PL, Carrera-Bastos P, Galvez BG, Ruiz-Hurtado G, Ordozas JM, Ruilope LM, Lucia A. Lifestyle interventions for the prevention and treatment of hypertension. *Nat Rev Cardiol* 2020.
 36. Blood Pressure Lowering Treatment Trialists Collaboration. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet* 2021;**397**:1625–1636.
 37. Ghatage T, Goyal SG, Dhar A, Bhat A. Novel therapeutics for the treatment of hypertension and its associated complications: peptide- and nonpeptide-based strategies. *Hypertens Res* 2021;**44**:740–755.
 38. Gupta P, Patel P, Strauch B, Lai FY, Akbarov A, Maresova V, White CMJ, Petrak O, Gulsin GS, Patel V, Rosa J, Cole R, Zelinka T, Holaj R, Kinnell A, Smith PR, Thompson JR, Squire I, Widimsky J, Jr., Samani NJ, Williams B, Tomaszewski M. Risk factors for nonadherence to antihypertensive treatment. *Hypertension* 2017; **69**:1113–1120.
 39. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005;**365**:217–223.
 40. Burnier M, Egan BM. Adherence in hypertension. *Circ Res* 2019;**124**:1124–1140.
 41. Berra E, Azizi M, Capron A, Hoiweggen A, Rabbia F, Kjeldsen SE, Staessen JA, Wallemacq P, Persu A. Evaluation of adherence should become an integral part of assessment of patients with apparently treatment-resistant hypertension. *Hypertension* 2016;**68**:297–306.
 42. Durand H, Hayes P, Morrissey EC, Newell J, Casey M, Murphy AW, Molloy GJ. Medication adherence among patients with apparent treatment-resistant hypertension: systematic review and meta-analysis. *J Hypertens* 2017;**35**:2346–2357.

43. Lauder L, da Costa BR, Ewen S, Scholz SS, Wijns W, Luscher TF, Serruys PW, Edelman ER, Capodanno D, Bohm M, Juni P, Mahfoud F. Randomized trials of invasive cardiovascular interventions that include a placebo control: a systematic review and meta-analysis. *Eur Heart J* 2020;**41**:2556–2569.
44. Lauder L, Azizi M, Kirtane AJ, Bohm M, Mahfoud F. Device-based therapies for arterial hypertension. *Nat Rev Cardiol* 2020;**17**:614–628.
45. Mahfoud F, Schlaich MP, Lobo MD. Device therapy of hypertension. *Circ Res* 2021;**128**:1080–1099.
46. Bruno RM, Taddei S, Borghi C, Colivicchi F, Desideri G, Grassi G, Mazza A, Muiesan ML, Parati G, Pontremoli R, Trimarco B, Volpe M, Ferri C. Italian Society of arterial hypertension (SIIA) position paper on the role of renal denervation in the management of the difficult-to-treat hypertensive patient. *High Blood Press Cardiovasc Prev* 2020;**27**:109–117.
47. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Oviagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. *Hypertension* 2018;**71**:e13–e115.
48. Schmieder RE, Mahfoud F, Mancia G, Azizi M, Bohm M, Dimitriadis K, Kario K, Kroon AA MDL, Ott C, Pathak A, Persu A, Scalise F, Schlaich M, Kreutz R, Tsioufis C, members of the ESH Working Group on Device-Based Treatment of Hypertension. European society of hypertension position paper on renal denervation 2021. *J Hypertens* 2021;**39**:1733–1741.
49. Kulkarni S, Rao R, Goodman JDH, Connolly K, O'Shaughnessy KM. Nonadherence to antihypertensive medications amongst patients with uncontrolled hypertension: a retrospective study. *Medicine (Baltimore)* 2021;**100**:e24654.
50. Du LP, Cheng ZW, Zhang YX, Li Y, Mei D. The impact of fixed-dose combination versus free-equivalent combination therapies on adherence for hypertension: a meta-analysis. *J Clin Hypertens (Greenwich)* 2018;**20**:902–907.
51. Parati G, Kjeldsen S, Coca A, Cushman WC, Wang J. Adherence to single-pill versus free-equivalent combination therapy in hypertension: a systematic review and meta-analysis. *Hypertension* 2021;**77**:692–705.
52. Kably B, Billaud EM, Boutouyrie P, Azizi M. Is there any hope for monitoring adherence in an efficient and feasible way for resistant hypertension diagnosis and follow-up? *Curr Hypertens Rep* 2020;**22**:96.
53. Burnier M, Polychronopoulou E, Wuerzner G. Hypertension and drug adherence in the elderly. *Front Cardiovasc Med* 2020;**7**:49.
54. Qvarnstrom M, Kahan T, Kieler H, Brandt L, Hasselstrom J, Bengtsson Bostrom K, Manhem K, Hjerpe P, Wettermark B. Persistence to antihypertensive drug treatment in Swedish primary healthcare. *Eur J Clin Pharmacol* 2013;**69**:1955–1964.
55. Poulter NR, Borghi C, Parati G, Pathak A, Toli D, Williams B, Schmieder RE. Medication adherence in hypertension. *J Hypertens* 2020;**38**:579–587.
56. Schoenthaler A, Knaf GJ, Fiscella K, Ogedegbe G. Addressing the social needs of hypertension patients: the role of patient-provider communication as a predictor of medication adherence. *Circ Cardiovasc Qual Outcomes* 2017;**10**.
57. Peacock E, Krousel-Wood M. Adherence to antihypertensive therapy. *Med Clin North Am* 2017;**101**:229–245.
58. Lane D, Lawson A, Burns A, Azizi M, Burnier M, Jones DJL, Kably B, Khunti K, Kreutz R, Patel P, Persu A, Spiering W, Toennes SW, Tomaszewski M, Williams B, Gupta P, Dasgupta I. Endorsed by the European society of hypertension working group on cardiovascular P, adherence. Nonadherence in hypertension: how to develop and implement chemical adherence testing. *Hypertension* 2022;**79**:12–23.
59. Qvarnstrom M, Kahan T, Kieler H, Brandt L, Hasselstrom J, Wettermark B. Medication persistence to antihypertensive drug treatment: a cross-sectional study of attitudes towards hypertension and medication in persistent and non-persistent patients. *Blood Press* 2019;**28**:309–316.
60. Milman T, Joundi RA, Alotaibi NM, Saposnik G. Clinical inertia in the pharmacological management of hypertension: a systematic review and meta-analysis. *Medicine (Baltimore)* 2018;**97**:e11121.
61. Ali DH, Kilic B, Hart HE, Bots ML, Biermans MCJ, Spiering W, Rutten FH, Hollander M. Therapeutic inertia in the management of hypertension in primary care. *J Hypertens* 2021;**39**:1238–1245.
62. Rea F, Corrao G, Merlino L, Mancia G. Initial antihypertensive treatment strategies and therapeutic inertia. *Hypertension* 2018;**72**:846–853.
63. Lin ND, Martins SB, Chan AS, Coleman RW, Bosworth HB, Oddone EZ, Shankar RD, Musen MA, Hoffman BB, Goldstein MK. Identifying barriers to hypertension guideline adherence using clinician feedback at the point of care. *AMIA Annu Symp Proc* 2006:494–498.
64. Anand TN, Joseph LM, Geetha AV, Prabhakaran D, Jeemon P. Task sharing with non-physician health-care workers for management of blood pressure in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet Glob Health* 2019;**7**:e761–e771.
65. Ogunge O, Cazabon D, Ajenikoko A, Jeemon P, Moran AE, Commodore-Mensah Y. Determining the frequency and level of task-sharing for hypertension management in LMICs: a systematic review and meta-analysis. *EClinicalMedicine* 2022;**47**:101388.
66. Finkelstein EA, Krishnan A, Naheed A, Jehan I, de Silva HA, Gandhi M, Lim CW, Chakma N, Ediriweera DS, Khan J, Kasturiratne A, Hirani S, Solayman AKM, Jafar TH, group C-Bs. Budget impact and cost-effectiveness analyses of the COBRA-BPS multicomponent hypertension management programme in rural communities in Bangladesh, Pakistan, and Sri Lanka. *Lancet Glob Health* 2021;**9**:e660–e667.
67. Murphy M, Scott LJ, Salisbury C, Turner A, Scott A, Denholm R, Lewis R, Iyer G, Macleod J, Horwood J. Implementation of remote consulting in UK primary care following the COVID-19 pandemic: a mixed-methods longitudinal study. *Br J Gen Pract* 2021;**71**:e166–e177.
68. Omboni S, McManus RJ, Bosworth HB, Chappell LC, Green BB, Kario K, Logan AG, Magid DJ, McKinstry B, Margolis KL, Parati G, Wakefield BJ. Evidence and recommendations on the use of telemedicine for the management of arterial hypertension: an international expert position paper. *Hypertension* 2020;**76**:1368–1383.
69. Rodriguez S, Hwang K, Wang J. Connecting home-based self-monitoring of blood pressure data into electronic health records for hypertension care: a qualitative inquiry with primary care providers. *JMIR Form Res* 2019;**3**:e10388.
70. Lv N, Xiao L, Simmons ML, Rosas LG, Chan A, Entwistle M. Personalized hypertension management using patient-generated health data integrated with electronic health records (EMPOWER-H): six-month pre-post study. *J Med Internet Res* 2017;**19**:e311.
71. Ralston JD, Cook AJ, Anderson ML, Catz SL, Fishman PA, Carlson J, Johnson R, Green BB. Home blood pressure monitoring, secure electronic messaging and medication intensification for improving hypertension control: a mediation analysis. *Appl Clin Inform* 2014;**5**:232–248.
72. Parati G, Torlasco C, Omboni S, Pellegrini D. Smartphone applications for hypertension management: a potential game-changer that needs more control. *Curr Hypertens Rep* 2017;**19**:48.
73. Frederix I, Caiani EG, Dendale P, Anker S, Bax J, Bohm A, Cowie M, Crawford J, de Groot N, Dilaveris P, Hansen T, Koehler F, Krstacic G, Lambrinou E, Lancellotti P, Meier P, Neubeck L, Parati G, Piotrowicz E, Tubaro M, van der Velde E. ESC e-Cardiology working group position paper: overcoming challenges in digital health implementation in cardiovascular medicine. *Eur J Prev Cardiol* 2019;**26**:1166–1177.
74. Scherrenberg M, Vangenechten G, Janssen A, Dendale P. What is the value of digital tools for cardiovascular patients? A comprehensive review of evidence for effectiveness and cost-effectiveness for prevention and management. <https://ehnhart.org/publications-and-papers/publications/1285.html> (June 9 2021).
75. Thangada ND, Garg N, Pandey A, Kumar N. The emerging role of mobile-health applications in the management of hypertension. *Curr Cardiol Rep* 2018;**20**:78.
76. Rowland SP, Fitzgerald JE, Holme T, Powell J, McGregor A. What is the clinical value of mHealth for patients? *NPJ Digit Med* 2020;**3**:4.
77. Bard DM, Joseph JI, van Helmond N. Cuff-less methods for blood pressure telemonitoring. *Front Cardiovasc Med* 2019;**6**:40.
78. Baderol Allam FN, Ab Hamid MR, Buhari SS, Md Noor H. Web-based dietary and physical activity intervention programs for patients with hypertension: scoping review. *J Med Internet Res* 2021;**23**:e22465.
79. Albini F, Xiaoqi L, Torlasco C, Soranna D, Faini A, Ciminaghi R, Celsi A, Benedetti M, Zamboni A, di Rienzo M, Parati G. An ICT and mobile health integrated approach to optimize patients' education on hypertension and its management by physicians: the patients optimal strategy of treatment (POST) pilot study. *Annu Int Conf IEEE Eng Med Biol Soc* 2016;**2016**:517–520.
80. Donevant SB, Estrada RD, Culley JM, Habing B, Adams SA. Exploring app features with outcomes in mHealth studies involving chronic respiratory diseases, diabetes, and hypertension: a targeted exploration of the literature. *J Am Med Inform Assoc* 2018;**25**:1407–1418.
81. Kagiyama N, Hiki M, Matsue Y, Dohi T, Matsuzawa W, Daida H, Minamino T, Kasai T. Validation of telemedicine-based self-assessment of vital signs for patients with COVID-19: a pilot study. *J Telemed Telecare* 2021:1357633X211011825.
82. Omboni S. Connected health in hypertension management. *Front Cardiovasc Med* 2019;**6**:76.
83. Omboni S, Gazzola T, Carabelli G, Parati G. Clinical usefulness and cost effectiveness of home blood pressure telemonitoring: meta-analysis of randomized controlled studies. *J Hypertens* 2013;**31**:455–467. discussion 467–8.

84. Pellegrini D, Torlasco C, Ochoa JE, Parati G. Contribution of telemedicine and information technology to hypertension control. *Hypertens Res* 2020;**43**:621–628.
85. Lu X, Yang H, Xia X, Lu X, Lin J, Liu F, Gu D. Interactive mobile health intervention and blood pressure management in adults. *Hypertension* 2019;**74**:697–704.
86. Kuwabara M, Harada K, Hishiki Y, Ohkubo T, Kario K, Imai Y. Validation of a wrist-type home nocturnal blood pressure monitor in the sitting and supine position according to the ANSI/AAMI/ISO81060–2:2013 guidelines: omron HEM-9601 T. *J Clin Hypertens (Greenwich)* 2020;**22**:970–978.
87. Kuwabara M, Harada K, Hishiki Y, Kario K. Validation of two watch-type wearable blood pressure monitors according to the ANSI/AAMI/ISO81060-2:2013 guidelines: omron HEM-6410T-ZM and HEM-6410T-ZL. *J Clin Hypertens (Greenwich)* 2019;**21**: 853–858.
88. Collins L. *Optimization of behavioral, biobehavioral, and biomedical interventions: the multi-phase optimization strategy (MOST)*. 1st ed Springer International Publishing AG; 2018.
89. Ataklte F, Erqou S, Kaptoge S, Taye B, Echouffo-Tcheugui JB, Kengne AP. Burden of undiagnosed hypertension in sub-saharan Africa: a systematic review and meta-analysis. *Hypertension* 2015;**65**:291–298.
90. Qin VM, Hone T, Millett C, Moreno-Serra R, McPake B, Atun R, Lee JT. The impact of user charges on health outcomes in low-income and middle-income countries: a systematic review. *BMJ Glob Health* 2018;**3**:e001087.
91. Ide N, Ajenikoko A, Steele L, Cohn J CJC, Frieden TR, Cobb LK. Priority actions to advance population sodium reduction. *Nutrients* 2020;**12**.
92. Cohn J, Kostova D, Moran AE, Cobb LK, Pathni AK, Bisrat D. Blood from a stone: funding hypertension prevention, treatment, and care in low- and middle-income countries. *J Hum Hypertens* 2021.
93. Kim SW, Skordis-Worrall J. Can voluntary pooled procurement reduce the price of antiretroviral drugs? A case study of efavirenz. *Health Policy Plan* 2017;**32**: 516–526.
94. Parati G, Lackland DT, Campbell NRC, Ojo Owolabi M, Bavuma C, Mamoun Beheiry H, Dzudie A, Ibrahim M, El Aroussy W, Singh S, Varghese CV, Whelton PK, Zhang XH, World Hypertension League. How to improve awareness, treatment, and control of hypertension in Africa, and how to reduce its consequences. A call to action from the world hypertension league. *Hypertension* 2022:Online. <https://doi.org/10.1161/HYPERTENSIONAHA.121.18884>