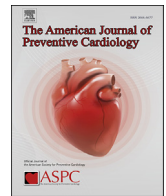


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State-of-the-Art Review

## State-of-the-Art review: Hypertension practice guidelines in the era of COVID-19

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### ABSTRACT

The global burden of hypertension (HTN) is immense and increasing. In fact, HTN is the leading risk factor for adverse cardiovascular disease outcomes. Due to the critical significance and increasing prevalence of the disease, several national and international societies have recently updated their guidelines for the diagnosis and treatment of HTN. In consideration of the COVID-19 pandemic, this report provides clinicians with the best strategies to prevent HTN, manage the acute and long-term cardiac complications of HTN, and provide the best evidence-based care to patients in an ever-changing healthcare environment. The overarching goal of the various HTN guidelines is to provide easily accessible information to healthcare providers and public health officials, which is key for optimal clinical practice. However, the COVID-19 pandemic has challenged the ability to provide safe care to the most vulnerable hypertensive populations throughout the world. Therefore, this review compares the most recent guidelines of the 2017 American College of Cardiology/American Heart Association and multiple U.S. societies, the 2018 European Society of Cardiology/European Society of Hypertension, the 2019 National Institute for Care and Health Excellence, and the 2020 International Society of Hypertension. While a partial emphasis is placed on the management of HTN in the midst of COVID-19, this review will summarize current concepts and emerging data from the listed HTN guidelines on the diagnosis, monitoring, management, and evidence-based treatments in adults.

### 1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus composed of a single stranded positive-sense RNA. The specifics of the detailed pathobiology and human cellular interactions have been described previously [1–4]. This virus binds to the angiotensin-converting enzyme 2 (ACE2), a cellular transmembrane homologue of angiotensin-converting enzyme (ACE), in order to enter most human cell lines, including pneumocytes and those in the cardiovascular system [4]. Consequently, in addition to the eponymous respiratory complications, COVID-19 is associated with increased vascular thrombosis, myocardial inflammation, arrhythmia, and potentially increased risk for adverse outcomes in patients with HTN [5]. In a recent meta-analysis of 6560 patients from 30 studies, HTN was associated with an increased composite poor outcome, which included mortality, acute respiratory disease syndrome, need for intensive care, and disease

progression in patients with COVID-19 [6]. Other studies have shown similar findings of the deleterious effects of COVID-19 patients with HTN [7,8]. Yet it remains unclear how contemporary guideline recommendations may be impacted in the setting of the COVID-19 pandemic.

Moreover, the current public health crisis of COVID-19 has already impacted patients with HTN from multiple aspects. Approximately 1.5 million people in the U.S. lost their employment-based health insurance coverage, directly affecting patients with HTN and other chronic conditions [9]. Coverage losses are likely the steepest in states without Medicaid expansion under the Patient Protection and Affordable Care Act. Unfortunately, access to health coverage is most deficient in states with the largest racial/ethnic disparities in cardiovascular care, potentially impacting adherence and medication affordability [10,11]. Specifically, African Americans may suffer worse outcomes related to COVID-19 exposure, due to a variety of reasons, including socioeconomic factors and limited health access [12].

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This review will compare and contrast contemporary evidence-based guidelines for the prevention and treatment of HTN: the 2017 American College of Cardiology/American Heart Association (ACC/AHA) Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults; the 2018 European Society of Cardiology/European Society of Hypertension (ESC/ESH) Guidelines for the Management of Arterial Hypertension; the 2019 National Institute for Health and Care Excellence (NICE) Hypertension in Adults; and the 2020 International Society of Hypertension (ISH) Global Hypertension Practice Guidelines. Accordingly, this review will summarize current best practices in HTN management, taken into account the current COVID-19 pandemic, emerging data on diagnosis and BP monitoring, and evidence-based treatment of certain special populations, including related to race/ethnicity. Guidelines-directed medical care will provide best strategies to battle the acute and long-term cardiac complications of HTN across diverse populations in the COVID-19 era and beyond.

## 2. The hypertension pandemic

HTN, the most widely prevalent and potent risk factor for atherosclerosis cardiovascular disease (ASCVD) and associated microvascular complications, affects an estimated 1.4 billion people worldwide, disproportionately so in low- and middle-income countries. Globally, upwards to 1 in 4 men and 1 in 5 women have the chronic HTN [13,14]. Consequently, HTN is the leading global cause of mortality, accounting for 10.4 million deaths per year and a major cause of premature death worldwide [15]. Regarding systolic blood pressures (SBP), there are over 7.8 million deaths and ~140,000 million disease adjusted life years (DALYs) attributed to a SBP > 140 mmHg alone [13–15].

As well, there are unique considerations and persistent world-wide disparities in HTN death and morbidity in specific populations, such as related to racial/ethnicity, female sex, advanced age, and socioeconomic status. Recent data from the Centers for Disease Control and Prevention (CDC) noted a significantly higher prevalence of uncontrolled HTN among U.S. racial/ethnic minority groups compared with non-Hispanic whites [16]. The prevalence of self-reported HTN in 2017 ( $\geq 140/90$  mmHg) was much higher in Non-Hispanic blacks (African Americans) and American Indians (40% vs. 37%, respectively) than the self-reported prevalence of HTN in Hispanics and whites (28% vs. 29%, respectively) [16]. After the introduction of the 2017 ACC/AHA and multi-society high blood pressure (HBP) guidelines, the prevalence of HTN increased from 32% in the U.S. to 46% using a BP threshold for HTN  $\geq 130/80$  mmHg, further disproportionately affecting blacks and older individuals [17]. Due to the increasing prevalence of HTN in younger patients, the U.S. Preventive Task Force recommendations now support office BP screening in patients 18 years of age and older [18]. Therefore, there may be further disparate prevalence among various groups with HTN as time progresses.

This review evaluates current recommended lifestyle interventions and pharmacotherapy within the major guidelines, and the ongoing efforts to combat the challenges of HTN management in the setting of COVID-19. Although recommended in evidence-based guidelines, the COVID-19 pandemic has limited physical activity secondary to social distancing, home quarantining, and fitness center shutdowns [19]. Moreover, the COVID-19 pandemic has forced the practice of medicine into a new paradigm, where telehealth technologies and self-monitoring techniques have developed more prominent roles for clinical management of HTN and ASCVD risk reduction.

## 3. Recent major guidelines for hypertension: similarities and differences

Current guidelines, despite major and minor differences, serve as tools for the advancement of “standard of care” recommendations in clinical practice, including specific populations, usually with a regional emphasis. The 2017 ACC/AHA recommendations for tighter BP control

were supported by several sources, including several meta-analyses of observational cohorts associated with a significantly higher range of hazard ratios (1.1–1.5) for cardiovascular disease (CVD) and stroke with SBP/DBP  $\geq 120$ –129/80–84 mmHg as compared to  $<120/80$  mmHg [17, 20]. Furthermore, data for the benefit of tighter BP control also emerged from the Systolic Blood Pressure Intervention Trial (SPRINT). This National Institute of Health landmark trial was a large randomized control study which evaluated the benefits of intensive BP goals ( $<120$  mmHg) compared with standard treatment goals ( $<140$  mmHg) [21]. As a result of an overwhelming positive effect, SPRINT was stopped early after demonstrating a 25% and 27% relative risk reduction (RRR) in the primary endpoint and all-cause mortality in the intensive BP lowering group compared to standard treatment (HR 0.75, 95% CI 0.64–0.89, HR 0.73, 95% CI 0.60–0.90, respectively). Thus, the prospect of encouraging patients and providers in the U.S. to manage HTN more intensively was recommended to decrease end-organ damage and mortality.

The 2018 ESC/ESH HTN guidelines reflected a broad scope, intended for the treatment of hypertensive individuals in countries with various socioeconomic populations [22]. The prevalence of HTN ( $\geq 140/90$  mmHg) in central and Eastern Europe is approximately 30–45%, affecting over 150 million adults, with an increasing prevalence of up to 60% in adults of advanced age. Instead of focusing on tighter BP control, the ESC/ESH guidelines defined HTN as the level of BP at which the benefits of treatment, whether lifestyle interventions or medications, outweighed the risks. Recommendations were based on meta-analyses of randomized controlled trials (RCTs), in which treatment of stage I BP values of  $\geq 140/90$  mmHg were considered beneficial [22]. Moreover, utilizing older and high-risk cohort studies may increase statistical power over a shorter duration of follow-up. These differences in the type of evidence used between the 2017 ACC/AHA and the 2018 ESC/ESH guidelines may provide clarity as to why the BP thresholds for HTN vary between the reports.

Most recently published are the NICE’s ‘Hypertension in Adults’ in 2019 and the 2020 ISH report [23,24]. The NICE guidelines only reviewed evidence beyond the year 2000, reflecting the current use of electronic BP devices. However, both guidelines use the SBP/DBP threshold of 140/90 mmHg to define Stage I HTN. The 2020 ISH proposes HTN guidelines for global use, fit for low and high resource settings by advising essential and optimal standards, in a concise and easy to use format. Therefore, the overarching goal of contemporary HTN development is to reduce the adverse outcomes in the populations of interest and regional differences often inhibit complete uniformity.

## 4. Current definitions of Arterial Hypertension in adult

Although the CVD morbidity and mortality of increased BP is linear, direct, and continuous, the definition of HTN varies among guidelines (Table 1). The current recommendations, in general, provide BP thresholds based on average measurements in an office setting. The rationale for these categorizations is determined primarily by in-office observational data related to the association of SBP/DBP and CVD risk, randomized-controlled trials (RCTs) of lifestyle modifications to lower BP, and RCTs of medication therapy to reduce BP [17]. The 2018 ESC/ESH HTN definition characterizes ‘optimal’ BP defined as SBP  $<120$  mmHg and DBP  $<80$  mmHg. On the other hand, this level of blood pressure is considered ‘normal’ by the 2017 ACC/AHA definitions [17] (Table 1).

The NICE and ISH publications use similar thresholds for the definitions of HTN ( $\geq 140/90$  mmHg). The BP for a visit is determined by the average of at least two measurements in the clinic setting, at least one minute apart. If the final BP measurement is between 140/90 and 180/120 mmHg, the NICE and ISH guidelines recommend offering ambulatory blood pressure monitoring (ABPM) to confirm the diagnosis [23,24]. Additionally, all of the reviewed guidelines strongly recommend the utilization of out-of-office BP measurements for monitoring and/titration antihypertensive therapies. The various reports reviewed herein support

**Table 1**  
Guideline Definitions of Hypertension [17,22,24,29].

BP Category (mmHg) <sup>a</sup>	ACC/AHA 2017	ESC/ESH 2018	NICE 2019	ISH 2020
<b>Normal</b>				
SBP	<120	120–129	<140	<130
DBP	<80	80–84	<90	<85
<b>Elevated</b>				
SBP	120–129	130–139	*	130–139
DBP	<80	85–89	*	85–89
<b>Hypertension</b>				
<b>Stage I</b>				
SBP	130–139	140–159	140–179	140–159
DBP	80–89	90–99	90–119	90–99
<b>Stage II</b>				
SBP	≥140	160–179	≥180	≥160
DBP	≥90	100–109	≥120	≥100
<b>Stage III</b>				
SBP	*	≥180	*	*
DBP		≥110	*	*

BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACC/AHA, American College of Cardiology/American Heart Association; ESC/ESH, European Society of Cardiology, European Society of Hypertension; NICE, National Institute for Health and Care Excellence; ISH, International Society of Hypertension.

<sup>a</sup> Blood pressure is defined as seated clinic BP and by the highest level of measurement, whether systolic or diastolic.

the initial or concomitant use of nonpharmacological interventions for most patients, which include lifestyle modifications of dietary and activity levels, prior to medications in most individuals to reduce BP values.

## 5. Contemporary recommendation of blood pressure techniques and devices

The accurate measurement of in-office and out-of-office BP is crucial in HTN diagnosis and management. Although the traditional use of devices calibrated to a column of mercury is still utilized in some regions, most guidelines report recommendations from data using electronic devices for BP monitoring. All of the guidelines recommend validated devices, whether electronic or manual [25,26]. The US Blood Pressure Validated Device Listing (VDLTM) was the first U.S. list of blood pressure (BP) measurement devices developed to assist physicians and patients in identifying BP devices that are validated for clinical accuracy. BP devices listed on the VDLTM have specific criteria detailed as determined through independent review. Visit [ValidateBP.org](http://ValidateBP.org) to view the current device listings for more information on the independent review process [27]. The ESC/ESH guidelines recommend validated devices by the Association of Medical Instrumentation [26].

As errors in BP measurements are common in most settings, the HTN guidelines all thoroughly describe protocols to obtain accurate results [28]. BP is measured in both arms to detect any differences in the first office visit. Most guidelines recommend using the arm with the higher BP reading for a subsequent visit. All of the reviewed guidelines suggest taking the BP 2–3 times, separated by at least 1 min apart, averaging at least two of the readings for the final result. The ESC/ESH and NICE guidelines also suggest measuring the standing BP at least once after standing for 1 min, to determine the likelihood of orthostatic BP changes [22,29]. All guidelines also suggest measuring BP in at least two separate office visits to diagnose HTN before any interventions are recommended. Expert panels of the AHA and ACC have published recent scientific statements evaluating the accuracy of BP measurements in further detail, emphasizing the need for proper and ongoing training of technicians and healthcare providers for the use of validated devices [28,30].

## 6. Guidance for out-of-office and ambulatory BP monitoring

The reviewed HTN guidelines acknowledge the benefits of ABPM and

home blood pressure monitoring (HBPM) and provide strong recommendations of these techniques to confirm the diagnosis of HTN and monitor medication adjustments. HBPM is an alternative to confirm the diagnosis of HTN if ABPM is not possible. The technology for ABPM has been available for many years and is recommended by the ACC/AHA, ESH/ESC, NICE, and ISH guidelines with similar protocols suggested for use. ABPM has a stronger association with hypertension-related target-organ damage and adverse clinical outcomes [30].

The ABPM devices usually measure BP every 15–30 min during the day and every 15 min to 1 h during the night over a 24-hour period. There are BP correlate values to in-office setting BP measurements within the guidelines for HTN management to assist with HTN management (Table 2). ABPM is also useful to detect certain BP phenotypes of HTN that may confer increased CVD risk. White-coat HTN occurs when individuals demonstrate higher BP measurements in the office setting when compared with measurements outside of the office. The white-coat effect is a term used to describe the same phenomenon in patients having a history of HTN and receiving antihypertensive medications [26]. Although the data are limited, there may be a modest increase in CVD risks for patients experiencing these conditions. Most studies demonstrating an increased CVD risk are in patients with other CVD risk factors that could explain the higher risk [31,32]. The guidelines also reference terminology of isolated office HTN and other subclasses of HTN, although these conditions are not covered extensively within this review [17,22,24].

ABPM has also been used to detect masked HTN, which refers to individuals demonstrating a mean out-of-office BP in the hypertensive range and normal BP measurements in an office setting. The ESC/ESH guidelines suggest incorporation of nighttime BP measurements with daytime readings for this diagnosis, although most guidelines use daytime readings of ABPM [22,30]. Incorporation of nighttime readings also increases the detection and prevalence rates of masked HTN in blacks, associated with higher rates of declining renal function [33,34].

Despite the evidence supporting the use of ABPM in HTN management, several issues limit its use and availability for patients. The monitoring requires proper training of patients and providers, as well as compliance of use to provide accurate and helpful information. The reimbursement rates for the utilization of ABPM is historically low, representing <1% of Medicare beneficiary claims in some studies [35]. There are also only modest data supporting better outcomes with the treatment of white-coat or masked HTN outside of standard treatment of existing CVD risk factors. Further investigations as to whether ABPM can specify individuals requiring additional treatments to reduce CVD risk may be warranted.

As recommended in all contemporary guidelines, HBPM and self-monitored blood pressure (SMBP) outside the office are considered a

**Table 2**  
Hypertension Correlation of Clinic, Home, and Ambulatory Blood Pressure Monitoring [17,22,24,29].

Guideline	Clinic (mmHg)	HBPM (mmHg)	Daytime ABPM (mmHg)	Nighttime ABPM (mmHg)	24-h avg ABPM (mmHg)
ACC/AHA	≥130/80	≥130/80	≥130/80	≥110/65	≥125/75
ESC/ESH	≥140/90	≥135/85	≥135/85	≥120/70	≥130/80
NICE*	≥140/90	≥135/85	≥135/85	*	*
ISH	≥140/90	≥135/85	≥135/85	≥120/70	≥130/80

HBPM, home blood pressure monitoring; ABPM, ambulatory blood pressure monitoring; ACC/AHA, American College of Cardiology/American Heart Association; ESC/ESH, European Society of Cardiology, European Society of Hypertension; NICE, National Institute for Health and Care Excellence; ISH, International Society of Hypertension.

more practical alternative to ABPM. The Agency for Healthcare Research and Quality (AHRQ) found strong evidence that SMBP plus additional support (defined below) was more effective than usual care in lowering blood pressure among patients with HTN [36,37]. SMBP protocols are likely to become much more useful in HTN control as the COVID-19 pandemic continues to direct current day medical care (see Fig. 1).

Public health organizations have recognized the devastating effects of HTN on the US population and have developed several initiatives to utilize the techniques of SMBP to manage CVD outcomes for HTN. The Million Hearts 2022 is a national initiative to prevent 1 million heart attacks and strokes within 5 years through the implementation of evidence-based strategies that can improve cardiovascular health for all. This effort recognizes the use of out-of-office BP monitoring and recommends use of these strategies, according to the best evidence [36]. The TargetBP national initiative, formed by the AHA and the American Medical Association, also assists health care organizations and care teams, at no cost, in improving BP control rates through a quality improvement program [38]. These large-scale efforts will provide new insights into the challenges and management of adherence with BP recommendations for all populations within the US.

In general, the use of HBPM/SMBP have been recommended by several societies, and most recently as a potential means to manage HTN during the COVID-19 outbreak in conjunction with the 2020 surge in telehealth [13,18,39]. It is likely these BP measuring methods will become more useful over time as the readings outside of the office may decrease the prevalence of white-coat hypertension and inconsistent readings within office measurements. These measures, in conjunction with advancing telehealth services, have the potential to provide more responsibility for the patient's HTN management. Thus, the increasing steps to use out of office BP monitoring and telehealth services may indirectly increase patient engagement and health literacy.

Many health centers and medical practices have quickly introduced more pronounced telehealth services into the current models of care

management, which is ideal at this time. Several barriers to overcome include payment and regulatory structures, state licensing, and credentialing across health centers [40]. Yet, the use of remote patient monitoring, patient-initiated messaging, telephone visits, and video visits are within the reach of telehealth medicine should be beneficial for BP control in a large population effort. Wosik and colleagues suggest the COVID-19 pandemic will stimulate the need for telehealth services in significant shifts or phases of care. Phase I, or the initial outpatient management of conditions such as HTN with the "stay at home", order has already begun as some health centers have increased the need for telehealth services to as much as 70% of total outpatient visits. Phase II is described as the telehealth needs during inpatient related surge, through the use of network care management and e-consultations. Phase III is considered the post-pandemic recovery period, which is still unknown at this time. The authors appropriately discuss the issues in delayed care for serious non-COVID-19 related medical conditions, such as acute coronary syndromes, which has already occurred in many communities. A "care debt" is described as well from the first two phases and will likely require intense sustained telehealth efforts [41].

In addition, mobile health services may become a preferred method of HTN management during and post the COVID-19 pandemic, particularly in poorer populations with less health care access. Mobile health interventions for HTN usually involve the use of a patient's mobile phone, along with a validated BP measuring device, to track and communicate measurements with providers. A recent meta-analysis of eleven randomized controlled trials (4271 participants) associated significantly lower systolic and diastolic BP measurements with the use of mobile health interventions in patients with HTN [42]. These findings were consistent through study duration and treatment intervention intensity within the trials. Further investigations, involving nonpharmacologic interventions and modes of patient engagement, may increase the effectiveness of future mobile and telehealth BP interventions.



Fig. 1. Feedback loop between patients and healthcare providers supporting SMBP [36].

## 7. Evidence-based approaches to nonpharmacologic management of HTN

Therapeutic lifestyle changes are necessary to prevent poor CVD outcomes with HTN. All of the major HTN guidelines support interventions of weight-control (weight loss if necessary), sodium restriction, smoking cessation, regular physical activity, healthy diet, and limiting alcohol consumption to reduce blood pressure in all individuals (Table 3) [17,22,29]. However, the Dietary Approaches to Stop Hypertension (DASH) pattern appears most effective to yield significant reductions in BP for all individuals (blacks with reductions of SBP as high as 20 mmHg) slowing the decline of renal dysfunction and for weight loss with overweight status [43–45].

Increased potassium intake (3500–5000 mg/day), aside from following the DASH diet, is recommended by the ACC/AHA to provide further reductions in BP (2–5 mmHg for hypertensive individuals) [17]. Dietary supplementation of potassium can help further lower blood pressure by easing tension on blood vessel walls. Behavioral therapies such as yoga and meditation, effectively reduce blood pressure [24]. Additionally, the 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease and a report from the American Society of Preventive Cardiology (ASPC) support the benefits of therapeutic lifestyle interventions for BP control [13,46].

Additionally, Mediterranean diet (MedDiet) may have a favorable effect on the risk of HTN in contrast to unfavorable dietary patterns such as red meat, processed meat, and poultry [47]. The MedDiet or DASH diet are also likely beneficial over the Western diet (WD) in relation to COVID-19 susceptibility, as the high rate of consumption of saturated fats, sugars, and refined carbohydrates in the WD contribute to the prevalence of obesity and type 2 diabetes (T2D) potentially increasing

**Table 3**  
Blood pressure reductions of nonpharmacological interventions [17].

Nonpharmacological Intervention	Dose	Reduction in SBP (mmHg)	
		HTN	Normal BP
Weight loss	Aim for at least 1-kg reduction in body weight for most adults who are overweight. Expect ~1 mmHg reduction for every 1-kg reduction in body weight.	5	2–3
DASH dietary pattern	Diet rich in fruits, vegetables, whole grains, low-fat dairy products, with reduced content of saturated and total fat. Available at <a href="https://www.nhlbi.nih.gov/health/resources/heart/hbp-dash-how-to">https://www.nhlbi.nih.gov/health/resources/heart/hbp-dash-how-to</a> .	11	3
Dietary sodium	Optimal goal <1500 mg/day. Aim for at least 1000 mg/day reduction in most adults	5–6	2–3
Dietary potassium	Approximately 3500–5000 mg/day. For a list of high potassium foods, visit <a href="https://www.drugs.com/cgi/potassium-content-of-foods-list.html">https://www.drugs.com/cgi/potassium-content-of-foods-list.html</a>	4–5	2
<b>Physical Activity</b>			
<b>Aerobic</b>	90–150 min/week at 65–75% of max heart rate	5–8	2–4
<b>Dynamic resistance</b>	90–150 min/week; 6 exercises, 3 sets/exercise, 10 repetitions/set	4	2
<b>Isometric resistance</b>	4 × 2 min (hand grip), 1 min rest between exercises; 3 sessions/week for 8–10 week duration	5	4
<b>Alcohol consumption</b>	In individuals who drink alcohol, reduce to: Men ≤ 2 drinks daily, Women ≤ 1 drink daily (~12 oz. beer, 5 oz. of wine, or 1.5 oz. distilled spirits)	4	3

the risk for severe COVID-19 pathology and mortality [48].

Patient engagement, in addition to nonpharmacologic interventions, will likely require more emphasis during and post COVID-19, as the prevalence of HTN could increase over time with decreased activity and attention to diet. The need for health coaching by clinicians and members of the community may increase in order to initiate or maintain adherence to nonpharmacologic BP interventions. A recent meta-analysis comparing implementation strategies for HTN control evaluated a total of 55, 920 patients, which included studies evaluating the use of patient-level health coaching. Health coaching was associated with a significant reduction in blood pressure over a minimum of 6 months (−3.9 mmHg, 95% CI −5.4 to −2.3 mmHg) [49]. Thus, multilevel interventions, including patient-level strategies, are likely to become more important in the treatment of HTN during and after the COVID-19 pandemic.

## 8. Impact of adherence on blood pressure control and outcomes

Nonadherence, affecting as much as 80% of patients with HTN, increases the associated risk for CVD morbidity and mortality, with approximately one of every four patients not filling their initial prescription [17,24]. The major HTN guidelines equally recognize the economic burden of HTN medications increasing nonadherence [50]. In a recent study, 67% of patients who do not experience financial barriers to pharmacotherapy are more likely adherent and have normal BP within the past 12 months [50–53]. There are promising data using highly sensitive high-performance liquid chromatography-tandem mass spectrometry biochemical measurements of drug levels in the serum or urine as a surrogate of compliance [54,55]. Although these measurements are now available for clinical use and covered by some insurance plans, more research is warranted for determining the effect on large populations and mainstream use.

Guideline-recommended strategies include adherence feedback to the patient, HBPM/SBPM, linkage of behavior with daily habits, electronic aids, such as mobile phones and reduction of polypharmacy utilizing a single pill combination is possible [24,46,56] (Table 4). As most patients will often require more than one antihypertensive agent to control BP, fixed-dose combinations (FDC) pills for HTN are supported by the major guidelines [17,22,24]. A recent meta-analysis of 62,481 patients with HTN reported a mean medication adherence difference of ~15% in patients receiving FDC medications vs. free separate equivalent dose pills [57]. Many common FDC HTN therapies are included in formularies at reduced co-pays and may attenuate HTN management costs during the COVID-19 pandemic and beyond.

The polypill concept, including HTN and lipid drugs, may help reduce prescribing complexities for CVD prevention [58–60]. A recent randomized, controlled polypill (atorvastatin 10 mg, amlodipine 2.5 mg, losartan 25 mg, and hydrochlorothiazide 12.5 mg) trial, involving adults with a CVD risk of >10% demonstrated significant BP and LDL reduction

**Table 4**  
Guideline recommendations for adherence to antihypertensive therapies [17,22,24].

● Link drug intake with daily habits for patients
● Give adherence feedback
● Use pillboxes or special packaging
● Integrate provider care with pharmacists and nurses (e.g., consider retrieving pharmacy refill patterns, multidisciplinary approach)
● Assess adherence with a “no blame” approach
● Telemetry transmission of recorded home BP values
● Use of long-acting drugs that require once-daily dosing
● Avoid complex dosing schedules
● Use of single-pill combinations when possible
● Consider the effects of treatment on patient’s budget
● Use of reminders (e.g., alerts or text messages on mobile devices)
● Assessment and resolution of individual barriers to adherence at every visit.
● Empowerment-based counseling for self-management
● Consider a combination of practical techniques to improve adherence

at 12 months versus standard care of participants at a federally qualified community health center in Alabama [61]. The mean estimated 10-year cardiovascular risk was 12.7% for the participants, with a mean baseline blood pressure LDL cholesterol of 140/83 mmHg and 113 mg per deciliter, respectively. The monthly cost of the polypill was \$26. At 12 months, polypill adherence was 86%. The mean systolic blood pressure decreased by 9 mm Hg in the polypill group, as compared with 2 mmHg in the usual-care group (difference, -7 mm Hg; 95% confidence interval [CI], -12 to -2;  $P = 0.003$ ) [61].

## 9. Telehealth and hypertension in the COVID-19 era

As previously noted, telehealth, prior to the COVID-19 pandemic, had been heralded as a potential advancement in successful HTN and CVD risk management. Moreover, due to safety concerns, the COVID-19 pandemic required telemedicine for routine outpatient visits, significantly affecting HTN and other chronic medical condition management. Initiatives, such as Million Hearts 2022 and Target BP, have emphasized the importance of SBPM with continual patient and provider feedback. In addition, the Centers of Medicare and Medicaid Services (CMS) recently published reimbursement information for telephone and other monitoring services [62] (See Table 5). As a significant amount of time and detail must be devoted to these modes of communication and assessment, it is important that providers receive adequate compensation. Therefore, CMS expanded telephone consultation payment on a temporary and emergency basis under the 1135 waiver authority and Coronavirus Preparedness and Response Supplemental Appropriations Act: particularly for high-risk COVID-19 beneficiaries and with widespread availability of smart phones, telehealth may become future standard medical practice [62,63].

Nevertheless, the use of digital technology may further increase disparities. A recent study evaluating telehealth in cardiac clinics suggested disparate use of video encounters in low income and black patients [64]. Of the 2940 patients scheduled for a telehealth encounter during the study, 1339 (46%) completed telehealth encounters and 1601 (54%) patients had a canceled/no-show visit. On unadjusted analysis, patients with a completed telehealth visit were slightly older, more likely to be male and speak English. However, low income and black patients were less likely to video visits possibly related to insurance coverage [64]. More investigation is warranted in the future to understand the risks and benefits of video telehealth encounters to enhance cardiac care.

## 10. Special populations: diabetes, race/ethnicity, sex, and older age

Although each guideline provides specific comments for the management of special populations, including persons with diabetes (DM) and certain involving race/ethnicity, sex, and older age, this review will only detail various aspects of care for certain groups [17,22,24,29,65].

The vast majority of adults with DM have 10-years ASCVD risk >10% placing them in a high-risk category. However, in the most recent ADA recommendations, patients with DM and a 10-year ASCVD risk <15% should maintain a target of <140/90 mmHg, with <130/80 mmHg for the highest risk patients [66]. In ACC/AHA 2017 and other major guidelines, antihypertensive drug treatment with diabetes should be initiated at a BP of 130/80 mmHg or higher with a treatment goal of <130/80 mmHg [17,67]. Moreover, major guidelines recommend the addition of renin-angiotensin modulators, including an angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blockers (ARB) in the setting of compelling comorbid issues such as diabetes with albuminuria, renal dysfunction, or HF [17,22,24,66,67].

The ACC/AHA, ESC/ESH, and ISH guidelines discuss the significance of race/ethnicity in HTN management. In the U.S., as well as globally, black ancestry may be associated with a higher prevalence of HTN than that of Hispanic Americans, whites, Native Americans, and other groups [17,22,24]. In some parts of the world, HTN prevalence is greater than 60% among blacks [15,68]. In comparison to the U.S., the prevalence of HTN in the black population in Europe is higher than the non-black population. The ESC/ESH guidelines emphasize the data are scarce for the European black populations and extrapolate much of their recommendations from U.S. studies [22]. Non-Hispanic U.S. white adults are more likely to have a higher prevalence of controlled HTN when compared to other groups. The lower rates of control in Hispanic Americans are likely secondary to decreased awareness. However, American blacks have lower controlled rates due to more severe HTN and possibly to less effective treatments [17].

Thiazide-type diuretics and calcium channel blockers (CCBs) are most effective as the first step in lowering BP and stroke in blacks. Although ACE-I and ARB are less effective in blacks as monotherapy when compared to whites, combination therapy is equally effective in whites and blacks [51,69,70]. Perhaps due to suppression of the renin-angiotensin aldosterone system, ACE-I and ARB may not only lower BP less effectively, but also for the prevention of heart failure and stroke [69-71]. ACE-I are also associated with a higher incidence of angioedema in blacks, and ARBs are recommended over an ACE-I by the ESC/ESH and ISH guidelines for HTN treatment, in combination with a diuretic or CCBs. The ACC/AHA, ESC/ESH, and ISH guidelines recommend two or more antihypertensive medications to achieve adequate BP control in blacks, with a diuretic or CCBs used as first-line agents. Patients with BP that is 20/10 mmHg above target may be considered for combination therapy at treatment onset. Given resistant hypertension (rHTN) is more common in African American patients, multidrug pharmacological therapy may be often indicated [17,22,24].

The ISH guidelines acknowledge ethnic-specific characteristics for East and South Asian populations, who have a greater likelihood of salt-sensitivity accompanied with mild obesity [24]. East Asians also have a higher prevalence of hemorrhagic stroke and nonischemic heart failure when compared to Western populations, associated with morning or

**Table 5**  
Summary of medicare telemedicine services [62].

Type of Service	What is the Service?	HCPCS/CPT Code	Type of Patient
<b>Medicare Telehealth Visits</b>	A visit with a provider that uses telecommunication systems between a provider and a patient	* <b>99201-99215</b> (Office or other outpatient visit) * <b>G0425-G0427</b> (Telehealth consultations, emergency department or initial inpatient) * <b>G0406-G0408</b> (Follow-up inpatient telehealth consultations furnished to beneficiaries in hospitals or SNFs)	New or Established
<b>Virtual Check-In</b>	A brief (5-10 min) check in with a patient via telephone or other telecommunications device to decide whether an office visit or other service is needed. A remote evaluation of recorded video and/or images submitted by an established patient	* <b>HCPCS code G2012</b> * <b>HCPCS code G2010</b>	Established
<b>E-Visits</b>	A communication between a patient and their provider through an online patient portal	* <b>99241-99243</b> * <b>G2061-G2063</b>	Established

HCPCS, The Healthcare Common Procedure Codign System; CPT, Common Procedural Technology; SNFs, Skilled nursing facilities.

nighttime HTN. Individuals from the Indian subcontinent have high risks for CVD and type 2D.

Although of considerable interest, special populations related to sex and older age are not detailed in this review, although detailed in the ACC/AHA and ESC/ESH guidelines [17,22]. Furthermore, the ISH guidelines also provide extensive recommendations for the treatment of HTN in pregnancy, whereas this area is covered in supplementary documents for the others [24]. Most recently, Aronow extensively reviewed the management of HTN in the elderly [65]. Overall, recognizing unique aspects in the treatment of various populations, including regional differences, is an important component for optimal care.

## 11. HTN and COVID-19: present and future concepts

According to the most recent data from the World Health Organization COVID-19 has infected over 11.1 million people, responsible for over 528,000 deaths worldwide [72]. Further clinical observation may be required to determine the long-term risk of COVID-19 and HTN. The devastating effects of COVID-19 have also disproportionately affected several vulnerable populations, including those with certain comorbid diseases, advanced age, and lower socioeconomic status. COVID-19 also has the potential to impact CVD outcomes via a 'domino effect', which is initiated by social fears and issues stemming from social distancing. Due to concerns of visiting hospital facilities, patients may not present for outpatient and emergent care needed, such as with acute coronary syndromes. Furthermore, physical inactivity and unhealthy eating due to home quarantine status, along with the social stressors related to increasing unemployment, may increase the rates of HTN, obesity, and CVD events in years to come [73].

Despite the early concern that ACEI/ARB therapy would worsen outcomes by upregulating ACE2, RAS inhibitors may actually improve the clinical status of COVID-19 patients with hypertension and may even be preferential for antihypertensive treatment [2,74–76]. In a recent study of 417 COVID-19 patients with HTN from China, the data suggest ACEI/ARB therapy attenuated the inflammatory response, potentially through the inhibition of IL-6 levels, which is consistent with the findings that ACEI and ARB therapy alleviated pneumonic injury [77]. Perhaps, ACEI/ARB therapy has a beneficial effect on the immune system by avoiding peripheral T cell depletion, thereby allowing for a better immune response to the virus in these patients.

As the standards of practice, the Heart Failure Society of America, ACC, AHA, and American Society of Preventive Cardiology currently recommend the continuation of RAS inhibitors with compelling complications such as: heart failure, hypertension, or ischemic heart disease [39,78]. Moreover, abrupt withdrawal of RAS inhibitors in high-risk patients, including those who have heart failure or have had recent myocardial infarction, may result in clinical instability and adverse health outcomes [79].

On the other hand, dihydropyridines CCBs (nifedipine and amlodipine) may be a benefit for the treatment of hypertensive patients with COVID-19. In a retrospective analysis, a small cohort of elderly hypertensive patients treated with a CCB during a COVID-19 infection, had a significantly higher survival rate and were much less likely to require mechanical intubation (50% vs. 14.6%, respectively) as compared to those not on CCBs [80]. Although further clinical studies are warranted, the data are promising that treatment of a CCB in hypertensive patients with COVID-19 may significantly improve outcomes.

## 12. Conclusion

Current guideline recommendations emphasize the importance of evidence-based care to curtail the widespread mortality and morbidity related to HTN and associated ASCVD. Additionally, the acute and long-term effects of COVID-19 may influence treatment in the hypertensive population and require further investigation. The importance of unifying

recommendations that help to curv the burden of HTN may become more significant in the coming years as we learn more about new treatments and the long-term effects of the current COVID-19 crisis. The COVID-19 associated morbidity and mortality including patients with underlying HTN and CVD are likely to have profound impact for several decades due to the worldwide medical, economic, and psychological effects. However, although contemporary guidelines suggest benefits of the use of telehealth technologies and out-of-office medical management, as recently required by the COVID-19 pandemic, these evolving techniques will be increasingly used for HTN control and CVD risk control. Ultimately, future HTN guidelines may increasingly reflect the impact of the COVID-19 pandemic and the utility of measures such as SMBP/HBMP over time.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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