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Review

Evolution of Blood Pressure Clinical Practice Guidelines: A Personal Perspective

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ABSTRACT

Before the second half of the 20th century, most clinical decision making was based on expert opinion. By the 1960s, experience in actuarial and research cohort studies had provided strong evidence that blood pressure was an important risk factor for cardiovascular disease. The landmark 1967 and 1970 Veterans Administration Cooperative Study trials confirmed the value of antihypertensive drug therapy in preventing stroke, myocardial infarction, and heart failure in adults with high levels of diastolic blood pressure. They also provided an impetus to develop the first blood-pressure–related clinical practice guideline in 1977. In subsequent years, more structured and comprehensive blood-pressure guidelines have evolved to become a major resource in clinical and public health practice. Despite some

RÉSUMÉ

Avant la seconde moitié du 20e siècle, la prise de décisions cliniques reposait pour l'essentiel sur des opinions d'experts. Dans les années 1960, les études actuarielles et les études de cohortes ont produit des données démontrant de façon probante que la pression artérielle était un facteur de risque important des maladies cardiovasculaires. Les volets de 1967 et de 1970 de la Veterans Administration Cooperative Study, un essai clinique déterminant, ont confirmé l'intérêt du traitement par un médicament antihypertenseur pour la prévention des accidents vasculaires cérébraux, de l'infarctus du myocarde et de l'insuffisance cardiaque chez les adultes présentant une pression artérielle diastolique élevée. Ces travaux ont également été le moteur de l'élaboration, en 1977, des premières lignes directrices de pratique

Evidence has always been a central tenet of clinical decision making. Historical examples of seminal advances based on previous scientific evidence include the use of cowpox inoculation to prevent smallpox, administration of citrus fruits to prevent scurvy, and demonstration that infectious diseases resulted from specific pathogens. For many years, however, clinical decisions were primarily based on expert opinion rather than on stronger scientific principles. As a result, such treatments as blood letting persisted for more than 2500 years before evidence demonstrated that it was, at best, of no value. During the early 20th century, William Welch and other leading figures in North American medicine were strong proponents of the premise that medical practice and education should be based on scientific principles rather than expert opinion and apprenticeship. However, the type of evidence available to make clinical judgements remained limited until the second half of the 20th century. Egas Moniz is recognized for his pioneering introduction of cerebral angiography but received the Nobel Prize in Medicine in 1949 for his "discovery of the therapeutic value of leucotomy in certain psychoses." Based on his original experience, Moniz concluded that "Prefrontal leucotomy is a simple operation, always safe." It was only later that the serious adverse consequences of lobectomy became apparent, and prefrontal lobotomy was replaced by the introduction of effective psychotropic drugs.[1] During the first half of the 20th century, radiation therapy was used to treat enlargement of the thymus in infants and to manage other benign conditions in children.[2] It was considered to be a safe and effective treatment until evidence eventually emerged documenting a strong relationship to cancer, especially in the thyroid gland.[3]

Measurement of Blood Pressure

Palpation of the pulse was practiced by the early Egyptians, and Hales description of blood pressure (BP) measurement in his 1733 "Haemostaticks: Volume II of the Statical Essays" attracted considerable interest and recognition by the major scientific societies of his era.[4] However, accurate measurement of BP in humans was not possible until the introduction of the mercury manometer by Poisuille in 1828.[4] During the mid- to latter part of the 19th century, there was intense interest in development of sphygmanometry devices for measurement of BP. However, when Osler's first edition of *The Principles and Practice of Medicine* was published in 1892,

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limitations, these guidelines provide useful evidence-based guidance for diagnosis and management of high blood pressure. The core advice in most of the current comprehensive blood pressure guidelines is more similar than different. Modelling studies suggest that better adherence to guideline recommendations would result in a lower average blood pressure and substantial improvement in public health.

clinique en lien avec la pression artérielle. Au cours des années ultérieures, des lignes directrices sur la pression artérielle plus structurées et plus exhaustives ont vu le jour et sont devenues une ressource de premier ordre dans la pratique, tant en milieu clinique qu'en santé publique. Malgré certaines limites, ces lignes directrices fournissent des conseils utiles et fondés sur des données probantes pour le diagnostic et la prise en charge de la pression artérielle élevée. Dans la plupart des lignes directrices exhaustives sur la pression artérielle qui existent actuellement, le message principal est sensiblement le même. D'après des études de modélisation, une meilleure observance des recommandations des lignes directrices se traduirait par une diminution de la pression artérielle moyenne et une amélioration substantielle de la santé de la population.

there was no mention of high BP because there was still no practical method of BP measurement in clinical practice.[5] It was not until Riva-Rocci introduced cuff-based sphygmomanometry, in 1896, that estimation of BP became feasible in clinical practice.[6] In 1901, Cushing introduced sphygmomanometry to US physicians as a simple tool for obliteration of the radial pulse and measurement of systolic BP (SBP).[7] Janeway and Crile were early supporters of the scientific utility of sphygmomanometry and its superiority over the traditional use of palpation to estimate the force of blood flow in the radial artery.[7] Much like today, however, there was great variation in measurement methods and little attention to quality control. In 1905, Korotkov described the auscultatory method of BP measurement, and this technique was disseminated remarkedly rapidly.[8]

Blood Pressure as a Risk Factor

Figure 1 provides a timeline for some of the most important studies that have informed our knowledge of BP-related cardiovascular disease (CVD) and all-cause mortality. Actuaries and life insurance company medical directors were among the first to recognize the value of BP in estimating future risk. By 1905, there was considerable discussion regarding the value of the sphygmomanometer and BP measurements. In 1911, Dr John Fisher, Medical Director of the Northwestern Mutual Life Insurance Company, wrote; "No practitioner of medicine should be without a sphygmomanometer. He has in this instrument a most valuable aid in diagnosis. The sphygmomanometer is indispensable in life-insurance examinations, and the time is not far distant when all progressive life-insurance companies will require its use in all examinations of applicants for life insurance."[9] In 1912, Osler published his initial clinical observations that only some patients with high BP had signs of cardiovascular disease.[10] Only 1 year later, Janeway reported clinical observations in 7872 patients that suggested a strong qualitative relationship between high BP and risk of cardiovascular disease (CVD).[11] In 1918, BP measurement became a standard part of insurance examinations for all companies.[12]

Beginning in the 1920s, large actuarial studies conducted by the insurance industry began to provide quantitative documentation of a strong association between level of BP and subsequent risk of CVD events, with a report published in 1925 being based on a study of 707,000 insured persons.[13] Although the data were imperfect, higher than average levels of both SBP and diastolic BP (DBP) were associated with increased mortality, whereas the reverse was true for lower than average levels of SBP and DBP. Unfortunately, these findings were ignored by many opinion leaders in the medical community. With the exception of malignant hypertension, high BP was generally thought to be relatively benign and a physiological consequence of aging.[14,15] As a result, the term *benign essential hypertension* was in common use well into the second half of the 20th century.

In 1957, the Framingham Heart Study (N = 5209) reported a 3-fold higher incidence of atherosclerotic heart disease in 98 adults with baseline SBP/DBP $\geq$ 160/95 mm Hg compared with 310 with baseline SBP/DBP $<$ 140/90 mm Hg.[16] The 1959 Build and Blood Pressure Study pooled data from 26 insurance companies to provide actuarial experience for 4,900,000 persons who were insured between 1934 and 1959.[17] This study identified a robust quantitative relationship between BP and mortality, both in men and women, with even small increments in SBP and DBP being associated with higher mortality. Cause of death analyses identified a strong relationship between level of BP and diseases of the heart and circulation. Important subsequent risk investigations have included the 1979 Blood Pressure Study, in which 4,350,000 insured men and women were followed for periods in excess of 20 years,[18] the Multiple Risk Factor Intervention Trial (MRFIT) cohort of 361,662 35- to 57-year-old men screened for trial participation whose baseline BPs were linked to CVD mortality and end-stage renal disease,[19] the Prospective Studies Collaboration study of BP as a risk factor in their meta-analysis of individual data for 1 million adults in 61 prospective studies,[20] and the Rapsomaniki et al. electronic health record study of 1.25 million patients in clinical practice.[21] Collectively, these reports have substantially enhanced and refined our knowledge of the BP-CVD relationship, but there was already little doubt as to the importance of BP as a risk factor for CVD by the 1960s. The 1979 Blood Pressure Study,[18] and many subsequent cohort study reports, especially the large MRFIT cohort investigation,[19,22] provided convincing evidence that SBP was more important than DBP as a predictor of risk, especially in older adults. Despite this, a misconception, which seems to have originated in 1926,[23] led to a widely held belief that high SBP reflected a strong heart, whereas high DBP resulted from raised peripheral resistance and should be the focus of clinical

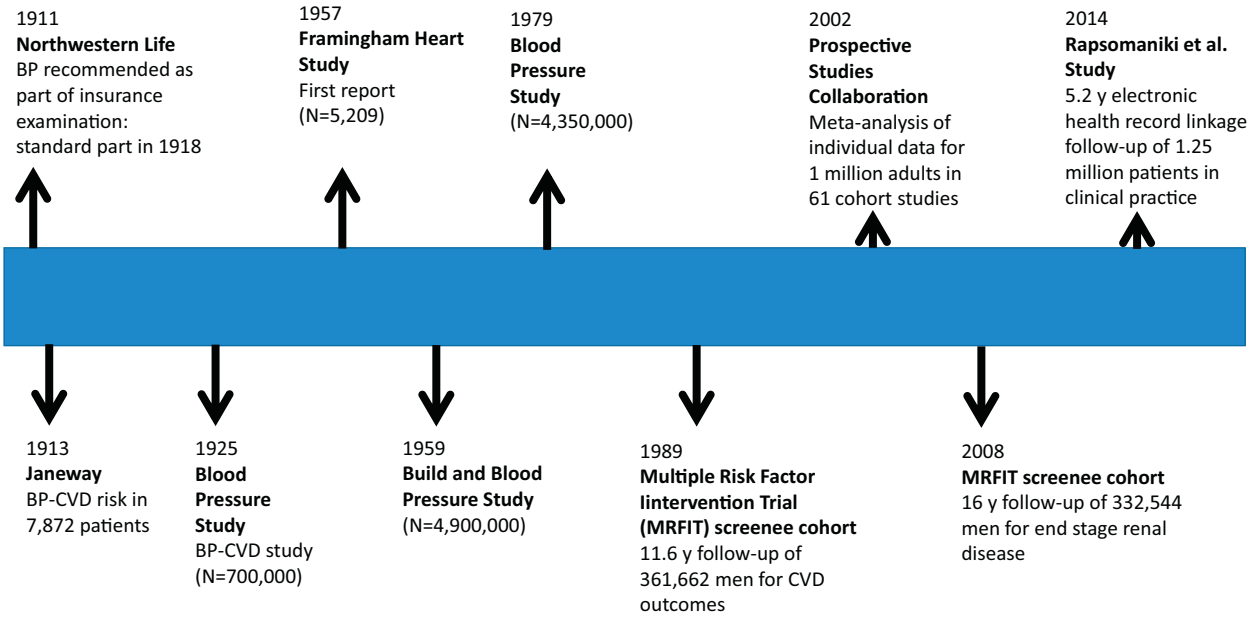

Figure 1. Timeline for selected advances in knowledge related to risks of high blood pressure.

attention. This type of thinking influenced the design of antihypertensive drug treatment trials well into the 1980s.

Treatment of High Blood Pressure

The era of effective antihypertensive drug therapy can be traced to the introduction of diuretics during the latter part of the 1950s. In the early 1960s, several historically controlled trials of antihypertensive drug therapy provided compelling evidence for benefit in adults with malignant hypertension or very high levels of BP. These studies were superseded by randomized controlled trials (RCTs), starting in the late 1960s. Figure 2 provides a timeline for some of the most important RCTs that have documented the value of antihypertensive drug therapy in adults with high BP. The first RCT of antihypertensive drug therapy was reported in 1966,[24] but it was quickly followed by 2 landmark Veterans Administration Cooperative Study Group multicentre trials that provided convincing evidence for treatment benefits in adults with a baseline DBP $\geq$ 105 mm Hg in 1967[25] and in those with a baseline DBP 90 to 104 mm Hg in 1970.[26] Subsequently, larger trials provided evidence of benefit for stepped-care compared with referred-care (usual) antihypertensive drug therapy,[27] and this treatment approach was widely recommended for many years. Until the late 1980s, RCTs were largely based on treatment of diastolic hypertension and DBP goals. Around this time, several RCTs were designed to test the value of antihypertensive drug therapy in older adults with high SBPs.[28-30] The **S**ystolic **H**ypertension in the **E**lderly **P**rogram (SHEP) trial was the first to prove the value of treating well defined isolated systolic hypertension in adults $\geq$ 60 years.[28] Later trials conducted in Europe and China also confirmed the value of drug treatment in older adults with a combination of high SBPs and low DBPs.[31,32] The 2008 **Hy**pertension in the **V**ery **E**lderly **T**rial (HYVET) established the value of BP lowering even in those 80 years of age or older.[33] More recently, the **S**ystolic Blood **Pr**essure **In**tervention **T**rial (SPRINT) demonstrated benefit with more intensive therapy to < 120 mm Hg compared with a goal of 140 mm Hg.[34] The benefit seemed to apply to all prespecified subgroups, including those $\geq$ 75 years at baseline.[35] In addition to the primary CVD composite outcome benefit, more intensive therapy significantly reduced mild cognitive impairment and the combination of mild cognitive impairment and dementia.[36,37] In the best-designed comparison of first-step antihypertensive drug therapy, the **A**ntihypertensive and **L**ipid-**L**owering to Treat **H**eart **A**ttack **T**rial (ALLHAT) investigators demonstrated the superiority of a long-acting diuretic (chlorthalidone) compared to an α-receptor blocker (doxazosin).[38] First-step therapy with chlorthalidone, the calcium channel blocker amlodipine, or the angiotensin-converting enzyme inhibitor lisinopril resulted in a similar incidence of the primary coronary heart disease outcome and all-cause mortality, but decompensated heart failure was less common with chlorthalidone, especially compared with amlodipine.[39] Meta-analyses of the many trials of antihypertensive drug therapy RCTs provide the scientific underpinning for pharmacologic treatment of hypertension in adults.[40-43] All the trials included in these meta-analyses were conducted in adults at high risk for CVD. The effectiveness of antihypertensive drug therapy for prevention of CVD events has not been proven in those at lower risk for CVD,[44] but low-dose pharmacotherapy has been demonstrated to be effective in preventing hypertension[45-47] and reducing left ventricular mass in adults with high normal BP.[47]

Figure 3 provides a temporal sequence for some of the more important RCTs that have confirmed the value of nonpharmacological therapy for prevention and treatment of high BP. In 1989, Stamler et al. demonstrated in 201 adults that a "nutritional-hygienic" behavioral intervention targeting weight, dietary sodium, physical activity, and alcohol consumption was effective for prevention of hypertension.[48] The

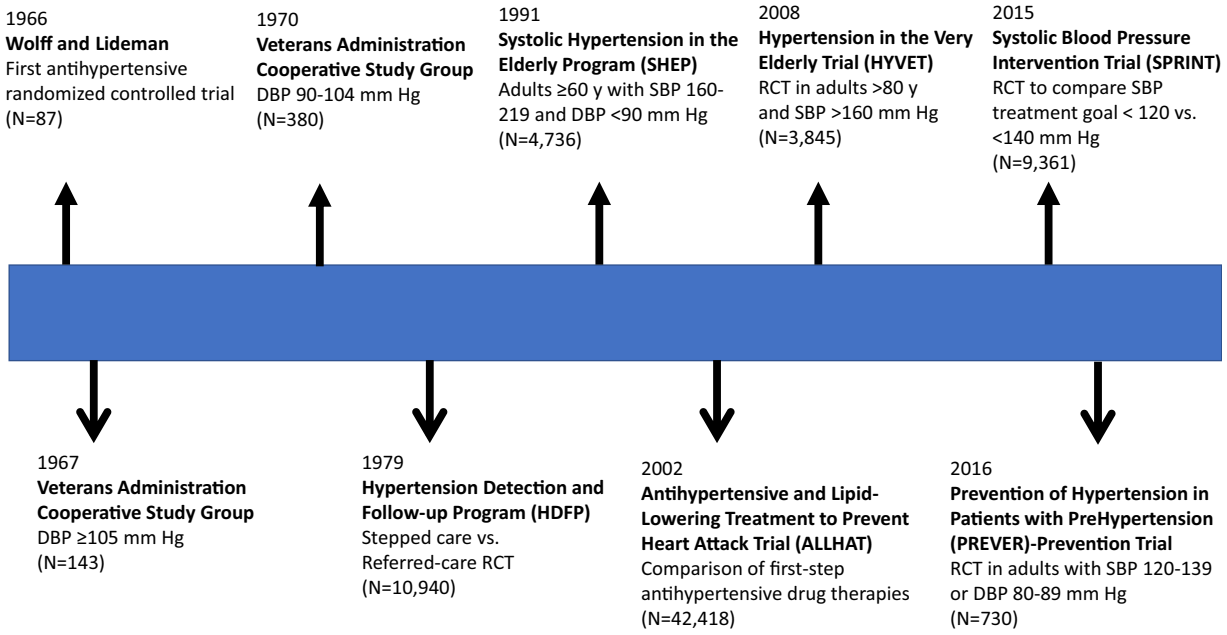

Figure 2. Timeline for selected advances in knowledge related to antihypertensive drug treatment of high blood pressure.

following year, many of the same investigators reported a larger (N = 841) 4-arm trial that suggested weight loss and sodium reduction as the most effective interventions for prevention of hypertension.[49] In a larger test of 7 behavioral and supplemental interventions in 2182 adults, Phase I of the **T**rials **o**f **H**ypertension **P**revention (TOHP) identified weight loss and reduction sodium intake as the 2 most effective approaches for prevention of hypertension.[50] TOHP, Phase II, confirmed the effectiveness of weight loss and sodium reduction during 3 to 4 years of follow-up in 2182 overweight adults but also demonstrated the difficulty of maintaining behavioural intervention effects during long-term follow-up.[51] A 3-arm 8-week feeding study demonstrated the value of the Dietary Approaches to Stop Hypertension (DASH) diet (high in fruits and vegetables and in low-fat dairy products) for BP lowering in 459 adults with and without hypertension.[52] In a subsequent crossover RCT conducted in 412 adults with and without hypertension, sodium reduction in combination with either the DASH or control diet was shown to be effective in lowering BP, with the greatest reduction in BP being noted in

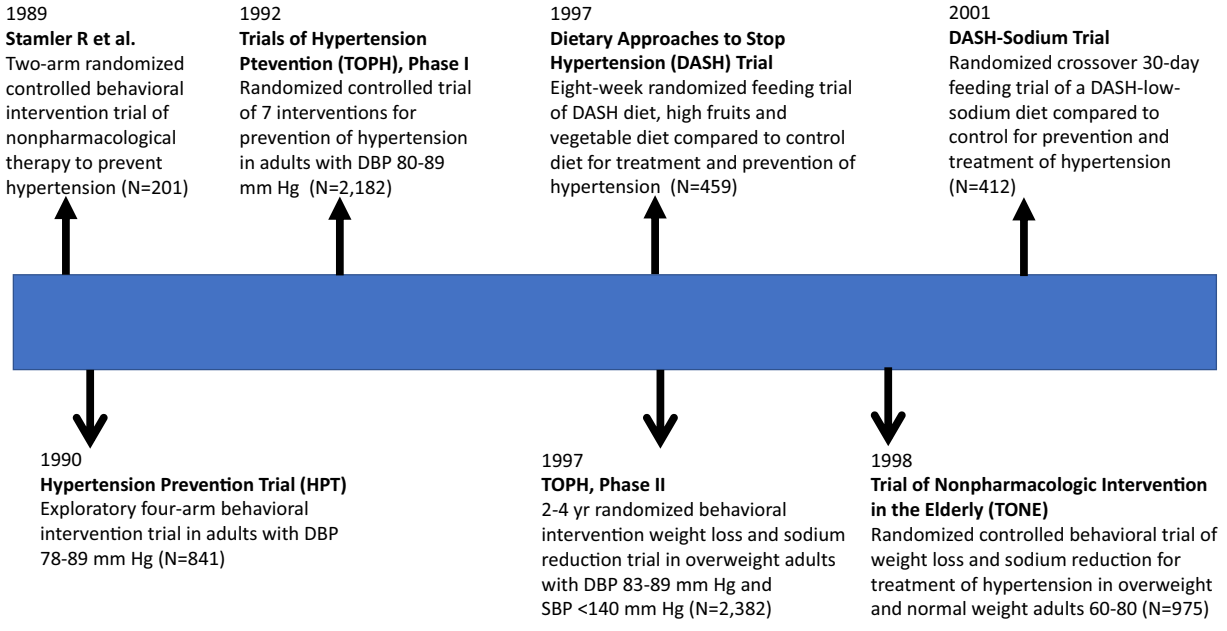

Figure 3. Timeline for selected advances in knowledge related to nonpharmacologic prevention and treatment of high blood pressure.

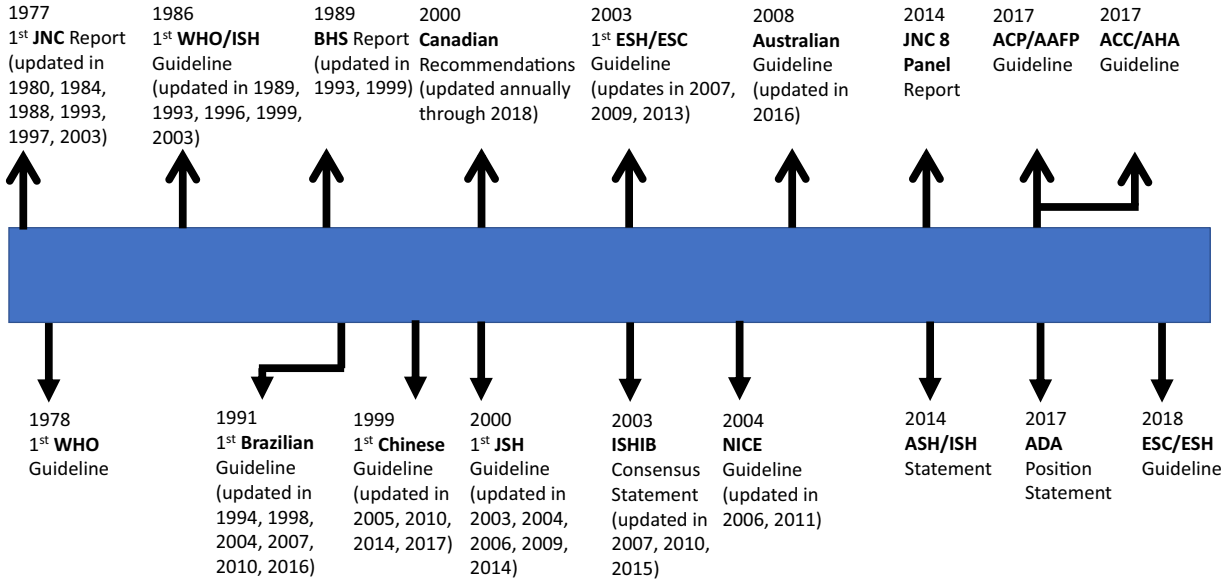

Figure 4. Timeline for selected major blood pressure clinical practice guidelines. AAFP, American Academy of Family Physicians; ACC, American College of Cardiology; ACP, American College of Physicians; ADA, American Diabetes Association; AHA, American Heart Association; ASH, American Society of Hypertension; BHS, British Hypertension Society; ESC, European Society of Cardiology; ESH, European Society of Hypertension; ISH, International Society of Hypertension; JNC, Joint National Committee; ISHIB, International Society of Hypertension in Blacks; JSH, Japanese Society of Hypertension; NICE, National Institute for Care and Excellence; WHO, World Health Organization.

those assigned to the DASH and the lowest level of sodium intake (1500 mg/day).[53] The **T**rial of N**on**pharmacologic Interventions in the **E**lderly (TONE) demonstrated the value of weight loss and sodium reduction, especially when combined, for BP lowering in 975 adults 60 to 80 years of age with hypertension already "controlled" on a single antihypertensive medication (mean SBP = 127.5 in the usual-care group) and the capacity to maintain an acceptable level of BP following withdrawal of their BP-lowering medication, particularly in those who maintained their behavioural intervention[54]. Long-term post-trial follow-up of the TOHP I and II participants has suggested sodium reduction is effective in preventing CVD and mortality from all causes in addition to lowering BP.[55-57]

Blood Pressure Clinical Practice Guidelines

Figure 4 provides a temporal sequence for some of the more important BP-related CPGs. Publication of Framingham Heart Study BP-related CVD risk results and demonstration of the benefits of antihypertensive drug treatment in the 2 Veterans Administration Cooperative Study Group trials provided the impetus for creation of a National High Blood Pressure Education Program (NHBPEP) at the National Heart, Lung, and Blood Institute (NHLBI) in 1972. Under the auspices of the NHBPEP, a task force was created to identify the prevalence of high BP, determine who would be expected to benefit from antihypertensive therapy, and recommend appropriate therapeutic regimens for lowering of BP. The task force issued a report in 1973, and this was followed by a more thorough Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure report (JNC 1) in 1977.[58] The 6-page JNC 1 report was a consensus-based document that provided advice on diagnosis of high BP in adults and recommended stepped-care antihypertensive drug therapy in those with DBP $\geq$ 105 mm Hg. The report did not address nondrug interventions, and staging of BP was based entirely on DBP. Three JNC updates were published during the 1980s,[59-61] reflecting the rapid expansion of biomedical research findings detailing BP-related risk of CVD and benefits of antihypertensive drug treatment. The 1980 JNC 2 Report recommended antihypertensive drug therapy for adults with DBP $\geq$ 104 mm Hg and possibly for adults with a DBP 90 to 104 mm Hg who had target organ damage or other evidence of increased CVD risk.[59] The 1984 JNC 3 Report was the first to include SBP in addition to DBP for diagnosis of hypertension and the first to emphasize the role of nonpharmacologic therapy for treatment of "mild" hypertension (DBP 90 to 94 mm Hg) and as an adjunct to drug therapy in adults with more severe hypertension. However, initial drug treatment recommendations were restricted to adults with DBP $\geq$ 95 mm Hg, with individualization of decisions in those with a DBP 90 to 94 mm Hg following nonpharmacologic therapy as well as those with isolated systolic hypertension. The goal of treatment was a DBP goal $<$ 90 mm Hg owing to lack of RCT evidence for a SBP goal.[60,61] The 1988 JNC 4 Report provided slightly modified treatment recommendations that included stepped-care antihypertensive drug therapy for all adults with an average DBP $>$ 94 mm Hg, for those with DBP of 90 to 94 mm Hg "despite vigorous attempts with nonpharmacologic approaches," and for those with isolated systolic hypertension (SBP $>$ 160 mm Hg and DBP $<$ 90 mm Hg) as well as a treatment goal (SBP/DBP $<$ 140/90 mm Hg) that included SBP for the first time.[61]

In 1989, the US Congress created the Agency for Health Care Policy and Research (AHCPR), now known as the Agency for Healthcare Research and Quality (AHRQ), to

focus on outcomes and effectiveness research. AHCPR contracted with the Institute of Medicine (IOM) to provide advice on development and formulation of clinical practice guidelines. In 1990, an IOM Committee to Advise the Public Health Service on Clinical Practice Guidelines issued what would be the first of several reports on the topic, *Clinical Practice Guidelines: Directions for a New Program.*[62] The most recent in the series, *Clinical Practice Guidelines We Can Trust*, was published in 2011.[63] Based on the IOM recommendations, progressively more structured and detailed JNC reports were published in 1993,[64] 1997,[65] and 2003.[66] The 1993 JNC 5 expanded the recommendation for nonpharmacologic therapy to include prevention of hypertension,[64] a concept that was published in greater detail in a NHLBI Working Group Report.[67] Although a SBP $<$ 140 mm Hg and DBP $<$ 90 mm Hg continued to be identified as the target during drug therapy, JNC 5 recommended consideration of "further reduction to levels of 130/85 mm Hg," especially in older persons. The 1997 JNC 6 recommended that treatment decisions be influenced by CVD risk stratification, specifically general reliance on "vigorous lifestyle modification" for adults with no CVD risk factors or target organ damage (Group A), consideration of initial combined lifestyle modification and antihypertensive drug therapy for those with at least 1 CVD risk factor but no diabetes, target organ damage, or clinical CVD (Group B), and prompt drug and lifestyle modification not only in adults with hypertension but in those with "high normal BP" (SBP 130 to 139 mm Hg or DBP 80 to 89 mm Hg) who manifested target organ damage, clinical CVD, or diabetes (Group C).[65] In addition, lower BP targets were recommended during treatment of adults with diabetes (SBP/DBP $<$ 130/85 mm Hg) and in those with renal disease (SBP/DBP of 125/75 mm Hg for those with heavy proteinuria and 130/85 mm Hg for those with less proteinuria). The final JNC Report (JNC 7), published in 2003, emphasized the importance of SBP in older adults, encouraged use of 2 or more antihypertensive drugs in most adults with hypertension, consideration of initial therapy with 2 or more drugs for those with SBP/DBP $>$ 20/10 mm Hg above goal, use of thiazide-type diuretics for first-step drug therapy, and a general SBP/DBP goal of $<$ 140/90 mm Hg but $<$ 130/80 in those with diabetes or chronic kidney disease.[66] In March 2008, NHLBI appointed a panel to develop a JNC 8 Report. In 2013, before publication of the panel's report, the NHLBI transferred responsibility for development of prevention of CVD clinical practice guidelines (CPGs) to the American College of Cardiology (ACC) and American Heart Association (AHA).[68,69] The members appointed to the JNC 8 panel elected to publish a guideline limited to 3 antihypertensive drug therapy questions in 2014, without endorsement from NHLBI or any professional society.[70] The most controversial of their recommendations was to employ a SBP treatment threshold of $\geq$ 150 mm Hg and a SBP treatment goal of $<$ 150 mm Hg during antihypertensive drug therapy in adults $\geq$ 60 years. Five members of the panel published a minority view that supported the JNC 7 recommendation for an SBP treatment threshold of 140 mm Hg and BP goal of $<$ 140 mm Hg during drug therapy in adults $\geq$ 60 years.[71] During the same year (2014), the ACC, AHA, and 9 partner professional societies with interest in BP appointed a 21-member writing committee to develop a comprehensive BP CPG, which was subsequently released in 2017.[72] The writing committee emphasized the importance of accurate BP measurements, averaging of readings within and between visits, use of out-of-office measurements to confirm high office readings and to recognize white coat and masked hypertension. In addition, the committee recommended a new BP classification system that characterized hypertension as an average of correctly measured SBPs $\geq$ 130 mm Hg or DBPs $\geq$ 80 mm Hg and also recommended quantification of atherosclerotic CVD (ASCVD) risk using the ACC/AHA pooled cohorts equation[73] for guidance of treatment decisions. Emphasis was placed on SBP, but DBP recommendations were also provided, with the DBP goals being based on expert opinion. Antihypertensive drug therapy, in addition to nonpharmacologic therapy, was recommended for the approximately 30% of US adults with stage 1 hypertension (SBP 130 to 139 mm Hg or DBP 80 to 89 mm Hg) with a 10-year risk of ASCVD $\geq$ 10% and all those with SBP $\geq$ 140 mm Hg or DBP $\geq$ 90 mm Hg. A general SBP/DBP treatment goal of $<$ 130/80 mm Hg was recommended, with the caveat that the focus should be restricted to SBP ($<$ 130 mm Hg) in noninstitutionalized ambulatory, community-dwelling adults $\geq$ 65 years. A variety of other US-based BP guidelines have been published by professional societies, such as the International Society of Hypertension in Blacks;[74-77] the American Society of Hypertension (in conjunction with the International Society of Hypertension);[78] the American College of Physicians (ACP)/American Academy of Family Physicians (AAFP), confined to pharmacologic treatment in adults $\geq$ 60 years of age;[79] and the American Diabetes Association.[80] In a quantitative analysis, identical antihypertensive treatment recommendations are advocated for a high percentage of US adults with diabetes in the 2017 ACC/AHA CPG and 2017 American Diabetes Association Position Statement.[81] For example, concordant management recommendations were made for 95.7% of those with BP above goal during treatment. Likewise, the BP treatment goals in the 2017 ACC/AHA, and the most recent major BP CPGs in Europe, Canada, and Australia have all been considerably lower than in previous CPGs. The most aberrant of the current US guidelines is the ACP/AAFP CPG, which provides recommendations for antihypertensive drug therapy in adults $\geq$ 60 years of age.[79] In contrast to the ACC/AHA CPG focus on functionality and recommendation to employ similar SBP goals ($<$ 130 mm Hg) in older compared with younger adults for noninstitutionalized community-dwelling patients who tolerate their treatment, the ACP/AAFP guideline recommends initiating treatment when SBP $>$150 mm Hg and a SBP treatment goal of $<$ 150 mm Hg, with consideration of $<$ 140 in high-risk patients. No guidance is provided regarding BP measurement methods for the ACP/AAFP treatment decisions. As indicated below, the other major English language CPG publications are more in keeping with the 2017 ACC/AHA recommendations than those suggested by the ACP/AAFP.

Outside the United States, the World Health Organization (WHO) issued a technical report with recommendations for detection and management of hypertension in 1978,[82] followed by a collaboration with the International Society of Hypertension that resulted in progressively more comprehensive CPGs in 1986,[83] 1989,[84] and 1993. A WHO Expert

Committee Report was released in 1996,[85] followed by a WHO/ISH statement on management of hypertension in 1999 and a statement that addressed the role of CVD risk for treatment decisions in 2003.[86] The British Hypertension Society published hypertension CPGs in 1989,[87] 1993,[88] and 1999,[89] followed by hypertension recommendations for England and Wales by the National Institute for Health and Clinical Excellence (NICE) in 2004,[90] 2006,[91] and 2011.[92] The European Society of Hypertension (ESH) and European Society of Cardiology (ESC) collaborated to produce their first comprehensive BP CPG in 2003,[93] which was subsequently updated in 2007,[94] 2009,[95] and 2013.[96] In 2018, the same 2 professional societies published an ESC/ESH hypertension CPG.[97] Despite some important differences, especially in classification of hypertension, the 2017 ACC/AHA and 2018 ESC/ESH have many common recommendations. These include lower than previous thresholds for initiation of therapy and lower BP targets during drug therapy as well as a focus on functionality rather than chronologic age during treatment in older adults.[98] The Canadian Hypertension Education Program was established in 1999 as a public-private partnership to develop and implement evidence-based CPGs for diagnosis and management of hypertension in Canadian primary care practices.[99] Starting with a hypertension CPG in 2000,[100,101] the recommendations have been comprehensively updated on an annual basis until the present.[102] The first (1999) hypertension CPG in China was published in 2000.[103] In subsequent years, a variety of hypertension CPGs have been released by different organizations, with some of the more important being published in 2005,[104] 2011,[105] 2015,[106] and 2017.[107] The Japanese Society of Hypertension produced its first hypertension CPG in 2001,[108] followed by updates in 2005,[109] 2009,[110] and 2014,[111] with an update expected in 2019. The Brazilian Society of Hypertension has published 7 hypertension CPGs in 1991,[112] 1994,[113] 1998,[114] 2004,[115] 2007,[116] 2010,[117] and 2016.[118] In Australia, a comprehensive hypertension CPG was published in 2008[119] (updated in 2010) and more recently replaced by a CPG published in 2016.[120] In a manner similar to the ACC/AHA, ESC/ESH, and Canadian BP CPGs, the 2016 Australian document recommends a much lower SBP treatment target (<120 mm Hg, if tolerated) than in the earlier Australian CPGs. Comprehensive hypertension CPGs have also been developed on a continuing basis by many other professional societies[121] and countries.[122,123]

Strengths and Challenges of Blood Pressure Clinical Practice Guidelines

In most countries, BP-related CPGs are now an established part of clinical and public health practice. CPGs are especially well suited to areas, such as high BP, that are common, result in substantial cost and use of health resources, demonstrate variation in practice patterns, and have high-quality evidence to support recommendations. One of the challenges in a "mature" area such as high BP is that many guidelines with variable rigour and quality are developed. To avoid the potential for a conflict of interest, membership of the 2017 ACC/AHA BP CPG writing committee was restricted to individuals devoid of any relationship with pharmaceutical companies or device manufacturers that have an interest in BP-related products. The review process was used to allow knowledgeable opinion leaders who were ineligible for committee membership to provide input. Although desirable, this approach is not feasible in all countries and may be less critical in the current era when many of the antihypertensive drugs used in clinical practice are generic.[124] At present, conflicting recommendations is a more serious issue. It is a natural consequence of CPGs generated by multiple writing committees because they may well interpret the same data in different ways,[72,79] and choice of CVD risk instruments as well as treatment recommendations are highly influenced by the country/region of focus. Even when the core recommendations are very similar,[81,98] there is a tendency to look for differences[125,126] and suggest that even the experts cannot agree. This is unfortunate because it can lead to confusion and uncertainty among clinicians and the general public. This inevitably results in therapeutic inertia, despite the inadequacy of hypertension control rates in such high-income countries as the United States[127] and Canada[128] and a dismal rate of hypertension control worldwide.[129] CPG treatment recommendations are heavily influenced by the results of RCTs and systematic reviews based on meta-analysis of clinical trials. RCTs provide the best evidence for treatment recommendations, but interpretation of their results is constrained by study participant selection and the knowledge that landmark trials have been based on efficacy rather than effectiveness studies. Although many BP CPGs are developed, only a small number are based on a comprehensive, rigourous, and independent review of the evidence. The 2017 ACC/AHA guideline,[72] 2018 ESC/ESH guideline,[97] annually updated Hypertension Canada series,[102] and 2016 National Heart Foundation of Australia guideline[120] are good examples of rigourous, comprehensive BP CPGs that have been developed by independent writing committees.

Many of the most careful BP CPGs have been designed to meet the needs of practitioners in specific countries or regions. Generalizing recommendations in these guidelines to other populations has the advantage that such reports tend to be based on thoughtful interpretation of the available evidence. Advice in some areas, such as BP measurement, has almost universal application. However, other areas—such as choice of CVD risk-prediction instruments, antihypertensive treatment decisions, and BP goals—are highly dependent on availability of valid instruments for measurement of CVD risk, economic conditions, existing systems of health care delivery, accessibility and affordability of antihypertensive medications, and the extent to which high BP—especially severe hypertension—is already being controlled. Most high BP and its complications are now centred in low- and middle-income countries, where CVD risk-estimating tools are imperfect;[130] few RCTs have been conducted;[131] systems of care are often imperfect; and control rates are extremely low, even for levels of BP at which combined nonpharmacologic and antihypertensive drug therapy are recommended in almost all BP CPGs.[129,132] In contrast to this dismal situation, control rates have improved progressively in high-income countries.[129] In the US general population, antihypertensive drug treatment and control to a SBP/DBP < 140/90 mm Hg has been slightly in excess of 50% in recent years.[127] However, when a focused approach is applied to management of high BP in RCTs[34,133] and in systems of care,[134,135] substantially better

control rates have been achieved. In a recent report from the Kaiser Permanente System in Northern California, control to a SBP/DBP < 140/90 mm Hg was reported in 90% of members receiving drug treatment for hypertension. Such reports from US systems of care have been based on Healthcare Effectiveness Data and Information Set (HEDIS) or similar requirements and are likely subject to some overestimation bias. However, there is little doubt that the level of BP control has improved progressively in settings in which there has been a commitment to a comprehensive plan aimed at improved treatment and control. Both the 2017 ACC/AHA and 2018 ESC/ESH CPGs placed considerable emphasis on approaches to improving treatment and control of high BP. Strategies recommended in the ACC/AHA CPG included improved adherence to prescribed therapy, promotion of lifestyle modification, team-based care, active use of electronic health record systems, telehealth initiatives, performance and quality improvement measures, and—to a lesser extent—financial incentives.[72] Many of the same strategies recommended to improve hypertension treatment and control in the ACC/AHA document were also identified in a subsequent systematic review and meta-analysis.[136] RCTs have repeatedly identified team-based care as having a major effect on rates of control.[136,137]

Recognizing the limitations of BP CPGs, they provide useful structured guidance for the clinical and public health communities. Implementation of CPG recommendations is challenging and involves several steps including dissemination of knowledge, commitment on the part of providers and policy decision makers, and funding agencies to implement all or some of the recommendations successfully. Many clinician survey reports suggest insufficient familiarity with the content of BP CPGs,[138-140] but these inferences are based on studies with serious methodologic limitations, including low response rates and use of selected practitioner samples. Surveys that have employed better methods and have achieved a relatively high response rate provide more convincing evidence that patients have limited awareness of important knowledge elements in BP CPGs. Whatever the knowledge and attitudes of providers and patients, control rates[127,129] support the need for better dissemination and implementation of BP CPGs. Modelling studies suggest this would result in a lower average level of BP and substantial improvement in the health of the public.[141-143] Fortunately, several large-scale initiatives are being implemented to improve detection and management of hypertension and CVD. In the United States, these include the Million Hearts Initiative,[144,145] sponsored by the Centers for Disease Control and Prevention (CDC) and the Centers for Medicare and Medicaid Services (CMS) and Target, BP,[146] sponsored by the American Heart Association and American Medical Association. Globally, major initiatives include the WHO-sponsored Global Hearts Initiative[147] and the Resolve to Save Lives Cardiovascular Health Initiative,[148,149] sponsored by private philanthropy. It is hoped that these and other initiatives will result in much improved treatment and control of high BP.

Conclusions

Clinical practice guidelines have evolved to become an important resource for advice on diagnosis and management of high BP. Most of the major BP guidelines provide recommendations that are more similar than different. Modelling studies suggest that better adherence to the advice in BP guidelines would result in a lower average level of BP and a substantial improvement in health status.

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