

## **Isometric Handgrip as an Adjunct for Blood Pressure Control - A Primer for Clinicians**

Cheri L. McGowan <sup>1,4,5</sup>; David N. Proctor <sup>2</sup>; Ian Swaine <sup>3</sup>; Robert D. Brook <sup>4</sup>; Elizabeth A. Jackson <sup>4</sup>; Phillip D. Levy <sup>5</sup>

<sup>1</sup> Department of Kinesiology, Faculty of Human Kinetics, University of Windsor, Windsor, ON, Canada

<sup>2</sup> Department of Kinesiology, The Pennsylvania State University, University Park, PA, USA

<sup>3</sup> Department of Life & Sport Sciences, University of Greenwich, Medway Campus, London, UK

<sup>4</sup> Division of Cardiology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA

<sup>5</sup> School of Medicine, Department of Emergency Medicine, Wayne State University, Detroit, MI, USA

Address for Correspondence: Dr. Cheri McGowan, Department of Kinesiology, Faculty of Human Kinetics, University of Windsor, 401 Sunset Avenue, Windsor, ON, Canada, N9B 3P4. Telephone: 519-253-3000 ex. 4979 Fax: 519-973-7056. Email: [mcgowanc@uwindsor.ca](mailto:mcgowanc@uwindsor.ca).

## **Abstract**

Considered a global health crisis by The World Health Organization, hypertension (HTN) is the leading risk factor for death and disability. The majority of treated patients do not attain evidence-based clinical targets, which increases the risk of potentially fatal complications. HTN is the most common chronic condition seen in primary care; thus implementing therapies that lower and maintain BP to within target ranges is of tremendous public health importance. Isometric handgrip (IHG) training is a simple intervention endorsed by the American Heart Association as a potential adjuvant BP-lowering treatment. With larger reductions noted in HTN patients, IHG training may be especially beneficial for those who a) have difficulties continuing or increasing drug-based treatment; b) are unable to attain BP control despite optimal treatment; c) have pre-HTN or low-risk stage I mild HTN; and, d) wish to avoid medications or have less pill burden. IHG training is not routinely prescribed in clinical practice. To shift this paradigm, we focus on: 1) the challenges of current HTN management strategies; 2) the effect of IHG training; 3) IHG prescription; 4) characterizing the population for whom it works best; 5) clinical relevance; and 6) important next steps to foster broader implementation by clinical practitioners.

## Introduction

Hypertension (HTN), defined as a systolic blood pressure (BP)  $\geq 140$  mmHg and/or a diastolic BP  $\geq 90$  mmHg, is a global epidemic [1]. It is the leading cause of cardiovascular disease (CVD) and related mortality worldwide [2-5], and is responsible for ~10 million deaths each year [6], making it a substantial contributor to global chronic disease burden [7;8].

HTN is now the most commonly diagnosed condition in primary care [9-11], yet between 50 - 70% of patients are not controlled to within clinical target ranges [12-18]. In the United States, approximately 34% of adults have HTN [4], with African Americans, and particularly African American women, having among the highest rates of HTN in the world [2;4]. Approximately 14% of American patients have true “resistant HTN” [4], which is a failure to effectively reduce BP to recommended levels despite compliance to optimal treatment [19].

Uncontrolled HTN is associated with a number of sequelae that are damaging to the cardiovascular system [20-29]. Long-term and potentially fatal pressure-related complications include coronary artery disease, heart failure, stroke, and renal failure, in addition to cognitive decline [1;30-33] and overall poor quality of life [34]. A recent call suggests increasing efforts to lower BP in individuals with resting BP between 110 - 140 mmHg (pre-HTN) to reduce the global HTN burden [7]. However, while HTN prevention and treatment are global health priorities for the World Health Organization [35;36], there is a lack of consensus on if and when antihypertensive therapy should be used in those with pre-HTN, making potential non-pharmaceutical alternatives appealing from a public health perspective.

## **The Challenges of Current Hypertension Management Strategies**

The objective of HTN-related clinical practice, in general, is to achieve a resting BP of  $\leq 140/90$  mmHg [10;12;37-42] using traditional office based oscillometric measurements, or  $\leq 135/85$  mmHg using newer, unattended automated office BP measurement devices [38;43]. However, these guidelines are always evolving and will likely become more stringent by lowering BP goals in the near future, at least for higher risk patients [7;10]. Adherence to HTN medication, a modified diet (e.g., sodium and alcohol reduction, Dietary Approaches to Stop Hypertension (DASH) eating plan), and increased physical activity are frontline components of BP management [44;45]. With respect to the latter, international guidelines overwhelmingly recommend aerobic exercise training with dynamic resistance training as an adjuvant intervention [38;44-47].

Despite the existence of these well-publicized management guidelines, non-compliance is common. Less than 50% of patients adequately adhere to their HTN medication regimen [48;49] for a myriad of reasons including sociocultural and economic considerations, and risk for non-compliance is particularly high in African Americans [50]. Further, adherence to dietary strategies is remarkably poor [47], and almost half of American adults are inactive (with even higher rates of inactivity reported among African Americans and those living in poverty) [51]. Common barriers to exercise include physical and other health limitations, lack of convenience, competing priorities and access difficulties [52-54]; these may extend to include an absence of social support, inflexible work schedules, unattainable costs and unsafe exercise environments [55-58].

In light of the above-noted realities, it is imperative to acknowledge that long-term compliance with traditional BP-lowering treatments is poor [47]. Thus, complementary treatments that can successfully reduce and maintain BP to within clinical targets are urgently needed, particularly for those that have a high potential for uptake and continuation over long periods of time.

## **Alternative Hypertension Treatments: Use of Isometric Handgrip Training as a Non-Pharmacological Approach to Blood Pressure Management**

A plethora of “alternative”, non-pharmacological complementary approaches to BP lowering have been investigated over the years, and have been implemented in patient cohorts ranging from pre- to resistant-HTN [47]. Falling broadly into three main categories, these alternative approaches include behavioral strategies (e.g., meditation, biofeedback), non-invasive procedures or devices (e.g., device-guided slow breathing, acupuncture), and novel exercise-based interventions (e.g., isometric handgrip (IHG) training) [47]. In their Scientific Statement on Alternative Approaches to Lowering Blood Pressure, the American Heart Association (AHA) supported the use of biofeedback techniques, device-guided breathing and IHG training as potentially effective BP-lowering adjuvant therapies, and amenable for use in clinical practice [47]. For the purposes of this report, we focus our attention on IHG training.

The weight of the evidence suggests that IHG training, a form of isometric resistance training comprised of multiple sustained forearm contractions separated by short rest periods, is a safe, simple, and easily-adoptable intervention to lower BP. The most recent meta-analysis of randomized controlled isometric resistance training trials (RCTs; N=302) cites post-training reductions in resting BP of ~5/4 mmHg, with larger reductions noted in HTN patients [59]. Early evidence suggests that ambulatory BP, a superior measure for diagnostic and prognostic purposes [60-63], may also be reduced. In the only trials involving ambulatory BP measurement, statistically significant reductions in mean 24-hour systolic BP were observed in young healthy adults following IHG training [64], while a clinically relevant post-training reduction was noted in a population of well-controlled HTN patients [65].

The time-efficient IHG protocol lasts as little as 12 minutes (11 if you discount the last minute of rest), and has proven effective in individuals with and without HTN (even in medicated hypertensives) and those who are already physically active [65-84]. Importantly, IHG training is well-tolerated by participants, and seems to present low levels of risk to safety. High compliance rates have been reported across isometric resistance training trials and there have been no published reports of acute or long-term adverse events [59;80]. While some clinicians may be concerned about the potential safety of IHG, current data supports only modest transient on-exercise increases in heart rate ( $\Delta$  3-8 bpm) and BP ( $\Delta$  12-38/7-23 mmHg) for most people studied thus far, even in those with pre-HTN and HTN [74;80;85-88]. Acute HR and BP changes are less than those elicited during moderate and vigorous aerobic exercise [88]. However, resistant hypertensives with more severe HTN (>160-180/100-110 mm Hg) may need to exert some caution because of the possible acute BP elevations during IHG, until its safety is established in this group. This is consistent with existing precautionary recommendations regarding the avoidance of aerobic exercise among these patients.

Plausible BP-lowering mechanisms supported by prior trials include: improved neural cardiac control (e.g., heart rate variability [71;73]), augmented arterial compliance and vascular function [68;80;85], reduced sympathetic outflow [73], and/or an enhanced oxidative capacity [82].

### **Isometric Handgrip Training Prescription**

The most common isometric resistance training protocol consists of four, 2-minute periods of sustained isometric exercise, separated by brief 1-minute rest periods, performed 3 to 5 times per week for up to 10 weeks on a handgrip dynamometer. Historically, training sessions have been conducted in laboratory settings, or via a combination of in-laboratory and at-home training. Recently completed pilot work from our group provides evidence, using a randomized single-blind

study in HTN patients, that IHG training is feasible and effective when prescribed in clinical settings using a home-based model.

IHG training trials have employed handgrip dynamometers ranging from computerized programmable devices to spring-loaded investigator calibrated handgrips, with the most widely studied to date in HTN patients being the former [59;80]. As the computerized devices are expensive, the financial burden of which may hinder patient uptake, a host of studies are being conducted to investigate cheaper and more readily available alternatives (e.g., stress ball, mechanical handgrips).

While the literature on the effectiveness of IHG training is still accumulating, handgrip resistance training was mentioned in the 2016 Canadian Hypertension Education Program guidelines, and as noted above, IHG training was featured in the AHA Scientific Statement as a potentially viable BP-lowering option [38;47]. In their Statement, the AHA provided an “Algorithm for implementing alternative approaches in clinical practice” which can be applied to IHG training prescription in clinical practice (Figure 1).

### **For Which Patients Does it Work Best?**

As with most BP-lowering treatments, IHG training appears to be particularly effective in those with higher initial resting BP [67;70;81]. In patients with HTN, data suggest that higher initial systolic BP elicits greater post-IHG training reductions [67;81]. Older individuals, and those with high pre-training systolic BP reactivity to cardiovascular stress tasks (e.g., serial subtraction task, 2-minute IHG task) also appear highly responsive to IHG training [67;70;77;89;90]. African Americans exhibit higher BP reactivity than other populations [91] and thus, IHG training may be particularly beneficial in this patient population. Data focused specifically on this population group,

however, is lacking. The effect of gender is also unclear [59;64;70] and may simply reflect the small overall number of women that have participated in IHG training trials to date.

### **Clinical Significance**

IHG training involves the use of a portable hand-held device, is of low time burden, is highly tolerable and requires no “refills” or other active maintenance efforts. Thus, this treatment is likely to be as attractive to HTN patients as it has been to research participants. From a provider perspective, prescribing an effective intervention that is safe, and one to which patients have a great likelihood to comply, is also enticing. With larger post-training reductions noted in HTN patients, IHG training may be especially beneficial for patients who a) have difficulties continuing or increasing drug-based treatment care; b) are unable to attain BP control despite optimal treatment; c) have pre-HTN or low-risk stage I mild-HTN, and; d) who wish to avoid medications or have less anti-hypertensive pill burden.

Taken together, this simple treatment has strong potential to impact patient care and improve the rates of BP control among those with HTN. It is important to acknowledge, however, that a post-IHG training reduction of  $\sim 5/4$  mmHg may not be enough to lower BP to within recommended targets (or within  $\sim 10$  mmHg of target) for some patients. In these individuals, IHG training may be more appropriate as part of a broader lifestyle approach, with the effects of IHG training adding to the effects of other lifestyle modifications. The effectiveness of this type of multi-modal intervention trial would need to be explored in future IHG training trials.

Despite its promise, IHG training is not routinely prescribed in clinical practice as a BP-lowering management strategy. This critical gap may be indicative of clinicians being unaware of IHG training or how to prescribe it, a lack of confidence in the ability of the patients to train at home, uncertainty about how to purchase the training devices and concern relating to the associated



cost. The aim of this report is to take the first steps towards addressing this gap, in an effort to shift this paradigm.

### **Important Next Steps**

In their 2017 Heart Disease and Stroke Statistics Update, the AHA stated that “the elimination of HTN is projected to have a larger impact on CVD mortality than the elimination of all other risk factors among females, and all except smoking among males” [4]. It is our over-arching goal to improve BP control and reduce the burden of HTN by incorporating IHG training as part of a comprehensive treatment strategy in clinical practice. Most IHG training studies to date have been small, short duration, proof-of-concept trials. Large-scale, high quality RCTs of longer duration are urgently needed to address these earlier limitations and further establish the merits of this effective treatment. Future work should aim to explore the potential additive effects of IHG training to traditional lifestyle modifications (e.g., DASH diet, aerobic exercise training), medical practice and home-based effectiveness models of IHG training, including trials in patients with resistant HTN and pre-HTN/mild-HTN wishing to avoid medication. Moreover, trials investigating the long-term persistence of BP-lowering, training interventions using less expensive handgrip devices, and those evaluating population-specific BP-lowering mechanisms, patient and physician burden, clinical outcomes, and economic benefit are also needed.

### **Conclusion**

Poor BP control puts many Americans and individuals around the world at risk for serious and often fatal complications of HTN. African Americans are disproportionately affected as are all individuals with treatment-resistant HTN. There is an urgent need to translate effective BP-lowering therapies, such as IHG training, into standard care that act alone or as an adjunct to traditional treatments. By increasing the proportion of patients achieving BP control, we take an important step towards reducing the burden of HTN in our country and beyond.

## References

- 1       Pescatello L, Franklin B, Fagard R, Farquhar W, Kelley GA, Ray CA. Exercise and hypertension. *Med Sci Sports Exerc.* 2004;36:533-553.
- 2       Joffres M, Falaschetti E, Gillespie C, Robitaille C, Loustalot F, Poulter N, McAlister F, Johansen H, Baclic O, Campbell N. Hypertension prevalence, awareness, treatment and control in national surveys from England, the USA and Canada, and correlation with stroke and ischaemic heart disease mortality: A cross-sectional study. *BMJ Open.* 2013;3: doi:10.1136/bmjopen-2013-003423.
- 3       Danaei G, Ding E, Mozaffarian D, Taylor B, Rehm J, Murray C, Ezzati M. The preventable causes of death in the United States: Comparative risk assessment of dietary, lifestyle, and metabolic risk factors. *PLoS Med.* 2009;6:e1000058.
- 4       Benjamin E, Blaha M, Chiuve S, Cushman M, Das S, Deo R, de Ferranti S, Floyd J, Fornage M, Gillespie C, Isasi C. Heart disease and stroke statistics - 2017 Update: A report from the American Heart Association. *Circulation.* 2017;135:e146-e603.
- 5       Ezzati M, Lopez A, Rodgers A, Vander Hoorn S, Murray C. Selected major risk factors and global and regional burden of disease. *Lancet.* 2002;360:1347-1360.
- 6       World Health Organization. A global brief on hypertension. Silent Killer, global health crisis. WHO Press 2013. World Health Day 2013.
- 7       Forouzanfar M, Liu P, Roth G, Ng M, Biryukov S, Marczak L, Alexander L, Estep K, Abate K, Akinyemiju T. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990-2015. *JAMA.* 2017;317:165-182.

8 Lim S, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, AlMazroa MA, Amann M, Anderson HR, Andrews KG, Aryee M, Atkinson C, Bacchus LJ, Bahalim AN, Balakrishnan K, Balmes J, Barker-Collo S, Baxter A, Bell ML, Blore JD, Blyth F, Bonner C, Borges G, Bourne R, Boussinesq M, Brauer M, Brooks P, Bruce NG, Brunekreef B, Bryan-Hancock C, Bucello C, Buchbinder R, Bull F, Burnett RT, Byers TE, Calabria B, Carapetis J, Carnahan E, Chafe Z, Charlson F, Chen H, Chen JS, Cheng AT-A, Child JC, Cohen A, Colson KE, Cowie BC, Darby S, Darling S, Davis A, Degenhardt L, Dentener F, Des Jarlais DC, Devries K, Dherani M, Ding EL, Dorsey ER, Driscoll T, Edmond K, Ali SE, Engell RE, Erwin PJ, Fahimi S, Falder G, Farzadfar F, Ferrari A, Finucane MM, Flaxman S, Fowkes FG, Freedman G, Freeman MK, Gakidou E, Ghosh S, Giovannucci E, Gmel G, Graham K, Grainger R, Grant B, Gunnell D, Gutierrez HR, Hall W, Hoek HW, Hogan A, Hosgood III HD, Hoy D, Hu H, Hubbell BJ, Hutchings SJ, Ibeanusi SE, Jacklyn GL, Jasrasaria R, Jonas JB, Kan H, Kanis JA, Kassebaum N, Kawakami N, Khang YH, Khatibzadeh S, Khoo JP, Kok C, Laden F, Lalloo R, Lan Q, Lathlean T, Leasher JL, Leigh J, Li Y, Lin JK, Lipshultz SE, London S, Lozano R, Lu Y, Mak J, Malekzadeh R, Mallinger L, Marcenes W, March L, Marks R, Martin R, McGale P, McGrath J, Mehta S, Memish ZA, Mensah GA, Merriman TR, Micha R, Michaud C, Mishra V, Hanafiah KM, Mokdad AA, Morawska L, Mozaffarian D, Murphy T, Naghavi M, Neal B, Nelson PK, Nolla JM, Norman R, Olives C, Omer SB, Orchard J, Osborne R, Ostro B, Page A, Pandey KD, Parry CD, Passmore E, Patra J, Pearce N, Pelizzari PM, Petzold M, Phillips MR, Pope D, Pope III CA, Powles J, Rao M, Razavi H, Rehfuess EA, Rehm JT, Ritz B, Rivara FP, Roberts T, Robinson C, Rodriguez-Portales JA, Romieu I, Room R, Rosenfeld LC, Roy A, Rushton L, Salomon JA, Sampson U, Sanchez-Riera L, Sanman E, Sapkota A, Seedat S, Shi P, Shield K, Shivakoti R, Singh GM, Sleet DA, Smith E, Smith KR, Stapelberg NJ, Steenland K, St+Ackl H, Stovner LJ, Straif K, Straney L, Thurston GD, Tran JH, Van Dingenen R, van Donkelaar A, Veerman JL, Vijayakumar

L, Weintraub R, Weissman MM, White RA, Whiteford H, Wiersma ST, Wilkinson JD, Williams HC, Williams W, Wilson N, Woolf AD, Yip P, Zielinski JM, Lopez AD, Murray CJ, Ezzati M. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990 - 2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2224-2260.

- 9 Hemmelgarn B, Chen G, Walker R, McAlister F, Quan H, Tu K, Khan N, Campbell N. Trends in antihypertensive drug prescriptions and physician visits in Canada between 1996 and 2006. *Can J Cardiol*. 2008;24:507-512.
- 10 James P, Oparil S, Carter B. 2014 evidence-based guideline for the management of high blood pressure in adults: Report from the panel members appointed to the eighth joint national committee (JNC 8). *JAMA*. 2014;311:507-520.
- 11 Centers for Disease Control and Prevention. National Ambulatory Medical Care Survey: 2013 State and National Summary Tables; 2017.
- 12 Chobanian A, Bakris G, Black H, Cushman W, Green L, Izzo J, Jr., Jones D, Materson B, Oparil S, Wright JT, Jr., Roccella E. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: The JNC 7 report. *JAMA*. 2003;287:1206-1252.
- 13 Sarafidis P. Epidemiology of resistant hypertension. *J Clin Hypertens*. 2011;13:523-528.
- 14 Wilkins K, Campbell N, Joffres M, McAlister F, Nichol M, Quach S, Johansen H, Tremblay M. Blood pressure in Canadian adults. *Stats Can Health Reports*. 2010;21:37-46.

- 15 Wolf-Maier K, Cooper R, Banegas J, Giampaoli S, Hense H, Joffres M, Kastarinen M, Poulter N, Primatesta P, Rodriguez-Artalejo F. Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States. *JAMA*. 2003;289:2363-2369.
- 16 Mills K, Bundy J, Kelly TN, Reed J, Kearney P, Reynolds K, Chen J, He J. Global burden of hypertension: Analysis of population-based studies from 89 Countries. *J Hypertens*. 2015;33.
- 17 Petrella R, Merikle E, Jones J. Prevalence, treatment, and control of hypertension in primary care: Gaps, trends, and opportunities. *J Clin Hypertens*. 2007;9:28-35.
- 18 Campbell N, Bovet P, Schutte A, Lemogoum D, Nkwescheu A. High blood pressure in Sub-Saharan Africa: Why prevention, detection, and control are urgent and important. *J Clin Hypertens*. 2015;17:663-667.
- 19 Ghofrani H, Weaver F, Nadim M. Resistant hypertension. Medical management and alternative therapies. *Cardiol Clin*. 2015;33:75-87.
- 20 Schiffrin E. Remodeling of resistance arteries in essential hypertension and effects of antihypertensive treatment. *Am J Hypertens*. 2004;17:1192-1200.
- 21 Ferroni P, Basili S, Paoletti V, Davi G. Endothelial dysfunction and oxidative stress in arterial hypertension. *Nutr Metab Cardiovasc Dis*. 2006;16:222-233.
- 22 Yamada Y, Miyajima E, Tochikubo O, Matsukawa T, Ishii M. Age-related changes in muscle sympathetic nerve activity in essential hypertension. *Hypertension*. 1989;13:870-877.

- 23 Anderson E, Sinkey C, Lawton W, Mark A. Elevated sympathetic nerve activity in borderline hypertensive humans. Evidence from direct intraneural recordings. *Hypertension*. 1989;14:177-183.
- 24 Fujita M, Ando K, Nagae A, Fujita T. Sympathoexcitation by oxidative stress in the brain mediates arterial pressure elevation in salt sensitive hypertension. *Hypertension*. 2007;50:360-367.
- 25 Nozoe M, Hirooka Y, Koga Y, Sagara Y, Kishi T, Engelhardt JF, Sunagawa K. Inhibition of Rac1-derived reactive oxygen species in nucleus tractus solitarius decreases blood pressure and heart rate in stroke-prone spontaneously hypertensive rats. *Hypertension*. 2007;50:62-68.
- 26 Biaggioni I. Sympathetic control of the circulation in hypertension: Lessons from autonomic disorders. *Curr Opin Nephrol Hypertens*. 2003;12:175-180.
- 27 Boos CJ, Lip GY. Is hypertension an inflammatory process? *Curr Pharm Des*. 2006;12:1623-1635.
- 28 Lassegue B, Griendling KK. Reactive oxygen species in hypertension. An update. *Am J Hypertens*. 2004;17:852-860.
- 29 Faulx M, Wright A, Hoit B. Detection of endothelial dysfunction with brachial artery ultrasound scanning. *Am Heart J*. 2003;145:943-951.
- 30 Braunwald E, Zipes D, Libby P. *Heart Disease. A textbook of cardiovascular disease medicine*. ed 6th, USA, W.B. Saunders Company, 2007.
- 31 Leite-Moreira AF. Current perspectives in diastolic dysfunction and diastolic heart failure. *Heart*. 2006;92:712-718.

- 32 Taylor C, Tillin T, Chaturvedi N, Dewey M, Ferri C, Hughes A, Prince M, Richards M, Shah A, Stewart R. Midlife hypertensive status and cognitive function 20 years later: The Southall and Brent revisited study. *J Am Geriatr Soc.* 2013;61:1489-1498.
- 33 Wysocki M, Luo X, Schmeidler J, Dahlman K, Lesser G, Grossman H, Haroutunian V, Beeri M. Hypertension is associated with cognitive decline in elderly people at high risk for dementia. *Am J Ger Psychiatry.* 2012;20:179-187.
- 34 Battersby C, Hartley K, Fletcher A, Markowe H, Styles W, Sapper H, Bulpitt C. Quality of life in treated hypertension: A case-control community based study. *J Hum Hypertens.* 1995;9:981-986.
- 35 World Health Organization. 2008-2013 Action plan for the global strategy for the prevention and control of noncommunicable diseases. *WHO Media.* 2008;1-42.
- 36 World Health Organization. World report on aging and health. *WHO Media.* 2015;1-260.
- 37 Arguedas J, Perez M, Wright J. Treatment blood pressure targets for hypertension. *Cochrane Database of Syst Rev.* 2009;4:CD004349.
- 38 Leung A, Nerenberg K, Daskalopoulou S, McBrien K, Zarnke K, Dasgupta K, Cloutier L, Gelfer M, Lamarre-Cliche M, Milot A, Bolli P, Tremblay G, McLean D, Tobe S, Ruzicka M, Burns K, Vallee M, Prasad G, Lebel M, Feldman R, Selby P, Pipe A, Schiffrin E, McFarlane P, Oh P, Hegele R, Khara M, Wilson T, Penner S, Burgess E, Herman R, Bacon S, Rabkin S, Gilbert R, Campbell T, Grover S, Honos G, Lindsay P, Hill M, Coutts S, Gubitza G, Campbell N, Moe G, Howlett J, Boulanger J, Prebtani A, Larochelle P, Leiter L, Jones C, Ogilvie R, Woo V, Kaczorowski J, Trudeau L, Petrella R, Hiremath S, Drouin D, Lavoie K, Hamet P, Fodor G, Gregoire J, Lewanczuk R,

Dresser G, Sharma M, Reid D, Lear S, Moullec G, Gupta M, Magee L, Logan A, Harris K, Dionne J, Fournier A, Benoit G, Feber J, Poirier L, Padwal R, Rabi D. Hypertension Canada's 2016 Canadian Hypertension Education Program guidelines for blood pressure measurement, diagnosis, assessment of risk, prevention, and treatment of hypertension. *Can J Cardiol.* 2016;32:569-588.

- 39 National Heart Lung and Blood Institute. Landmark NIH study shows intensive blood pressure management may save lives. <http://wwwnhlbinihgov/news/press-releases/2015/landmark-nih-study-shows-intensive-blood-pressure-management-may-save-lives> 2015.
- 40 The SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *New Engl J Med.* 2015;373:2103-2116.
- 41 Yusuf S, Lonn E, Pais P, HOPE-3 Investigators. Blood-pressure and cholesterol lowering in persons without cardiovascular disease. *New Engl J Med.* 2016;COI: 10.1056/NEJMoa1600177.
- 42 Flack J, Sica D, Bakris G, Brown A, Ferdinand K, Grimm R, Hall W, Jones W, Kountz D, Lea J, Nasser S, Nesbitt S, Saunders E, Scisney-Matlock M, Jamerson K, on behalf of the International Society on Hypertension in Blacks. Management of high blood pressure in blacks: An update of the International Society on hypertension in blacks consensus statement. *Hypertension.* 2010;56:780-800.
- 43 Myers M, Kaczorowski J, Paterson J, Dolovich L, Tu K. Thresholds for diagnosing hypertension based on automated office blood pressure measurements and cardiovascular risk. *Hypertension.* 2015;66:489-495.



- 44 Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A. 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Blood Press.* 2013;22:193-278.
- 45 Weber M, Schiffrin E, White W, Mann S, Lindholm L, Kenerson J, Flack J, Carter B, Materson B, Ram C, Cohen D, Cadet J, Jean-Charles R, Taler S, Kountz D, Townsend R, Chalmers J, Ramirez A, Bakris G, Wang J, Schutte A, Bisognano J, Touyz R, Sica D, Harrap S. Clinical practice guidelines for the management of hypertension in the community. *J Clin Hypertens.* 2014;16:14-26.
- 46 Pescatello L, MacDonald H, Ash G, Lamberti L, Farquhar W, Arena R, Johnson B. Assessing the existing professional exercise recommendations for hypertension: A review and recommendations for future research priorities. *Mayo Clinic Proceedings.* 2015;90:801-812.
- 47 Brook R, Appel L, Rubenfire M, Ogedegbe G, Bisognano J, Elliott W, Fuchs F, Hughes J, Lackland D, Staffileno B, Townsend R, Rajagopalan S. Beyond medications and diet: Alternative approaches to lowering blood pressure. A scientific statement from the American Heart Association. *Hypertension.* 2013;61:1360-1383.
- 48 Sabate E. Adherence to long-term therapies: Evidence for action. World Health Organization, 2003.
- 49 Rajpura J, Nayak R. Medication adherence in a sample of elderly suffering from hypertension: Evaluating the influence of illness perceptions, treatment beliefs, and illness burden. *J Manage Care Pharm.* 2014;20:58-65.

- 50 Hyre A, Krousel-Wood M, Muntner P, Kawasaki L, DeSalvo K. Prevalence and predictors of poor antihypertensive medication adherence in an urban health clinic setting. *J Clin Hypertens*. 2007;9:179-186.
- 51 Liao Y, Bang D, Cosgrove S, Dulin R, Harris Z, Stewart A, Taylor A, White S, Yatabe G, Liburd L, Giles W. Surveillance of health status in minority communities --- racial and ethnic approaches to community health across the U.S. (REACH U.S.). Risk Factor Survey, United States, 2009. *Adult and Community Health, National Center for Chronic Disease Prevention and Health Promotion 2011; Surveillance Summaries: 60(SS06)*.
- 52 Bethancourt H, Rosenberg D, Beatty T, Arterburn D. Barriers to and facilitators of physical activity program use among older adults. *Clin Med & Res*. 2014;12:10-20.
- 53 Franco M, Tong A, Howard K, Sherrington C, Ferreira P, Pinto R, Ferreira M. Older people's perspectives on participation in physical activity: A systematic review and thematic synthesis of qualitative literature. *Br J Sports Med*. 2015;Br J Sports Med doi:10.1136/bjsports-2014-094015.
- 54 Jefferis B, Sartini C, Lee I, Choi M, Amuzu A, Gutierrez C, Casas J, Ash S, Lennon L, Wannamethee S. Adherence to physical activity guidelines in older adults, using objectively measured physical activity in a population-based study. *BMC Pub Health*. 2014;14:2-9.
- 55 Pekmezi D, Barbera B, Bodenlos J, Jones G, Brantley P. Promoting physical activity in low income African Americans: Project LAPS. *J Health Dispar Res Pract*. 2009;3:82-91.

- 56 Richter DL, Wilcox S, Greaney M, Henderson K, Ainsworth B. Environmental, policy, and cultural factors related to physical activity in African American women. *Women & Health*. 2002;36:89-107.
- 57 Walcott-McQuigg J, Prohaska T. Factors influencing participation of African American elders in exercise behavior. *Public Health Nurs*. 2001;18:194-203.
- 58 Henderson K, Ainsworth B. A synthesis of perceptions about physical activity among older African American and American Indian women. *Am J Public Health*. 2003;93:313-317.
- 59 Inder J, Carlson D, Dieberg G, McFarlane J, Hess N, Smart N. Isometric exercise training for blood pressure management: A systematic review and meta-analysis to optimize benefit. *Hypertens Res*. 2016;39:88-94.
- 60 Boggia J, Thijs L, Hansen T, Li Y, Kikuya M, Bjorklund-Bodegard K, Richart T, Ohkubo T, Jeppesen J, Torp-Pedersen C, Dolan E, Kuznetsova T, Olszanecka A, Tikhonoff V, Malyutina S, Casiglia E, Nikitin Y, Lind L, Maestre G, Sandoya E, Kawecka-Jaszcz K, Imai Y, Wang J, Ibsen H, O'Brien E, Staessen J, on behalf of the International Database on Ambulatory blood pressure in relation to Cardiovascular Outcomes (IDACO) Investigators. Ambulatory blood pressure monitoring in 9357 subjects from 11 populations highlights missed opportunities for cardiovascular prevention in women. *Hypertension*. 2011;57:397-405.
- 61 Fagard R, Celis H, Lutgarde T, Staessen J, Clement D, De Buyzere M, De Bacquer D. Daytime and nighttime blood pressure as predictors of death and cause-specific cardiovascular events in hypertension. *Hypertension*. 2008;51:55-61.

- 62 Pickering T, Shimbo D, Haas D. Ambulatory blood pressure monitoring. *New Engl J Med.* 2006;354:2368-2374.
- 63 Sarafidis P, Bakris G. Resistant hypertension: An overview of evaluation and treatment. *J Am Coll Cardiol.* 2008;52:1749-1757.
- 64 Somani Y, Baross A, Levy P, Zinszer K, Milne K, Swaine I, McGowan C. Reductions in ambulatory blood pressure in young normotensive men and women after isometric resistance training and its relationship with cardiovascular reactivity. *Blood Press Monit.* 2017;22:1-7.
- 65 Stiller-Moldovan C, Kenno K, McGowan C. Effects of isometric handgrip training on blood pressure (resting and 24 h ambulatory) and heart rate variability in medicated hypertensive patients. *Blood Press Monit.* 2012;17:55-61.
- 66 Badrov M, Bartol C, Dibartolomeo M, Millar P, McNevin N, McGowan C. Effects of isometric handgrip training dose on resting blood pressure and resistance vessel endothelial function in normotensive women. *Eur J Appl Physiol.* 2013;113:2091-2100.
- 67 Badrov M, Horton S, Millar P, McGowan C. Cardiovascular stress reactivity tasks successfully predict the hypotensive response of isometric handgrip training in hypertensives. *Psychophysiol.* 2013;50:407-414.
- 68 McGowan C, Visocchi A, Faulkner M, Verduyn R, Rakobowchuk M, Levy AS, McCartney N, MacDonald M. Isometric handgrip training improves local flow-mediated dilation in medicated hypertensives. *Eur J Appl Physiol.* 2007;99:227-234.

- 69 McGowan C, Levy A, McCartney N, MacDonald M. Isometric handgrip training does not improve flow-mediated dilation in persons with normal blood pressure. *Clin Sci*. 2007;12:403-409.
- 70 Millar P, Bray S, MacDonald M, McCartney N. The hypotensive effect of isometric handgrip training using an inexpensive spring handgrip training device. *J Cardiopulm Rehabil Prev*. 2008;28:203-207.
- 71 Millar P, Levy A, McGowan C, McCartney N, MacDonald M. Isometric handgrip training lowers blood pressure and increases heart rate complexity in medicated hypertensive patients. *Scand J Med Sci Sports*. 2013;23:620-626.
- 72 Ray C, Carrasco D. Isometric handgrip training reduces arterial pressure at rest without changes in sympathetic nerve activity. *Am J Physiol*. 2000;279:H245-H249.
- 73 Taylor A, McCartney N, Kamath M, Wiley R. Isometric training lowers resting blood pressure and modulates autonomic control. *Med Sci Sports Exerc*. 2003;35:251-256.
- 74 Hanik S, Badrov M, Stiller-Moldovan C, DiBartolomeo M, Millar P, Clarke D, McNevin N, McGowan C. Isometric handgrip training induces equal blood pressure reductions in normotensive males and females without influencing heart rate variability. *Can J Cardiol*. 2012;28:S118-S119.
- 75 Wiley R, Dunn C, Cox R, Hueppchen A, Scott M. Isometric exercise training lowers resting blood pressure. *Med Sci Sports Exerc*. 1992;24:749-754.
- 76 Hanik S, Somani Y, Baross A, Swaine I, Milne K, McGowan C. The mechanism underlying the hypotensive effect of isometric handgrip training: Is it cardiac output mediated? *Appl Physiol Nutr Metab*. 2014;39:S21.

- 77 Somani Y, Hanik S, Malandruccalo A, Freeman S, Caruana N, Badrov M, Baross A, Swaine I, Milne K, McGowan C. Isometric handgrip (IHG) training-induced reductions in resting blood pressure: Reactivity to a 2-minute handgrip task identifies responders and non-responders in young normotensive individuals (LB661). *The FASEB Journal*. 2014;28:LB661.
- 78 Somani Y, Hanik S, Badrov M, Baross A, Swaine I, Milne K, McGowan C. Can blood pressure reactivity to a 2-minute isometric handgrip task predict reductions in ambulatory blood pressure? *Appl Physiol Nutr Metab*. 2014;39:S43.
- 79 Badov M, Freeman S, Zokvic M, Millar P, McGowan C. Isometric exercise training lowers resting blood pressure and improves local brachial artery flow-mediated dilation equally in men and women. *Eur J Appl Physiol*. 2016;116:1289-1296.
- 80 Millar P, McGowan C, Cornelissen V, Araujo C, Swaine I. Evidence for the role of isometric exercise training in reducing blood pressure: Potential mechanisms and future directions. *Sports Med*. 2014;44:345-356.
- 81 Millar P, Bray S, McGowan C, MacDonald M, McCartney N. Effects of isometric handgrip training among people medicated for hypertension: A multilevel analysis. *Blood Press Monit*. 2007;12:307-314.
- 82 Peters P, Alessio H, Hagerman A, Ashton T, Nagy S, Wiley R. Short-term isometric exercise reduces systolic blood pressure in hypertensive adults: Possible role of reactive oxygen species. *Int J Cardiol*. 2006;110:199-205.
- 83 Owen A, Wiles J, Swaine I. Effect of isometric exercise on resting blood pressure: A meta analysis. *J Hum Hypertens*. 2010;24:796-800.

- 84 Carlson D, Dieberg G, Hess N, Millar P, Smart N. Isometric exercise training for blood pressure management: A systematic review and meta-analysis. *Mayo Clin Proc.* 2014;89:327-334.
- 85 McGowan C, Levy A, Millar P, Guzman J, Morillo C, McCartney N, MacDonald M. Acute vascular responses to isometric handgrip exercise and effects of training in persons medicated for hypertension. *Am J Physiol Heart Circ Physiol.* 2006;291:1797-1802.
- 86 Millar P, MacDonald M, Bray S, McCartney N. Isometric handgrip exercise improves acute neurocardiac regulation. *Eur J Appl Physiol.* 2009;107:509-515.
- 87 Araujo C, Duarte C, Gonzalves F, Medeiros H, Lemos F, Gouveia A. Hemodynamic responses to an isometric handgrip training protocol. *Arq Bras Cardiol.* 2011;97:413-419.
- 88 Carlson D, McFarlane J, Dieberg G, Smart N. Rate pressure product responses during an acute session of isometric resistance training: A Randomized Trial. *J Hypertens Cardiol.* 2017;2:1-11.
- 89 Badrov M, Millar P, McGowan C. Role of isometric handgrip training in the management of hypertension: Insights from cardiovascular stress reactivity testing. *Crit Revs Phys Rehabil Med.* 2010;22:13-28.
- 90 Millar P, Bray S, MacDonald M, McCartney N. Cardiovascular reactivity to psychophysiological stressors: Association with hypotensive effects of isometric handgrip training. *Blood Press Monit.* 2009;14:190-195.

91 Berenson G, Chen W, DasMahapatra P, Fernandez C, Giles T, Xu J, Srinivasan S. Stimulus response of blood pressure in black and white young individuals helps explain racial divergence in adult cardiovascular disease: The Bogalusa Heart Study. J Am Soc Hypertens. 2011;5:230-238.



## **Figure Legend**

Figure 1. Algorithm for implementing alternative approaches in clinical practice (Brook R, Appel L, Rubenfire M, Ogedegbe G, Bisognano J, Elliott W, Fuchs F, Hughes J, Lackland D, Staffileno B, Townsend R, Rajagopalan S: Beyond medications and diet: Alternative approaches to lowering blood pressure. A scientific statement from the American Heart Association. *Hypertension* 2013;61:1360-1383). Reprinted with permission from Wolters Kluwer Health, Inc.