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Should We Treat Hypertension in Patients 80 Years of Age and Older? Results from the HYVET Trial

By Luc Poirier

Hypertension is an extremely prevalent disease and continues to be a major risk factor for cardiovascular mortality and morbidity around the world. Unlike diastolic blood pressure (BP) which decreases in patients' mid 50s, systolic BP increases linearly through life, and this elevation is closely correlated to the occurrence of stroke, coronary artery disease, heart failure and death due to cardiovascular events.

The benefits of antihypertensive treatment are well established in most age groups. However, some meta-analyses of large cohorts tried to demonstrate that benefits of treatment decrease with age. In one study, compared to a normal BP, a 180mmHg systolic BP was associated with a risk 16 times greater in the group aged 50-59 years and three times greater in subjects aged 80-89 years. Another study involving subjects aged 80 years or older suggested a 14% increase in the risk of mortality ($p = 0.05$) despite a 36% reduction in the risk of stroke. Finally, numerous morbidity/mortality studies describing the advantages associated with the treatment of isolated systolic hypertension could not demonstrate clear benefits in the group of subjects aged 80 years or older, perhaps because of insufficient sample size. Thus, it appeared that benefits of treatment in patients aged 80 years or older remained uncertain.

The Hypertension in the Very Elderly Trial (HYVET), carried out in Europe, Australia, China and Tunisia, has recently been published. A total of 3,845 subjects aged 80 years or older (mean age 83.6 years) having sustained systolic BP of ≥ 160 mmHg a diastolic BP < 110 mmHg (mean BP 173.0/90.8 mmHg) were randomized to either a diuretic (sustained-release indapamide at a dose of 1.25 mg per day, $n = 1,933$), or matching placebo ($n = 1,912$). An angiotensin converting enzyme (ACE) inhibitor (perindopril at a dose of 2 mg to 4 mg per day) was added if the BP target of $< 150/80$ mmHg was not achieved. The primary endpoint was fatal or nonfatal stroke.

Of note, despite the fact that it was supposed to end in 2009, the study was terminated prematurely in August 2007 due to a significant 21% reduction ($p = 0.02$) in the risk of mortality from all causes in favour of the group receiving active treat-

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Hypertension in the Very Elderly

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ment. After a median follow up of 1.8 years, active treatment resulted in additional reductions of systolic and diastolic BP of 15.0/6.1 mmHg vs. placebo. More than 48% of patients in the active-treatment group achieved the target BP, which was significantly more than seen in the placebo group (19.9%). The reduction of BP was associated with a decreased relative risk of fatal and nonfatal strokes by 30% ($p = 0.06$), of mortality from stroke by 39% ($p = 0.05$), of mortality from cardiovascular causes by 23% ($p = 0.06$) and the incidence of heart failure by 64% ($p < 0.001$). The treated group also presented significantly fewer serious adverse events than the placebo group ($n = 358$ vs. 448, $p < 0.001$).

When considering this study, it is possible to draw conclusions from the results that undermine some apprehensions based on previous studies. One remembers that the pilot phase of the HYVET trial was in line with other meta-analyses that suggested a reduction in the incidence of stroke but an increased mortality from all causes. Based on the full HYVET trial results, it now appears clear that the treatment of hypertension lends as much benefit in the population of subjects called 'very old' while showing an unexpected significant reduction in total mortality.

However, the main hypothesis—to demonstrate a significant risk reduction for fatal and nonfatal strokes by the active treatment—was not verified. As the study was terminated before its planned term, a sufficient number of events was not reached. Nevertheless, a clear trend can be observed with a borderline threshold of statistical significance ($p = 0.06$). From the results, we can predict that 94 patients will need to be treated for two years in order to prevent one stroke. It is well known that the risk of mortality from stroke increases with age and is strongly correlated with the BP level. This aspect of the study concerned with stroke prevention assumes a great importance, since the rate of death from stroke was decreased by 45% with active treatment vs. placebo. The HYVET trial thus reinforces the benefits of treating hypertension by demonstrating a reduction of mortality from all causes, but also mortality from stroke.

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Canada Chair in Hypertension Prevention and Control

1: Initiatives to Improve Public and Patient Education on Hypertension and to Prevent Hypertension by Reducing Dietary Sodium

By Norm RC Campbell and Solina Omer
In the early 2000s, Blood Pressure Canada, the Canadian Hypertension Society and the Canadian Institute for Health Research developed a proposal to fund a leadership position for prevention and control of hypertension in Canada. The project was co-funded by sanofi-aventis Canada, the Canadian Hypertension Society and the Canadian Institute for Health Research.

As the recipient of the initial five-year funding, Norm Campbell proposed four major initiatives: 1) increase public and patient self-efficacy to prevent and manage hypertension; 2) decrease the prevalence and incidence of hypertension by reducing dietary sodium; 3) increase the interdisciplinary dissemination and partnership of the Canadian Hypertension Education Program (CHEP) and develop a CHEP business plan; and 4) develop a national surveillance program for hypertension.

The initiatives have received strong support. The hypertension community, the Public Health Agency of Canada, the Heart and Stroke Foundation of Canada, some provinces, and many Canadian healthcare professional and scientific organizations have implemented programs that address the initiatives. In this report, we discuss progress made on the first two initiatives in the first two years of the Hypertension Chair, noting that many of the activities are the work of, and led by, other like-minded individuals and organ-

izations. The second two initiatives will be the focus of a later report.

Improving Self-efficacy of the Public to Prevent Hypertension and of Patients with Hypertension to Manage Hypertension

A multi-pronged approach was developed by Blood Pressure Canada and partner organizations to sustain a public and patient hypertension-education program. The approach uses development of a variety of educational tools specifically for different public and patient audiences (Table 1) and broad dis-

semination of material through healthcare professionals, healthcare-professional journals, lay-public journals, and via online resources (www.hypertension.ca, www.heartandstroke.ca/BP), specifically looking for potential opportunistic media releases based on new research as well as the annual World Hypertension Day releases. The different tools are available online at www.hypertension.ca. Train-the-

Trainer sessions are used to train healthcare professionals to use tools for public and patient education. Blood Pressure Canada has developed a Task Force with 24 interdisciplinary members to aid the development, dissemination, and evaluation of tools to enhance public and patient self-efficacy. Multiple partner organizations have contributed significantly. The Heart and Stroke Foundation, for example, has developed a sophisticated website to provide individualized advice and tracking for patients with hypertension (www.heartandstroke.ca/BP). Of note, provincial Heart and Stroke Foundations

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Table 1
High-quality Hypertension Resources for Your Patients

Resource	Content	Availability
2008 patient recommendations	<ul style="list-style-type: none"> • Blood-pressure basics • Blood-pressure targets • Lifestyle changes • Salt intake • Diagnosis of hypertension • Home monitoring • Medication adherence 	www.hypertension.ca www.heartandstroke.ca
Online personalized BP plan	<ul style="list-style-type: none"> • Self-assessment tool: <ul style="list-style-type: none"> – to identify risk of heart disease and stroke – to provide tips, advice and support to help prevent or control high blood pressure – to create a personalized action plan for healthy living 	www.heartandstroke.ca/bp
World Hypertension Day	<ul style="list-style-type: none"> • Brochures and posters • Public awareness campaigns in most Canadian cities 	www.worldhypertensionday.org
DASH diet	<ul style="list-style-type: none"> • Facts about the DASH Eating Plan • Healthier eating with DASH • Getting started with DASH • Heart-healthy recipes • Tips on how to make healthier meals • Award about tats 	www.nhlbi.nih.gov/ohp/prevent/d_eating/d_eating.htm
Canada's Food Guide	<ul style="list-style-type: none"> • Food Guide basics: choosing foods • Using the Food Guide and choosing foods • Maintaining healthy habits 	www.hc-sc.gc.ca/food/affair/food-guide/dimention/index_e.html
Dietitians of Canada	<ul style="list-style-type: none"> • Eat well, live well: <ul style="list-style-type: none"> – tips, resources, tools – EATracker 	www.dietitians.ca
Online health and fitness calculators	<ul style="list-style-type: none"> • Body mass index • Waist:hip ratio • Smoking cost • Optimal weight calculator 	www.healthtoolsforlife.com/health-fitness/

With permission of Blood Pressure Canada.

Pressure Canada has led the development of a national survey to examine knowledge, attitudes, practices, sources of information, and barriers to care. The survey results will be representative of Canadians with hypertension and are expected in 2009-2010. The survey will be repeated periodically to monitor progress and assess knowledge gaps.

Particular projects of interest include the development of annually updated public recommendations for the management of hypertension, a public-awareness DVD, a standardized slide presentation for use by healthcare professionals in educating the public, and a resource centre for community-based hypertension proj-

ects (www.hypocanada.net/youchange.net/). A comprehensive patient-education DVD is planned. Education of politicians is an important part of the program and several meetings have been held with politicians and government officials. It is expected that a more informed public will not only aid in the detection and management of hypertensive individuals, but will also encourage policy changes required to prevent hypertension.

Reducing the Prevalence of Hypertension by Decreasing Salt Additives in Food

Hypertension is expected to increase in prevalence dramatically throughout the

world and affect 30% of the adult population.⁴ Awareness, treatment and control of hypertension have dramatically improved in Canada.⁵ To avoid the need to treat very large proportions of the population with drugs, a concerted effort to prevent hypertension is required. A mandate of the Hypertension Chair is to lead an effort to reduce dietary sodium. Well recognized scientific groups have concluded that the current levels of dietary sodium are unsafe and cause hypertension.⁶ Canadian policy has called for reduced dietary sodium for several decades but the lack of a concerted health-sector lobby has hindered efforts to reduce dietary sodium in Canada and around the world.



Initial efforts were to increase the prominence of sodium in Canada's Food Guide to Healthy Eating. A lobby by 10 major national healthcare and scientific organizations was organized. The Food Guide was revised to increase the prominence of dietary sodium as a health issue of equal importance to sugar and saturated fats (www.hc-sc.gc.ca/fo/food/guide-aliments/index_e.html). A strategic planning committee with representation from seven national organizations was developed to form strategies for government and food-industry action. This committee has assisted Blood Pressure Canada in the development of a policy statement calling on the Canadian government and food industry to reduce sodium additives to food and for healthcare-professional organizations to educate Canadians and their membership about the risks. The policy statement (available at www.hypertension.ca/BFC) called for specific actions with timelines by government and the food sector and was signed by most major national healthcare professional and scientific organizations that are involved in cardiovascular disease in Canada. The Dieticians of Canada organized a meeting of the food sector, government and health sector to discuss issues around dietary sodium which resulted in an informal agreement to collaborate to reduce sodium additives to food. A request was made by the health and food sector for government oversight of the process to reduce dietary sodium. The Canadian government announced the formation of an inter-sectoral workgroup that has now met twice, conceptually agreed on terms of reference and is performing background data-finding to support the effort. The strategy to reduce sodium additives and educate the public is the next step for the workgroup. Many of the organizations that signed the policy statement have organized clinical and scientific sessions at regional and national meetings and/or published infor-

mation to their membership on dietary sodium. Specific studies have been conducted to estimate the impact on hypertension and cardiovascular disease of high dietary sodium in Canada.⁴⁵ Notably, a reduction in dietary sodium is estimated to reduce hypertension by about 30%, cardiovascular disease by almost 9% and healthcare costs by roughly \$2 billion per year.

Blood Pressure Canada has formed an 18-member workgroup to develop tools to educate the public and healthcare professionals about the health risks of sodium. This has resulted in the development of several educational tools and publications made available to healthcare professionals and the public (available at www.hypertension.ca), as well as multiple media releases (through the Canadian Stroke Network and the Heart

Blood Pressure Canada plans to independently monitor and report on the sodium content of specific foods that are high in sodium. Around the world, there has been increased interest in reducing sodium additives to food. The reduction, however, will take many years and sustained oversight and interest from the health community.

Some Thoughts

The last two years have laid the foundation for a comprehensive, sustained public- and patient-education program on hypertension and for a reduction in dietary sodium in Canada. Much work remains to ensure the programs are sustainable and meet the comprehensive needs of the Canadian population. It is hoped that the development of the National Cardiovascular Strategy will as-

A mandate of the Hypertension Chair is to lead an effort to reduce dietary sodium. Well recognized scientific groups have concluded that the current levels of dietary sodium are unsafe and cause hypertension. Canadian policy has called for reduced dietary sodium for several decades but the lack of a concerted health-sector lobby has hindered efforts to reduce dietary sodium in Canada and around the world.

and Stroke Foundation of Canada). A grant from PHAC will allow the development of comprehensive summaries and educational material on dietary sodium.

Many groups have become active in the effort. Notably, the Canadian Stroke Network has recently launched a sodium website to consolidate information on sodium (www.sodium01.ca) and provincial governments are now considering regulations to limit high-sodium foods within their jurisdictions. Although several food companies reported starting to reduce sodium additives to food, objective monitoring is required to ensure there is a broad reduction in sodium additives to food.

assist in sustaining successful programs like those outlined. Over the past two years, hypertension has gained prominence in many organizations and this has resulted in several important initiatives. In particular, there has been a substantive increase in hypertension activity by the Heart and Stroke Foundation of Canada, the provincial Heart and Stroke Foundations (particularly in Ontario), the Canadian Stroke Network, the Public Health Agency of Canada, Health Canada, Statistics Canada, and provincial governments. Healthcare-professional organizations, especially the Canadian Pharmacists Association, the Canadian Council of Cardiovascular Nurses and the College of Family

The 19th Annual Scientific Meeting of the Ontario Hypertension Society

By Robert Gros

The 19th Annual Scientific Meeting of the Ontario Hypertension Society (OHS) was held May 2-4, 2008 at the Nottawasaga Inn and Conference Centre in Alliston, Ontario. The meeting started on Friday afternoon with a well attended poster session, where trainees and faculty from the participating universities and research institutes presented their latest research findings.

Saturday morning kicked off with a Clinical Update in Hypertension which was presented by Dr. Sheldon Tobe from Sunnybrook Hospital in Toronto. This was followed by oral trainee presentations given by Yohan D'Souza (Supervisor: Brian Bennett, Queen's University), Topher Morris (Robert Gros and Ross Feldman, Robarts Research Institute/University of Western Ontario), Augusto Montezano (Rhian Touyz, University of Ottawa), Stephane Bouque (Michael Adams, Queen's University), Carlo Cifelli (Scott Heximer, University of Toronto) and Theodor Small (Geoffrey Pickering, Robarts Research Institute/University of Western Ontario). The morning oral sessions ended with a State-of-the-Art Lecture which was presented by Dr. Peter Backx, from the University of Toronto and was entitled "The Role of Cl⁻ Currents in Pulmonary Smooth Muscle Cell Proliferation: Implication on Pulmonary Hypertension." The oral sessions were followed by poster session II and lunch.

The afternoon oral sessions started off with a second State-of-the-Art Lecture which was presented by Dr. Peter Liu, University of Toronto and entitled "Predict, Prevent and Personalize: Ge-

nomie and Proteomic Approaches to Cardiovascular Medicine." This was followed by more oral trainee presentations by Danae Benjamin (Supervisor: Karji Nakatsu, Queen's University), Matthew Frontini (Geoffrey Pickering, Robarts Research Institute/University of Western Ontario), Steven Gu (Scott Heximer, University of Toronto), Johanna Harman (Michael Adams, Queen's University), Marina Komolova (Michael Adams, Queen's University) and Alvaro Yogi (Rhian Touyz, University of Ottawa). These proceedings were followed by what has now become an annual tradition: the Faculty vs. Trainee Basketball Challenge. For the first time, the long and heated battle ended up in a 50-50 tie.

The basketball game/free time was followed by dinner and the presentation of awards for most outstanding oral and poster trainee presentations. The competition was again very tough this year and this made judging the oral and poster presentations extremely difficult. The best-presentation award in the BSc/MSc category was a tie between Tina Maio (Queen's University, supervisor Michael Adams) and Lisa Pritchard (Queen's University, supervisor Donald Maurice). The best-presentation award in the PhD category was presented to Theo Small (Robarts Research Institute/University of Western Ontario, supervisor Geoff Pickering), and the best presentation in the post-doctoral category was presented to Augusto Montezano (University of Ottawa, supervisor Rhian Touyz). We thank all those who participated in judging the trainee poster and oral presentations for their time and effort and the interaction and dis-

ussion they provided for the presenting trainees.

Sunday morning saw the final State-of-the-Art Lecture, which was presented by Dr. Duncan Stewart from the Ottawa Health Research Institute and entitled "From Genes to Schemes: How Insight Into the Genetic Basis of Pulmonary Hypertension Can Lead to New Therapies." This was followed by a workshop presented by Dr. Robert Gros (Robarts Research Institute/University of Western Ontario), entitled "Cell in Motion: Single Cell Assessment of Vascular Smooth Muscle Cell Contractility." Following these Sunday-morning sessions, we bid our farewells over brunch.

This meeting would not have been possible without the continued educational support of the Principle Program sponsor, Pfizer Canada, and the Supporting Program sponsors AstraZeneca, Bayer HealthCare, Boehringer Ingelheim, and Merck Frost. In addition, this meeting would also not be possible without the excellent organizational support provided by Kathy Christmas. Lastly, the planning for the 20th Annual Spring Meeting of the OHS has begun. The co-chairs for the meeting will be Drs. Ross Feldman and Robert Gros from the Robarts Research Institute/University of Western Ontario. Please watch for the announcement of the OHS annual meeting in early 2009, and we hope to see you there.

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Physicians of Canada, have markedly increased their involvement in hypertension-related activities, largely through Blood Pressure Canada and CHEP. The Canadian Hypertension Society has increased its role in prevention and clinical management of hypertension, providing more content at the annual meeting, resources, collaboration and visibility.

The marked increase in independent activities comes with a loss of ability to coordinate and lead. Nevertheless, the Chair recognizes that the resulting increase in capacity is required for prevention and control of hypertension on

a national level. Recently, it has become evident that Ontario has the lowest prevalence of hypertension in the developed world and has by far the highest rate of treatment and control. Other data indicate these findings are likely to reflect those of the Canadian population. To continue to benefit the health of Canadians, programs must continue to evolve to stay ahead of and take advantage of the rapid and profound changes occurring in healthcare in Canada. The future is challenging but bodes well to prevention and control of hypertension.

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Hypertension in the Very Elderly

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Almost 75% of subjects randomized to active treatment received the diuretic + ACE inhibitor combination. Recall that earlier studies in older subjects with systolic hypertension showed that diuretics were beneficial unless hypokalemia or arrhythmias ensued. In HYVET, the diuretic + ACE inhibitor combination could have avoided these deleterious effects and could explain the reduction in total mortality observed in this study compared to previous studies. Active treatment with a diuretic and an ACE inhibitor could also have reduced the risk of heart failure, since the combination has been proven efficacious in trials of patients with this condition.

The HYVET-COG study, aimed at identifying a reduction in the incidence

of dementia in subjects enlisted in the HYVET trial, was also recently published. Evaluation of cognitive function using the Mini Mental State Examination (MMSE) hypothesized a 33% reduction of risk in favor of active treatment. However, after a median follow-up period of 2.2 years, no significant difference was observed between the two study groups for all types of dementia evaluated.

Do the results from the HYVET trial allow us to say that it is beneficial and safe to treat arterial hypertension in subjects aged 80 years or older? The results show benefits in reduction of events like total mortality, mortality from stroke and heart failure despite the absence of gains on the risk of dementia. Moreover, the study underlines previous studies that suggested treatment caused increased total mortality. This study allows us to recommend treatment of

hypertension in subjects aged 80 years or older by aiming at a conservative BP target of < 150/80 mmHg. However, since the overall health of subjects in HYVET seems to have been better than that of the general population, we must very carefully apply treatment to more vulnerable very elderly hypertensive patients with a more precarious state of health.

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Readers of *Hypertension Canada* are invited to visit the CHS homepage at www.hypertension.ca/home and submit suggestions on its improvement.

