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IN THIS ISSUE

FROM THE EDITOR

The ISH meeting 2022 in Kyoto – We are coming soon!

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Editor

Dear reader,

It is again a pleasure for me to present a new issue of Hypertension News (Opus 70) to you. The Newsletter has now served as the ISH's source of news and scientific exchange for almost 20 years. As we reach our 70th issue, we have asked the Deputy editor Dylan Burger to look back on the history of this Society flagship, its growth, and how that has shaped our current efforts (see pages 4-6). In short, there has been a dramatic expansion in content and in the reach with an increase from below 1,000 views per issue to 6,000-10,000 downloads today.

Our heavily read "Learning the Ropes" feature, first introduced in March 2019, has allowed for some of the most distinguished leaders in the hypertension field to introduce key topics in hypertension research and management to our readership. This expansion has, of course, required growth of our editorial board. Our current team with eight scientists from different parts of the world is our largest, and most diverse to date and I am confident that we will continue to produce a letter worth reading. In Dylan Burger's review, you will also find a brief biography of the members of the editorial board. Our board members have been selected so they cover most types of hypertension research and management.

Very few studies have investigated the effects of initiating, increasing, decreasing, or stopping antihypertensive treatment in the very old (≥85 years). We have therefore chosen this topic for the "Learning the ropes" section and you will find four papers written by experts in the field in this issue (see pages 11-26): Hiromi Rakugi, Osaka, Japan, Paul Whelton, New Orleans, USA, Kazem Rahimi, Oxford, UK, and Bo Carlberg, Umeå, Sweden. It is reasonable to assume that there is a benefit from treatment in the very old but increasing presence of co-morbidities and side effects, however, will affect the risk/benefit ratio.

The burden of hypertension remains one of the major public health concerns in Africa, where awareness, treatment, and control levels all remain lower than in many other countries. This calls for intensification of research on accessible and affordable treatment options, and implementation of strategies aimed at improving hypertension management. In this issue of Hypertension News, we have expanded this section, (introduced by Lebo Gafane-Matemane) with two papers, one written by Neusa Jessen and Albertino Damasceno, Mozambique and another by Tiny Masupe, Botswana (see pages 42-46). There is also a lovely report from Robert Fagard, Loewen (see pages 39-41), entitled "My 10 years of ISH activities in Africa – 2005 to 2015", which I strongly recommend you read! Maybe more education in Africa is something the new ISH Council (2022-24) should consider!

Moreover, in this issue there are two papers I recommend you top read: First, an interesting "Institute Focus" from the Laval University in Québec City, Canada (see pages 27-31) written by Mohsen Agharazii and co-workers and second, a paper by Alta Schutte, Sydney, Australia (see pages 35-37) on paracetamol treatment and CV risk.

Continued on next page.

You will find a final update on the 2022 ISH meeting in Kyoto by Professor Hiroshi Itoh on pages 32-33. The meeting will be a hybrid event, due to the ongoing COVID-19 situation in Japan and elsewhere. The members of the Local Organising Committee are getting ready to welcome everyone and their efforts should be commended. The help they give with the papers needed (quite a lot) for a business visa to Japan is considerable and Juko is doing a remarkable job. I understand that delegates from the US and Canada can now apply online, whereas many of us have to visit a Japanese embassy in person.

Finally, let me thank my talented Deputy editor Dylan Burger, the ISH Secretariat, and all the members of the editorial team for their endless support and help! Thanks also to all the authors for their valuable contributions.

Have a good read!
Lars H Lindholm

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From the Executive Committee - News highlights

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Activity always increases as we approach our Scientific Meeting and this year is no different.

First and foremost, let me congratulate **Bryan Williams** on his selection as President-Elect of the ISH. Bryan has served as a member of the ISH Council since 2018 and is the current Secretary of the society. He is a distinguished clinician and scientist and experienced leader who is well suited to continue to raise the profile of our organization. I look forward to working with him. Bryan will take up his role as 26th President of the ISH at the conclusion of the Kyoto meeting.

Speaking of the Kyoto meeting, this is fast approaching. As outlined by Hiroshi Itoh elsewhere in this issue this will be a hybrid meeting, however I am looking very much forward to attending in person. There are a lot of questions surrounding attendance in person but it really isn't much more complicated than any other country that requires a visa to attend. The ISH2022 committee has done an excellent job of providing information for those who want to attend in person which, for most countries, is as simple as booking your flight and accommodation, obtaining a visa (with support from the organizing committee), a pre-departure PCR test, and use of the MySOS App to collate your vaccination and test result information. Having been through the process I have to say that it was quite simple.

Scientifically, the past few months have also been notable for the ISH as we have published two position papers in the Journal of Hypertension.

The first "Virtual management of hypertension: lessons from the COVID-19 pandemic: International Society of Hypertension position paper endorsed by the World Hypertension League and European Society of Hypertension" (DOI: 10.1097/HJH.0000000000003205) identifies key modalities for the virtual assessment and management of hypertension and provides recommendations based on consensus of an international writing group.

The second "Bedtime dosing of antihypertensive medications: systematic review and consensus statement: International Society of Hypertension position paper endorsed by World Hypertension League and European Society of Hypertension" (DOI: 10.1097/HJH.0000000000003240) was published in late August and is a response to controversy on the timing of antihypertensive medications.

Third, a meta-analysis of randomized controlled trials on use of renin-angiotensin system inhibitors (RASi) in patients with COVID-19 was released just this week (DOI: 10.1161/JAHA.122.026143). The study, led by ISH Immediate Past-President Aletta Schutte provides strong evidence that RASi can be used safely in patients with COVID-19.

These position statements showcase the ISH as a global leader in hypertension care, management and research. Further statements are planned in the coming year so stay tuned.

Finally, and perhaps most significantly, the ISH recently signed a memorandum of understanding with the World Health Organization (WHO) to work together on joint projects over the next five years. This represents a key step in the process of becoming a WHO non-State actor which would facilitate greater influence over global health policy. The ISH has a long history of partnership with WHO including joint hypertension guidelines and it is exciting to see us strengthening this relationship once more. The first fruits of this partnership will be seen with a joint WHO-ISH session at the 2022 Scientific Meeting. Be sure to attend this session.

Until next time,

Dylan Burger
Chair, ISH Communications Committee

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Hypertension News: A Brief History

Hypertension News has served as the ISH's source of news and scientific exchange for almost 20 years. As we reach our 70th issue, the editorial board asked me to take a look back on the history of the society's flagship newsletter, its growth, and how that has shaped our current efforts.

The newsletter was first published in September of 2003. It was developed by current editor-in-chief Lars Lindholm with founding advisory board members Michael Alderman, Susan Davenport, Serap Erdine, Anna Dominiczak, Giuseppe Mancia, and Lawrie Beilin. From its inception the newsletter focused on accessibility (it was shared in Word '95 format due to its ubiquity at the time) and diverse coverage with contributions from Australia, Italy, South Africa, Brazil, and Spain in the first issue. It grew into a key chronicle of ISH activities, highlighting every scientific meeting, position statement, guideline, and major activity of the ISH since our 2004 meeting in São Paolo. It has also served as a mechanism for promoting activities of ISH members and partners through features such as our "Institute Focus". This first began in 2006 with an overview of the BHF Glasgow Cardiovascular Research Centre and continues to this day. The Institute Focus provides exposure for ISH members and their home institutions while also serving as a useful resource for trainees and investigators who are new to the field.

In December 2006, Lawrie Beilin took on the role of editor of Hypertension News for two years, coinciding with Lars Lindholm's term as ISH president. He oversaw growth of the newsletter both in terms of content and in improvements to its visual presentation. Central to these improvements was the addition of Helen Horsfield of the ISH secretariat to the Hypertension News team. She played a key role in the modernization and expansion of Hypertension News in the ensuing years. In October 2008 Lars Lindholm returned to his role as Editor-in-Chief. His first issue back was notable because it was the first to introduce new council members to the society through brief introductory profiles. To me, this has always been an important feature because it familiarizes our members with their representation, makes the council more accessible, and serves as a historical reference.

Another major change to Hypertension News came in December 2010 when Bo Carlberg joined the editorial board as co-editor. This is notable because Bo was the Chair of the newly established ISH New Investigator Committee and his involvement led to an increased focus on ISH New Investigators in Hypertension News. Hypertension News had always been a platform for New Investigators prior to this (I note that Issue 5 actually includes a "New Investigator Perspective" from our current President Maciej Tomaszewski), however the attention to early career researchers really came to the forefront with the rise of the NIC under Stephen Harrap's presidency and it continues to this day with our New Blood content.

In June of 2014 I joined the Hypertension News editorial board; initially contributing with "Hot off the Press" basic science content and NIC updates. Eventually I was invited to serve as Deputy Editor-in-Chief under an expanded editorial board with Thomas Kahan, and Maciej Tomaszewski (then ISH Secretary). This editorial team was responsible for obtaining ISSN registration and CrossRef membership (which allows Hypertension News to assign DOIs to its scientific content). Again this was a major step forward for Hypertension News because it allows us to better track our readership, reward authors for their contributions, and promote newsletter content on social media. The result has been a dramatic expansion in content and in the reach of our newsletter with an increase

from ~1000 views per issue to 6000-10000. We have added a dedicated section for Early Career Researchers and features such as "African Voices". Our heavily read "Learning the Ropes" feature, first introduced in March 2019, has allowed for some of the foremost leaders in hypertension to introduce key topics in hypertension research and management to our readership. This expansion has, of course, required growth of our editorial board as well. Our current team is our largest, and most diverse to date and I am confident that we will continue to produce a tremendous product under Lars Lindholm's leadership. Below you will find a brief biography of our editorial board members. Our team aims to be representative and develop content that is of interest to all ISH members, however we also welcome suggestions and/or contributions from any ISH member. Please reach out to myself (dburger@uottawa.ca), or the ISH secretariat (membership@ish-world.com) should you wish to contribute.

Dylan Burger - dburger@uottawa.ca

Editorial board members

Lars H Lindholm (Editor-in-Chief), MD, PhD.

Professor senior, Department of Public Health and Clinical Medicine, Umeå University, Sweden. Distinguished fellow of the ISH. Lars Lindholm started Hypertension News in 2003 and has edited all issues except the ones published when he was President of ISH in 2006-8. His main interest in hypertension concerns high blood pressure and its cardiovascular risks as well as pros and cons with different types of blood pressure lowering therapy, especially beta-blockers as first-line therapy.

Dylan Burger (Deputy Editor), PhD, ISHF

Senior Scientist and Associate Professor at the Ottawa Hospital Research Institute, University of Ottawa, Canada. He joined Hypertension News in June 2014 and currently serves as deputy editor. He is also the current Chair of Communications for the ISH. His research interests are in extracellular vesicles as markers and mediators of vascular and renal injury in diabetes and hypertension.

Lebo F Gafane-Matemane, PhD, ISHF

Associate Professor of Physiology, Hypertension in Africa Research Team, North-West University, South Africa. Lebo joined Hypertension News in September 2021 and is currently leading the new section on African Voices. She is also a member of the ISH Mentorship and Training Committee since October 2020. Her main research interest is the Renin-Angiotensin-Aldosterone System and cardiovascular risk in populations of African ancestry.

Continued on next page.

Thomas Kahan, MD, PhD, FESC, FAHA.

Professor of medicine at Karolinska Institutet, Stockholm (Sweden) and senior consultant in cardiology at Danderyd University Hospital, Stockholm (Sweden) where he has long been head of the Cardiovascular Risk Assessment Unit, an European Society of Hypertension Centre of Excellence. Current (2020-22) Chair of the European Society of Cardiology Council on Hypertension, a Board Member of the European Society of Hypertension, and the current (2022) President of the International Society on Cardiovascular Pharmacotherapy. Main research areas are neurohormonal mechanisms in the control of blood pressure and cardiac function, with a focus on structural myocardial and vascular changes, and neuroendocrine mechanisms in heart failure. Other areas of interest are cardiovascular risk assessment and prevention.

Charlotte Mills, PhD.

A Hugh Sinclair Assistant Professor in Human Nutrition from Department of Food and Nutritional Sciences, University of Reading, UK. Charlotte is a member of the ISH New investigator Committee and joined the Editorial Board for Hypertension News in 2020 where she coordinates new investigator contributions.

Charlotte's research employs a multidisciplinary approach combining clinical and basic/analytical science to investigate the impact of plant bioactives and other nutrients on cardiovascular disease risk and the mechanisms underpinning these effects.

Hiromi Rakugi, MD, PhD.

Professor, Department of Geriatric and General Medicine, Osaka University Graduate School of Medicine. Hiromi Rakugi is the President of the Japanese Society of Hypertension in 2020-2022 and was the President of the Japan Geriatrics Society in 2015-2019. His research interests include geriatric medicine, hypertension in older people, and the role of the renin-angiotensin system in aging.

Thomas Unger, MdD, PhD, FAHA, FESC.

Professor and Scientific Director em. CARIM-Cardiovascular Research Institute, Maastricht University, The Netherlands. Council Member and Former Secretary of the ISH. Former president of the European Council for Cardiovascular Research (ECCR) and the German Institute for High Blood Pressure Research. Founder of the Cardiovascular Research Center (CCR) of the Charité, Berlin, Germany. Main interest brain-related peptidergic mechanisms and the renin-angiotensin system (RAS) in cardiovascular regulation. Has developed new therapeutic approaches modifying the RAS. First author of the recent ISH Hypertension Guidelines.

Maria-Christina Zennaro, MD, PhD.

Research Professor at the French National Institute of Health and Medical Research (Inserm), head of the team "Genetic mechanisms of aldosterone related disorders - towards integrative precision medicine" at the Paris Cardiovascular Research Center, Inserm and Université Paris Cité, and associated investigator at the Genetics Department of the European Hospital Georges Pompidou (HEGP) in Paris, France. Her research team has developed a genome-wide strategy to explore the genetics and genomics of aldosterone related disorders and endocrine hypertension, in order to generate knowledge translatable to patient's care.

HOT OFF THE PRESS

The benefit of lower target blood pressure in hypertension during pregnancy

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Hypertension in pregnancy is associated with short term risks for both mothers (preeclampsia and eclampsia, stroke, heart failure, pulmonary oedema, acute kidney injury, placental abruption, and death) and for offspring (preterm birth or birth at small-for-gestational age, and perinatal death). However, whereas recommendations for treating hypertension in adults are clear and there is evidence supporting treatment at increasingly lower levels[1,2] the case for treating mild-to-moderate hypertension in pregnancy has remained unclear[3,4].

The Chronic Hypertension And Pregnancy (CHAP) study by Tita and colleagues[5] provides important new information to this issue. This open labelled randomized parallel group study aimed to evaluate antihypertensive therapy compared with control among pregnant women with mild chronic hypertension. Inclusion criteria were singleton pregnancies with gestational age less than 23 weeks and mild hypertension (defined as systolic blood pressure 140–159 mm Hg or diastolic blood pressure 90–104 mm Hg, or documented hypertension with previous or current antihypertensive treatment). Thus, 1208 participants with mild chronic hypertension were randomized to a blood pressure target below 140/90 mm Hg, and 1200 women to the control group, where antihypertensive therapy was withheld unless blood pressure was 160/105 mm Hg or higher. Baseline blood pressure was 134/84 mm Hg, body mass index 38 kg/m^2, diabetes was present in 16%, 48% were non-Hispanic black women, 28% non-Hispanic white, and 20% Hispanic. The preferred drug therapy was labetalol or nifedipine (62 and 36% of participants, respectively); aspirin was taken by 45% at enrollment and 74% at the time of delivery. Primary outcome was a composite of preeclampsia with severe features, medically indicated preterm birth at a gestational age less than 35 weeks, placental abruption, or fetal/neonatal death. The primary safety outcome was poor fetal growth. Major secondary outcomes included a composite of maternal death or serious complications, and a composite of serious neonatal complications.

Mean blood pressure between randomization and delivery was 129/79 mm Hg in the active treatment group and 133/82 mm Hg in the control group, corresponding to a 3.1/2.3 mm Hg difference. The primary outcome was reduced in the active treatment group (30.2 vs. 37.0% of the control group, risk ratio and 95% confidence interval 0.82 [0.73–0.92], P < 0.001). These results were driven by reductions in preeclampsia with severe features and by medically indicated preterm birth (23.3 vs. 29.1%, 0.80 [0.70–0.92], and 12.2 vs. 16.7%, 0.73 [0.60–0.89], respectively). The authors determined the numbers needed to treat to prevent one primary outcome to be 14-15 participants. The safety outcome of newborns showed no difference between the two study groups.

Taken together, this study[5] provides new evidence supporting treatment of mild chromic hypertension in pregnancy to a target of less than 140/90 mm Hg. The improvement in pregnancy outcome (a primary composite outcome including preeclampsia with severe features, medically indicated preterm birth, placental abruption, or fetal or neonatal death)

was largely due to reduction in preeclampsia with severe features and in medically indicated preterm birth. Second, there were no safety concerns to the outcome of newborns. However, there are limitations to this study to consider. The authors did not include out of office blood pressure measurements, which is increasingly used in pregnancy. The lower boarder of target blood pressure remains to be demonstrated. The results may not be generalized to women with hypertension in pregnancy diagnosed after gestational week 23. This notwithstanding, these novel findings suggest treatment of hypertension in pregnancy at lower levels than previous practice. There may be reasons to revise current recommendations for the treatment of elevated blood pressure in pregnancy.

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HOT OFF THE PRESS

Insights into the mechanisms of inhibition of aldosterone production by mutant atrial natriuretic peptide (MANP)

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In this study, Chen et al investigated the molecular mechanisms of aldosterone inhibition by mutant atrial natriuretic peptide (MANP), a novel atrial natriuretic peptide (ANP) analog, in the human adrenal cortical cell line H295R[1].

Aldosterone is one of the major hormones contributing to blood pressure regulation and a potent sodium-retaining factor in the organism. Excessive aldosterone leads to hypertension, but also facilitates pathophysiologic fibrosis, and organ remodeling in the heart, vasculature, and kidney, contributing to heart failure and chronic kidney disease. Mineralocorticoid receptor antagonists have been used for decades to lower blood pressure in resistant hypertension and primary aldosteronism, and have shown potent effects in reducing morbi-mortality in heart failure. However, given that they increase aldosterone levels by a counter-regulatory mechanism, drug development efforts have focused on direct aldosterone inhibition.

ANP is a cardiac hormone involved in blood pressure homeostasis through vasodilation and natriuretic actions via activation of pGC-A (particulate guanylyl cyclase A receptor) and production of the second messenger cGMP. ANP is also an endogenous inhibitor of aldosterone production[2]. However, the therapeutic use of ANP is limited because of its instability due to degradation by neprilysin. Recently, MANP, a novel ANP analog, has been engineered to overcome this limitation. MANP possesses a more potent aldosterone inhibitory action than ANP *in vivo* and is reported to be resistant to neprilysin degradation[3]. MANP is now entering into phase 2 clinical trial after it was shown to lower blood pressure in a phase 1 clinical study in patients with resistant hypertension[4]. The mechanisms whereby the natriuretic peptides (NP) lower aldosterone has not been clearly elucidated. It has been suggested that this effect may be mediated by pGC-A activation, while other studies suggested that this inhibition is caused by the NP clearance receptor (NPRC). Therefore, this work aimed to better understand the mechanisms of aldosterone inhibition by natriuretic peptides.

The authors demonstrated the presence of pGC-A and NPRC in human adrenocortical H295R cells, and showed that treatment of these cells with MANP increased the production of cGMP in a dose-dependent manner. Aldosterone production in H295R cells stimulated by ANGII or KCl was reduced by treatment with MANP. Similarly, MANP treatment also suppressed aldosterone production stimulated by forskolin (a direct activator of adenylyl cyclase producing cAMP). In order to investigate if NPRC also inhibits aldosterone biosynthesis, H295R cells were treated with the NPRC-specific agonist cANF and antagonist AP-811. cANF did not suppress aldosterone production and AP-811 did not affect the inhibitory effect of MANP.

cGMP-AM, a non-specific cGMP analog, mimicked MANP's aldosterone-suppressive effects in H295R cells. Since PKG and PDEs are two important downstream protein targets of cGMP, the authors explored which one is responsible for the aldosterone-mediated inhibition of MANP. PKG activator did not lower aldosterone levels and PKG inhibitor had no effect on the aldosterone decrease induced by MANP. In contrast, they observed reversal of the inhibitory effect of MANP when using a nonspecific PDE inhibitor and they showed that this effect was mediated through PDE2 and not PDE3. They further showed that MANP treatment 10 minutes before forskolin stimulation reduced cAMP levels suggesting an activation of PDE2. MANP also lowered intracellular Ca^{2+} levels following AngII stimulation, as well as expression of *CYP11B2*, the gene encoding aldosterone synthase, and this effect was reversed by the PDE2 inhibitor Bay 60-7550. These results were confirmed by *in vivo* studies showing that the expression of *CYP11B2* was higher in homozygous PDE2 knockout mouse embryos compared to wild-type mice.

In summary, this study demonstrated that MANP inhibits aldosterone production via the pGC-A/cGMP/PDE2 pathway and plays an important role in reducing aldosterone and CYP11B2 levels, therefore highlighting the therapeutic potential of MANP in treating hypertension. Additional potential approaches may target an increase of cGMP and PDE2 activity, the increase of endogenous NPs through neprilysin inhibitors or exogenous NP administration.

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LEARNING THE ROPES: HIGH BLOOD PRESSURE IN THE VERY OLD

Introduction

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When health care became critically strained under the COVID-19 pandemic, there was news that an age limit for older people was applied to health care priorities in some countries. Some people felt ageism, some thought another age group should separate it, and some thought it was inevitable that there should be priorities for the lives that could be saved. In daily practice, some feel that it made no sense to separate older people by age, as their health varied greatly at the same age. On the other hand, some felt that the definition of older people makes sense because there is an age group where the majority is unhealthy or not independent. Although hypertension treatment differs from highly invasive treatments, which strictly indicate age criteria, it is reasonable to be aware of older people in hypertension management. There should be no ageism, but appropriate management of the diversity of older people would be possible by taking into account age and the presence of frailty and multimorbidity.

In guidelines for the treatment of hypertension, the ISH and European guidelines define the older age group as 65 years or older and the very old age group as 80 years or older.[1, 2] In particular, concerning initial therapy with dual combination in general patients, very old and frailer patients are recommended starting with monotherapy. These different recommendations for the very old are based on the characteristics of the populations included in the randomised controlled trials (RCTs). Most RCTs do not include patients with severe frailty or nursing home residents in their studies, and very few RCTs have included patients who are considered very old.

There are two scientific ways of defining very old people who require a more specific response in antihypertensive treatment decisions. One is based on the age above the age group for which a certain level of evidence is available to make recommendations. The other is based on the age at which the prevalence of multimorbidity and severe frailty becomes prominent. Regarding the former, the results of a Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC) meta-analysis based on data from 358,707 participants from 51 randomised clinical trials are informative.[3] It concluded that pharmacological blood pressure reduction should be considered an important treatment option regardless of age, with the removal of age-related blood-pressure thresholds from international guidelines. However, there was no statistically significant beneficial effect of blood pressure reduction in the over 85 age group. For the latter, a meta-analysis on the prevalence of frailty in 11,414 community-dwelling individuals is informative: 10%, 20.4% and 35.1% in the 75-79, 80-84 and 85+ age groups, respectively.[4] According to such information, it seems appropriate to define 85+ as very old. Apart from the debate on how old is very old, it is essential to consider not only age categories but also frailty status.

In this special issue about hypertension in the very old, the epidemiology, the usefulness of treatment, the optimal treatment regimen, and the decision to stop treatment will be presented expertly. These special features will be helpful to readers in their clinical practice and provide awareness of new research questions.

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2. Concor®/Concor® COR Product Information, updated November 2020. To be replaced by the local Product Information.

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LEARNING THE ROPES:

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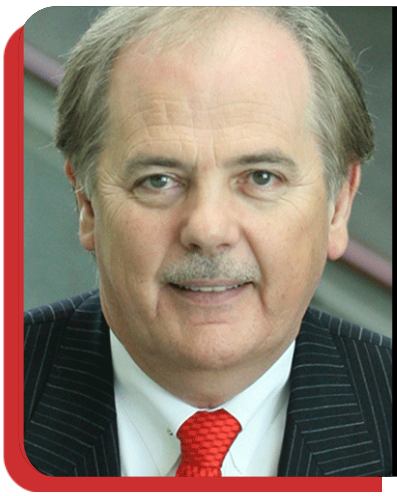

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Aging populations leading to more older adults

In most economically developed counties, including the United States, survivorship rates have improved progressively for many decades[1]. Average life expectancy for US adults aged 85 years was 5.5 years in 1972 but increased to 6.5 years by 2010 and is projected to increase to between 7 and 8.5 years, depending on race/ethnicity, by 2050. The corresponding life expectancy estimates for Sweden were 4.9 years in 1972 and 6.2 years in 2010.

Table 1 provides the number and percent of the US population ≥85 years in 2012, overall, and by the four largest race/ethnicity groups (Whites, Blacks, Hispanics, and Asians). The number ≥85 years is projected to increase progressively in future decades and the percentage of Blacks, Hispanics (especially), and Asians in this age range is also projected to increase. The percentage of Whites is expected to decline progressively but they will remain the dominant race/ethnic group in US adults ≥85 years.

Although the US population is aging progressively, it is younger compared with almost all other economically developed countries, with only Russia having a younger population. With nearly 24% of its population ≥65 years, Japan has the oldest population among the most economically developed countries, but the corresponding percentage was >20% in several European countries, including Germany and Italy. In contrast, the US percentage was <14%.

Cumulative incidence of hypertension in older adults

In most adults, systolic blood pressure (SBP) rises progressively throughout life, at least into the eight decade. As a result, high BP is very common during the second half of life. Even in those who remain free of hypertension in their fifth or sixth decade of life, the risk of developing it in later years is high. In a 2002 report, Vasan et al calculated cumulative incidence to estimate the residual risk of hypertension during 8469 person-years of observation in 1298 Framingham Heart Study

Table 1. Number, in thousands (%), of US adults ≥85 years who were White, Black, or Hispanic in 2012 and projected numbers (%) through 2050. US Census Bureau, 2014[1].

	2012	2020	2030	2040	2050
Total	5,887	6,693	8,946	14,115	17,987
White	5,232 (88.9%)	5,845 (87.3%)	7,667 (85.7%)	11,830 (83.8%)	14,657 (81.5%)
Black	424 (7.2%)	539 (8.1%)	774 (8.7%)	1,356 (9.6%)	1,950 (10.8%)
Hispanic	329 (5.6%)	502 (7.5%)	759 (8.5%)	1,331 (9.4%)	2,246 (12.5%)
Asian	172 (2.9%)	224 (3.3%)	359 (4.0%)	650 (4.6%)	928 (5.2%)

Table 2. Residual lifetime risk of hypertension (SBP ≥140 mm Hg, DBP ≥90 mm Hg, or taking antihypertensive medication) by age at baseline (≥55 or ≥65 years) in Framingham Heart Study men and women.

	Average % risk (95% CI) for participants without hypertension at age ≥55 years		Average % risk (95% CI) for participants without hypertension at age ≥65 years	
Years of follow-up	Women (n=709)	Men (n=589)	Women (n=549)	Men (n=438)
10	52 (46-58)	56 (49-63)	64 (60-69)	72 (67-78)
15	72 (68-76)	78 (74-82)	81 (77-84)	85 (81-89)
20	83 (80-86)	88 (85-91)	89 (86-92)	90 (87-93)
25	91 (89-93)	93 (91-95)	----	----

Adapted from Vasan SV et al.[2] Lifetime risk of developing hypertension is represented by the risk over 25 years of follow-up in those aged 55 years or older at baseline and 20 years in those aged 65 years and older.

(FHS) participants (589 men and 1298 women) who were aged 55-65 years and free of hypertension at baseline in 1976-1998. Two blood pressures were measured by trained physicians at each biannual FHS visit using a standard protocol and a mercury sphygmomanometer. Hypertension was based on an average SBP ≥140 mm Hg, average diastolic BP ≥90 mm Hg, or reported use of antihypertensive medication. As shown in Table 2, the residual risk of developing hypertension for men and women who were free of hypertension at ages 55 and 65 years was high, with an estimated lifetime risk of about 90%. Adjustment for competing causes of mortality had only a marginal effect on the estimates.

In a more recent 2019 report[3], Chen et al. used individual pooled data from three contemporary cohort studies (Framingham Offspring Study, Coronary Artery Risk Development in Young Adults Study, and Atherosclerosis Risk in Communities Study) to estimate lifetime risk of hypertension, based on the ACC/AHA Stage 1 (SBP ≥130 mm Hg, DBP ≥80 mm Hg, or taking antihypertensive medications) or stage 2 (SBP ≥140 mm Hg, DBP ≥90 mm Hg, or taking antihypertensive medication) classification of hypertension in 13, 160 study participants who contributed 227,600 person-years of follow-up. At baseline, median age was 25 years and the prevalence of stage 1 hypertension in those 20-30 years of age was 30.7% in white men, 23.1% in African-American men, 10.2% in white women, and 12.3% in African-American women. In the participants without hypertension at baseline, the lifetime risk of stage 1 hypertension was 83.8% in white men, 86.1% in African-American men, 69.3% in white women, and 85.7% in African-American women. The corresponding lifetime risks for stage 2 hypertension were 60.5%, 74.7%, 53.9%, and 77.3%, respectively.

Prevalence of hypertension in very old adults

Limited published information is available to estimate the prevalence of hypertension in very old adults. In a 2005 manuscript, Lloyd-Jones et al. reported the prevalence of ACC/AHA stage 2 hypertension in the FHS original and offspring cohort studies[4]. As expected, the prevalence of hypertension increased progressively with higher age and was 74% in those ≥80 years (69.1% in men and 76.5% in women). In a more recent 2014 publication, Bromfield et al. reported on trends in SBP and DBP, and prevalence of ACC/AHA stage 2 hypertension among US adults ≥80 years in the 1988-1984 (n=1,164), 1999-2004 (n=1,1,026), and 2005-2010 (n=1,048) US National Health and Nutrition Examination Surveys[5]. The overall prevalence of hypertension increased from 69.2% in 1988-1984 to 76.5% in 1999-2004 and remained 76.5% in 2005-2010 (Figure). The corresponding prevalence of isolated systolic hypertension (SBP≥ 140 mm Hg and DBP<90 mm Hg) among those with stage 2 hypertension was 52.8%, 55.3%, and 43.9%, respectively. Much of the increase in prevalence seemed to result from greater use of antihypertensive medication over time, with a doubling in the mean number of antihypertensive medication classes being taken between 1988-1994 and 2005-2010 and the proportion of those taking ≥3 antihypertensive medications increasing from 7.0% to 30.9%. In a 2020 KORA-age 1 study report[6], Muli et al. identified the prevalence of hypertension (SBP≥140 mm Hg, DBP≥90 mm Hg, or

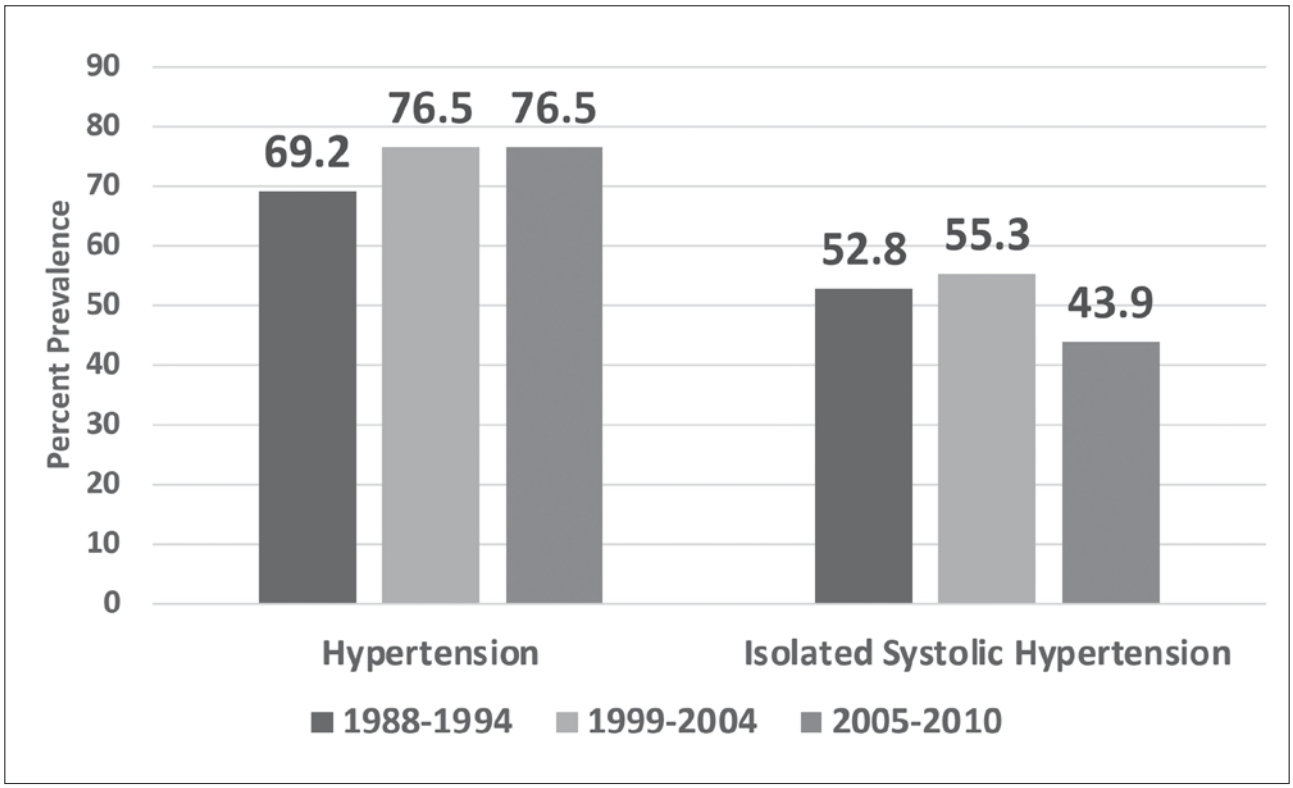

Figure: Prevalence of hypertension (SBP ≥140 mm Hg, DBP ≥90 mm Hg, or taking antihypertensive medication) and isolated systolic hypertension (SBP ≥140 mm Hg and DBP <90 mm Hg) among those with hypertension in US adults ≥80 years of age. Results based on findings in serial National Health and Nutrition Examination Surveys (1988-1994, 1999-2004, and 2005-2010). Adapted from Bromfield et al.[5]

taking antihypertensive medication) in 1052 adults 65-94 years in the Augsburg region in Germany. Of the 125 participants aged 85-94 years, 92 (74%) had hypertension. In a multivariate analysis of the entire cohort, increasing age, obesity, and diabetes were the factors most associated with a higher prevalence of hypertension.

Cardiovascular risk associated with hypertension in the very old

In the study by Lloyd-Jones et al., 336 major cardiovascular events were observed during follow up, including 127 major coronary heart disease events, and 194 congestive heart failure hospitalizations. In those ≥80 years, the corresponding adjusted hazard ratios among the participants with an SBP 140-159 mm Hg or DBP 90-99 mm Hg were 1.8, 1.5, and 0.9, and for the participants with an SBP ≥160 mm Hg or DBP ≥100 mm Hg were 2.4, 2.2, and 1.7. These hazard ratios were quite similar to those seen in the participants who were <60 or 60-79 years. However, the absolute rates of cardiovascular disease were much higher in those ≥80 years compared with the two younger age groups.

Over and above the direct risks resulting from hypertension, older adults have a high prevalence of co-morbidity. In an analysis of almost 31 million US Medicare beneficiaries, Salive assessed the prevalence of 15 co-morbid conditions[7]. In those ≥85 years, 81.5% had two or more of the index co-morbidities (82.3% in women and 79.5% in men). In the same manuscript, a review of 17 previous general population reports confirmed the high prevalence of multimorbidity (two or more co-morbid conditions) in previous US reports and documented multimorbidity in ≥50% of older adults in Israel, Canada, Ireland, Australia, Germany, Sweden, and the Netherlands. It seems likely that the prevalence of co-morbidity, including multimorbidity, is even higher in clinical practice settings.

Summary

In summary, the percentage and number of older adults is increasing in most countries and this pattern is expected to continue in the coming decades. The prevalence of hypertension increases in an age-dependent fashion and there is a high cumulative incidence and residual risk of hypertension in later life in those who have previously remained free of the condition. As a consequence, the prevalence of hypertension in very old adults is high, approximating 75% for hypertension defined as an average SBP ≥140 mm Hg, DBP ≥90 mm Hg, or taking antihypertensive medication. In the very old, hypertension results in an approximately two-fold increase in the risk of cardiovascular disease and co-morbidity is very common, with multimorbidity being noted in >50% in most older general population samples and likely even higher in clinical practice settings.

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LEARNING THE ROPES:
Effects of blood pressure lowering treatment in the very old

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Treatment of high blood pressure (BP) in very old adults is challenging due to variable life expectancy and a high prevalence of comorbidities, polypharmacy and cognitive impairment. In this article, we summarise the latest evidence on antihypertensive medication effects in the very old and areas of remaining uncertainty that future studies should investigate.

Evidence from landmark observational studies has shown a continuous, graded association between higher systolic and diastolic BP (SBP and DBP, respectively) and increased risk of major cardiovascular outcomes, even at very old age.[1] These associations, however, show two quantitative differences amongst the age groups. First, the slope of the association tends to be flatter at older age; likely explained by accumulation of multiple risk factors for CVD and competing risk of other outcomes. Second, the absolute risk of CVD increases substantially with older age. While the flatter slope for the BP-CVD association suggests a smaller relative effect of BP reduction in the very old, the higher absolute risk for CVD suggests a bigger benefit of antihypertensive medication in the older patient groups. As the impact of age on absolute CVD risk is much stronger than the dilution of BP-CVD associations by age, one would expect the same amount of BP reduction to lead to the prevention of even more CVD events in the very old than in the younger adults.

However, the aforementioned epidemiological findings are typically based on relatively healthy cohorts without pre-existing diseases. As such, their findings might not generalise to the typical older patient seen in clinical practice with a high burden of comorbidities. On the other hand, observational studies with fewer exclusion criteria are prone to residual confounding and reverse causation by incipient and undiagnosed diseases that cannot always be addressed through adjustment. Therefore, randomised trials are needed to provide more definitive answers to the question of the benefits and harms of antihypertensive medication, especially in the very old.

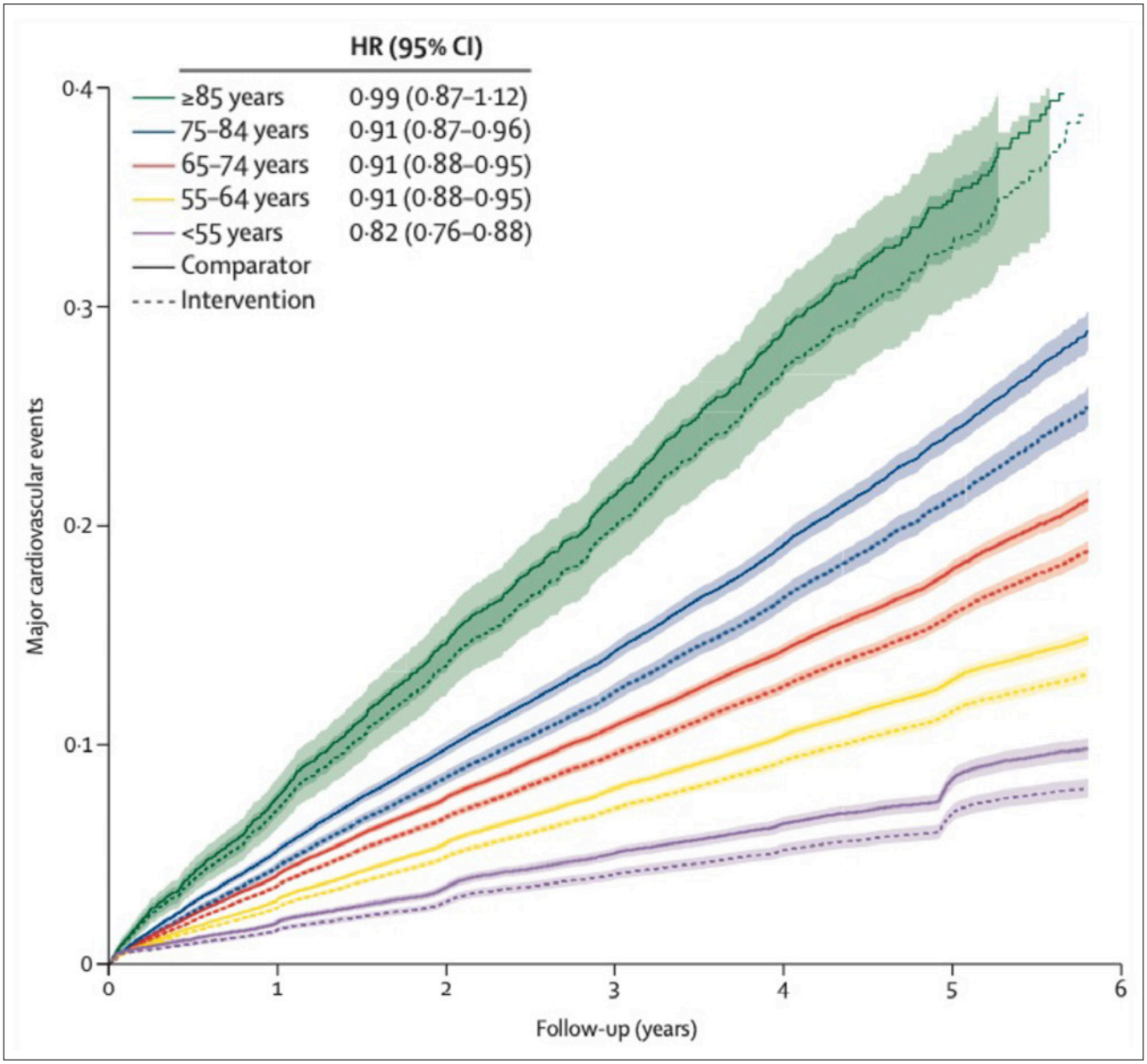
While there is overwhelming evidence from randomised trials that antihypertensive treatment reduces the risk of cardiovascular disease (CVD),[2] its effects on CVD risk in the very old has been uncertain and subject to debate. This controversy is reflected in multiple clinical practice guidelines published over the past five years that have provided different recommendations on the level of BP at which antihypertensive medication should be initiated and to which it should be lowered.

Some individual trials have reported beneficial effects of antihypertensive medication on CVD risk in very old adults. But most participants included in these trials had SBP ≥ 160 mm Hg. For instance, the Hypertension in the Very Elderly

Trial (HYVET) investigated the effect of BP lowering in about 4000 patients aged 80 years and older with SBP ≥ 160 mm Hg at study entry.[3] This study found 30% and 23% reductions in risk of stroke and cardiovascular death, respectively, with antihypertensive medication versus placebo. Other randomised trials that have investigated the effects of BP reduction by age also included few participants who were very old with a narrow range of pre-treatment BP.

This gap in evidence was addressed in a recent large-scale study by the Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC).[4] The study included individual participant-level information from about 360,000 participants from 51 randomised trials, of whom about 22,000 participants were aged ≥80 years at randomisation. The study divided the patient population into five age groups and seven categories for systolic BP (<120 mm Hg to ≥ 170 mm Hg) and six categories of diastolic BP (<70mm Hg to ≥110 mm Hg). The oldest group comprised about 5000 participants aged ≥85 years at randomisation (average age 90 years at the end of the study), with a broad distribution of BP at randomisation. The average follow-up duration of 2.8 years was comparatively short in this oldest age group. Consequently, with

Figure 1. Rate of major cardiovascular events per 5 mm Hg reduction in systolic blood pressure by treatment allocation and age categories at baseline (Figure taken from the Lancet, 2014).



only about 1000 CVD events accrued during the study, the confidence intervals for treatment effect were wide (Figure 1). Nonetheless, the comparison of the effect of BP lowering effect on CVD events with other age groups suggested that there is no age threshold beyond which the beneficial effects of BP lowering on major CVD would cease to exist. Moreover, the study found consistent relative risk reductions by baseline BP levels in all age groups, down to SBP less than 120 mm Hg and DBP less then 70 mm Hg. Indeed, because older patients were at a substantially higher risk of CVD, the absolute effect of a fixed level of BP reduction appeared to be higher in older participant groups.

As with any drug treatment, the decision to initiate and intensify antihypertensive medication should weigh its benefit and potential harm. The aforementioned evidence on prevention of CVD in the very old would only be worthwhile when it is not outweighed by detrimental effects on other health outcomes. To this end, the BPLTTC study reported effects on all-cause death and found no clear reduction or increase in risk of death with BP lowering in people older than 75 years.[4] This should provide reassurance that treatment does not result in excess fatal events in the very old.

Concerns have been raised that BP lowering among the very old increases the risk for non-fatal adverse outcomes, in particular at lower BP levels. Support for such concerns have come from some non-randomised studies that have reported associations between low BP and a higher risk for several important outcomes including cognitive function, falls and acute renal injury. The BPLTTC has proposed meta-analyses of randomised trials to study such effects among older adults.[5] Other planned and ongoing trials might also be able to specifically investigate treatment effects in very high-risk older adults such as those with multimorbidity, polypharmacy and frailty. In the meantime, published randomised studies have found largely reassuring results on outcomes other than major cardiovascular disease. For instance, in a subgroup analysis of the Systolic Blood Pressure Intervention Trial (SPRINT), the total serious adverse event rates were similar between the intensive and standard BP lowering study arms,[6] and there was some evidence to suggest that intensive BP reduction might actually prevent cognitive decline.[7] Several other age-stratified analyses of randomised trials have also shown no worsening in functional status, physical wellbeing, or quality of life with antihypertensive medication among the very old.[8] In other recent BPLTTC studies, antihypertensive treatment did not increase the risk of cancer[9] but there was an additional beneficial effect of BP lowering on reducing the risk of type 2 diabetes[10], which could further add to the net benefit of treatment.

In conclusion, the population world-wide is ageing and elevated BP is common among older adults. There is overwhelming evidence that BP lowering with antihypertensive medication reduces CVD risk among the very old, at least up to 85 years, and across a wide spectrum of baseline BP, down to 120/70 mm Hg. There are residual evidence gaps on the unintended consequences of BP lowering with antihypertensive medication in the very old, especially in presence of multimorbidity and polypharmacy. A patient-centric approach for BP lowering that considers the CVD risk reduction benefits with patient's comorbidities and life expectancy should be considered among the very old. However, age alone should not be a barrier to antihypertensive treatment, even when BP is not highly elevated.

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LEARNING THE ROPES:

Should treatment with blood pressure lowering drugs be stopped in the very old?

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Very few studies have investigated the effects of initiating, increasing, decreasing or stopping antihypertensive treatment in the very old (≥85 years). It is reasonable to assume that there still is a benefit from treatment in the very old, but increasing presence of co-morbidities and side effects will affect the risk/benefit ratio.

High blood pressure as a risk factor in very old

Even in high age, high blood pressure is a risk factor for stroke. A Swedish population-based study in very old with a mean age of 89 years found that, during a mean follow-up of 2.9 years, high blood pressure and atrial fibrillation were associated with an increased risk for stroke[1]. On the other hand, in many countries, most very eldery are already on treatment with blood pressure lowering drugs. Withdrawal of treatment is probably a much more common measure.

Effects of treatment with blood pressure lowering drugs in very old

The benefits from stopping antihypertensive treatment should be contrasted with the benefit from treating high blood pressure in the very old. The number of subjects aged 85+ in randomized controlled outcome trials of hypertension treatment is very small, and with uncertain results. The largest trial in this age group is the HYVET (HYpertension in the Very Elderly Trial) study[2]. It included subjects aged 80 or more, and active treatment resulted in lower total mortality and fewer cardiovascular events compared with subjects randomized to placebo. Also, there was no association between Frailty Index and the effects of treatment on the outcomes.

In the HYVET-subgroup of subjects aged 85 or more at randomization (n=1038), the treatment effects on cardiovascular outcomes were not statistically different from subjects aged 80-84. In a 1-year extended follow-up of 80 years + subjects, starting after finishing double blind treatment (baseline mean age 84.8 years), total mortality and cardiovascular mortality during the following year was lower in those previously randomized to active treatment, with a hazard ratio of 0,48 (95% confidence interval 0.26-0.87) and 0.19 (95% confidence interval 0.04-0.87), respectively. But, there were no significant differences in cardiovascular morbidity[3].

Which treatment regimen is the best in the very old?

With this very sparse data, it is not possible to gain specific evidence about potential differences between different antihypertensive drugs or treatment regimens in the very old compared with younger individuals. In the HYVET study, a thiazide-like diuretic (indapamide) and the ACE-inhibitor perindopril were used. Guidelines recommend using Angiotensin receptor blockers (ARB), ACE-inhibitors, diuretics and calcium antagonists. A systematic review of beta-blockers in older adults concluded that it could not be recommended to use beta-blockers as first line drugs in older adults[4]. However, there were no specific data from the very old.

Many hypertension guidelines recommend a combination pill containing two different drugs as initial blood pressure lowering drug therapy. The European Society of Hypertension Guideline have a quite strong recommendation for this initial combination therapy. However, due to the potential risk of initial hypotension and other side effects, they recommend that in people above 80 years and in frailer patients, initial monotherapy should be preferred.

Stopping treatment

In clinical practice, stopping antihypertensive drug treatment in old people is a very common measure. Reasons differ; symptomatic orthostatism, polypharmacy, hypotension due to a concomitant acute situation, other severe diseases etc. Very little is known about the effects on blood pressure, side effects, cognitive function or cardiovascular outcomes. There are a few observational studies in this area, but with this research question, it is very difficult to draw conclusions about the risks and benefits without a control group.

A Cochrane review titled "Withdrawal of antihypertensive drugs in older people", published in 2020 included randomized controlled trials of stopping antihypertensive drugs[5]. The review defined "older" as 50 years and older, and only three of the included trials were performed in studies with a mean age over 80 years. Of these, two included only subjects treated with diuretics and the indication could have been hypertension, heart failure or ankle edema. Thus, only one study covered the question about very old persons, the DANTE (Discontinuation of Antihypertensive Treatment in Elderly people) study[6].

The DANTE Study

DANTE included very old persons with drug treated hypertension, SBP below 160 mmHg, and a Mini-Mental State Examination score of 21-27 but not fulfilling the diagnostic criteria of dementia. The mean age was 81 years. Patients with heart failure or a history of myocardial infarction, CABG/PCI or stroke during the last three years were excluded. Participants (n=385) were randomized to continue or discontinue their blood pressure lowering drugs. Primary outcome was the change in a cognitive score from baseline to 4 months. The baseline mean SBP was 148 mmHg and increased by 5.4 mmHg in the discontinuation group and decreased by 2.0 mmHg in the control group.

Discontinuation of antihypertensive treatment did not improve cognitive function[6]. Nearly half of the patients with orthostatic hypotension in the discontinuation group could not discontinue all antihypertensive drugs. Therefore, the prevalence of orthostatic hypotension was not significantly reduced in the intention-to-treat analysis, but only in the as-treated analysis[7]. In total, there were only a few cardiovascular events during the four months of the study.

The OPTiMISE Study

Since then, the OPTiMISE (Optimizing Treatment in for Mild Systolic Hypertension in The Elderly) study has been published[8]. It included subjects with a mean age of 84.8 years with a SBP lower than 150 mmHg on 2 or more antihypertensive drugs. In addition, the physicians had to assess that the patient could benefit from treatment reduction due to polypharmacy, co-morbidity, nonadherence, frailty or dislike of medicines. Patients with heart failure due to left ventricular dysfunction, myocardial infarction or stroke during the last year, secondary hypertension or lacking capacity to consent were excluded.

Patients were randomized to follow a detailed medicine reduction scheme or to usual care for 12 weeks. In the end of the study, patients in the medication reduction group took 0.6 antihypertensive drugs fewer than the usual care group. Mean SBP at baseline was 130 mmHg and after 12 weeks, 3.4 mmHg higher in the deprescribing group compared with the usual care group. During this short follow-up, there were only a few cardiovascular events, but the number of patients experiencing at least 1 adverse event was significantly higher in the medication reduction group.

A cost-effectiveness estimation was performed with a Markov Modelling from a life-time time horizon. The conclusion from this analysis, besides

the uncertainty around many of the assumptions, was that antihypertensive medication reduction should not be attempted in all older patients. A more targeted approach should be required in routine practice.

The HYVET study revisited

Thus, there are very few randomized controlled studies examining the effects of stopping treatment with antihypertensive drugs in the very old. There are no studies with enough power to detect effects on cardiovascular outcomes.

Interestingly, the HYVET study mentioned above might give some more information. In total, 3845 subjects were randomized to active treatment or placebo. One third of the subjects had not been treated with antihypertensive drugs before randomization. They were thus randomized to start treatment or continue without treatment. Two thirds of the participants in the study were already on treatment before randomization. They could be regarded as being randomized to continue treatment of high blood pressure or stopping treatment. Interestingly, total mortality was reduced only in the last group (continue vs stopping treatment). Those who were randomized to continue treatment had lower mortality than those who were randomized to stop antihypertensive drugs (table). This was not a preplanned analysis, only one of many subgroup analyses and one should therefore be careful about interpreting the finding[9].

Epilogue

We know very little about the effect of stopping treatment with blood pressure lowering drugs in the very old or frail. There are sometimes obvious reasons for stopping or reducing treatment; symptomatic orthostatism, co-morbidity, nonadherence, dehydration, etc. However, it is always a risk/benefit estimation with many uncertain parameters. Also, with these sparse data, it is obvious that stopping treatment is often difficult to carry through and might be dangerous. When treatment is withdrawn, the effects on blood pressure, symptoms and signs have to be monitored.

Table. Subgroups, starting and stopping treatment with blood pressure lowering drugs in the HYVET study (table modified from ref 9, with permission)

	Subgroup HYVET Starting treatment vs no treatment (placebo) n=1359 Hazard Ratio (95% CI)	**Subgroup HYVET Continuing treatment vs stopping treatment (placebo) n=2486 Hazard Ratio (95% CI)**
All-cause mortality	0.95 (0.69-1.31)	O.71 (0.56-0.90)
Cardiovascular mortality	0.94 (0.61-1.47)	0.69 (0.50-0.97)
All cardiovascular events	0.69 (0.48-0.99)	0.65 (0.50-0.86)
Fatal or nonfatal Stroke	0.73 (0.39-1.36)	0.69 (0.44-1.07)
Fatal or nonfatal Myocardial infarction	No data	No data
Fatal or nonfatal Heart failure	0.28 (0.12-0.65)	0.42 (0.23-0.76)

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LEARNING THE ROPES

INVITED PAPER

Hypertension Research at Université Laval

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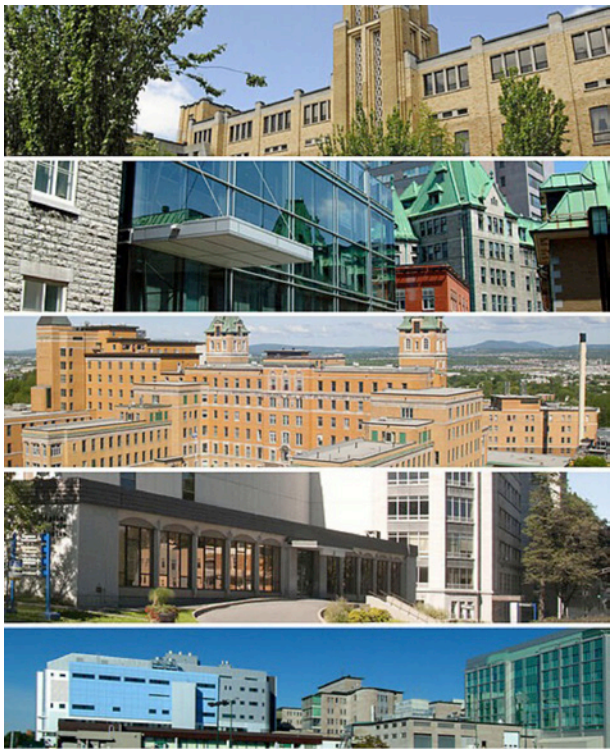
Université Laval was officially founded in 1852, but its origin dates to 1663 with the founding of the Grand Séminaire de Québec making it the oldest centre of higher education in Canada and the first North American institution to offer higher education in French. Located in the beautiful Québec City area, the affiliated health research centers are physically located close to university hospitals. At the **CHU de Québec-Université Laval**, the **Québec Heart and Lung institute** and the **VITAM** research centers, investigators use complementary approaches to tackle the challenges of hypertension in kidney disease, pregnancy, metabolic syndrome and pulmonary hypertension.

Hypertension and Kidney

A group of dynamic clinician scientists and basic scientists work closely together to unravel the mechanisms of hypertension in chronic kidney disease (CKD) within the **Endocrinology and Nephrology research axis** of **CHU de Québec-Université Laval research center**. This research group, originally under the leadership of Dr. Marcel Lebel, has significantly contributed to the role of kidney in hypertension and to the understanding of the mechanisms of erythropoietin-induced hypertension in the context of CKD. More recently, the research group has focused their clinical research work towards understanding the consequences of the evolution of biomechanical properties of the arterial wall and their clinical significance as novel mechanical biomarkers. In a longitudinal study, **Dr. Agharazii's team** discovered that aortic pulse wave velocity (stiffness) increased with time, while the brachial

Université Laval. Photo credit: Marc Robitaille



CHU de Québec-Université Laval Research Centre
Photo credits: CHU de Québec-U. Laval

pulse wave velocity decreased in patients on dialysis **(PMID: 23648699)**. This puzzling finding led them to explore the concept of arterial stiffness gradient and underline the potential contribution of the medium-sized muscular conduit arteries in the regulation of pulse pressure transmission along the arterial path into the microcirculation **(PMID: 25452473)**. To understand the arterial tree as a whole, they proposed a novel non-invasive method to assess stiffness of smaller arteries by using radial-digital pulse wave velocity **(PMID: 33481697)**. They propose that this will allow them to consider the mechanical properties of vessels from large, to medium and small-sized arteries in health and disease, and their respective responses to pharmacological interventions.

This research group is also composed of basic scientists who are conducting *in vitro* and *in vivo* experimental studies to understand the process of vascular calcification in the context of CKD (Drs D. Richard, R. Lariviere and. F. Mac-Way). This process is tightly linked to the abnormal mineral metabolism in CKD, but other pathways can come into play either to promote or to attenuate this process. For example, through *in vitro* studies they have shown that hypoxia-inducible factor-1 plays a role in phosphate-induced vascular smooth muscle cell calcification **(PMID: 27470678)**, while their *in vivo* studies show that endothelin type A receptor blockade attenuates vascular calcification, stiffness, and inflammation in rat models of CKD-related medial vascular calcification **(PMID: 28005706)**.

Through these clinical and experimental approaches, they aim to continue their work for a better understanding of the hemodynamic consequences of arterial remodelling in CKD, and their underlying mechanisms related to bone mineral metabolism and ion transport systems.

Hypertension in Pregnancy

For more than 40 years, many clinical researchers at Université Laval (JM Moutquin, JC Forest, Y Giguère, E Bujold) have been interested in different aspects of hypertension during pregnancy, mainly in biomarkers for predicting preeclampsia. They were pioneers in demonstrating, as early as the 1980s, that it was possible to identify women at risk as early as the first trimester by measuring blood pressure. Subsequently, they have periodically demonstrated that the addition of different variables, ultrasound, biochemical and biophysical, could also contribute to the early detection of gestational hypertension and preeclampsia. In 2009, **Dr. Bujold** and his doctoral student Ms. Stéphanie Roberge made a major discovery by demonstrating, with the help of systematic reviews and targeted meta-analyses, that aspirin at adequate doses and initiated at the end of the first trimester allowed the prevention of preterm and severe preeclampsia **(PMID: 20664402)**. Based on these data; an international multicenter trial demonstrated that first trimester screening for preeclampsia combined with the treatment proposed by Dr. Bujold prevents the majority of severe preeclampsia. Since then, Dr. Bujold has been conducting large cohort studies (over 25,000 pregnant women recruited in the last 15 years) to better characterize the disease, using cardiovascular maternal evaluation, 3D and Doppler evaluation of the placenta, and maternal urine and blood proteomic profiling; and to develop new screening tools that would be available to all populations worldwide **(PMID: 25175335; PMID: 34682802; PMID: 32777265)**

Hypertension and cardiometabolic risk

Research initially launched at Université Laval by **Jean-Pierre Després** in 1986 and then pursued at the Quebec Heart and Lung Institute **(QHLI)** since 1999 has contributed to a better understanding of the links between visceral obesity and features of the metabolic syndrome including hypertension. Dr Després and an expanding group of colleagues have shown that the selective deposition of adipose tissue in the abdominal cavity was characterized by insulin resistance, atherogenic dyslipidemia and a proinflammatory state, which conspire to induce vascular dysfunction and atherosclerosis. Visceral obesity was not only reported to be associated with insulin resistance, type 2 diabetes and various cardiovascular outcomes (including valvular disease); other clinical conditions were found to be associated with this high risk adiposity phenotype such as sleep apnea, impaired cognitive function and dementia. In the cohort of middle-aged men of Quebec Cardiovascular Study, they reported, in several high-profile publications **(PMID: 8994419; PMID: 8596596; PMID: 9643858)**, that some features of the metabolic syndrome such as fasting hyperinsulinemia, an elevated apo B concentration and an increased proportion of small dense LDL particles were found to substantially increase risk of coronary heart disease, independently from traditional cardiovascular risk factors. A large group of basic and clinical investigators at the QHLI are conducting additional studies to understand the mechanisms responsible for individual differences in body fat partitioning and their influence on various features of cardiometabolic risk, the latter term having been introduced in the literature in 2006 **(PMID: 17167477)**.

Hypertension and lifestyle vital signs

At the **QHLI**, the team of investigators (P Poirier, E Larose, ME Piché, P Pibarot, P Mathieu, B Arsenault) interested by visceral obesity and features of the metabolic syndrome (including hypertension) were not only interested by the primary and secondary prevention of various cardiovascular outcomes, but they have also embraced the notion of primordial prevention and promotion of cardiovascular health. To do so, lifestyle modification approaches have been and are still tested using clinical and field studies

Québec Heart and Lung Institute.
Photo credit: IUCPQ

in order to investigate to what extent assessing and targeting so-called "lifestyle vital signs" could help manage non pharmacologically traditional risk factors such as blood lipids, glycemic control and blood pressure. First, lifestyle intervention studies conducted specifically in patients with visceral obesity and features of the metabolic syndrome (with and without type 2 diabetes and with/without coronary heart disease) have shown that it is indeed possible to substantially mobilize visceral adiposity, even in the absence of major weight loss. Furthermore, such loss of visceral adipose tissue was found to be accompanied by major improvements in features of the metabolic syndrome including a reduced blood pressure. Additional field studies assessing what we have called lifestyle vital signs (waist circumference as a marker of abdominal obesity, cardiorespiratory fitness, level of reported physical activity, and overall diet quality) have shown the remarkable effects of targeting these lifestyle vital signs on traditional CVD risk factors including blood pressure. Since 2019, considerable additional efforts are devoted by Dr Després and a new group of colleagues at **VITAM** (Centre de recherche en santé durable) to implement a so-called "Precision Lifestyle Medicine" approach in primary care.

Pulmonary Hypertension

Pulmonary arterial hypertension (PAH) is a progressive obstructive vasculopathy affecting the small pulmonary arteries (PAs) characterized by enhanced inflammation, vasoconstriction, and proliferation/apoptosis imbalance within the artery wall. During the past 15 years,

S. Bonnet and **S. Provencher** created the Pulmonary Hypertension Research Group (https://phrg.ca/en/) at the QHLI. The group is the repository for ongoing basic science, translational, and clinical studies on PAH and developed the largest cardiopulmonary biobank for PAH tissues (lungs, heart, skeletal muscle) and blood samples in Canada, allowing unique access to human tissues and fostering collaborations with colleagues from other centres in Canada and worldwide.


Sébastien Bonnet

Among their findings, they first confirmed the key role of epigenetics in the PAH pathobiology, contributing to the development and progression of PA remodeling and right ventricle (RV) dysfunction, including several microRNAs, long-non-coding RNAs, histone deacetylases. More recently, the key role of bromodomain-containing proteins in PA progression and RV dysfunction were confirmed in the first multicentre preclinical study ever performed in PAH and translated to the realization and publication of the first epigenetic-based clinical trial in PAH, with a subsequent phase 2 clinical trial currently ongoing (APPROACH trials, NCT03655704 and NCT04915300). They also provided key evidence of the numerous similarities shared by cancer and PAH at the cellular level. Among those, the group pioneered the demonstration that enhanced DNA damage and impaired DNA repair machinery are etiologically implicated in PAH progression. This hypothesis is currently tested in the first DNA damage-based clinical trial in PAH (OPTION trial, NCT03782818). Along with findings on the key role of aberrantly expressed transcription factors, these publications have contributed to the establishment of the "cancer theory" of PAH, which has now been accepted by the field. As secondary RV dysfunction remains the main driver for functional impairment and poor outcomes, the group has also been largely involved in RV-related biomarkers discovery and validation, as well as therapeutic interventions specifically supporting the overloaded RV. In addition, they have also significantly contributed to the concept of PAH as a multisystemic disease. Using both human tissues and animal models, they documented skeletal muscle and mitochondrial dysfunction, impaired systemic angiogenesis and premature BRD4-related coronary artery disease contributing to RV failure, which were subsequently shown as clinically relevant factors influencing patient outcomes. Finally, the group has led several seminal meta-analyses and empirical works on PAH clinical study design, confirming the added value of combination therapy in PAH long-term outcomes.

Taken together, their discoveries have significantly contributed to the field and is already impacting PAH patients' management and health.

Hypertension and the work environment

The prevalence of psychosocial stressors at work (PSW) is approximately 25% in countries from the Organisation for Economic Co-operation and Development, highlighting the public health importance of these exposures. A such, a multidisciplinary team of epidemiologists, clinicians, public health physicians and statisticians of the **Population health and optimal health practices axis** of the CHU de Québec-U. Laval research center (Chantal Brisson, Gilles R Dagenais, Mahée Gilbert-Ouimet, Alain Milot, Xavier Trudel, Michel Vézina), work together to understand the impact of PSW on cardiovascular disease (CVD) and its risk factors. They have set in motion and expanded two cohorts: the 24-year PROspective Québec (PROQ) Study on Work and Health (N=9188) and the 6-year post myocardial infarction cohort (N=972). The aim was to examine the effect PSW on 1) CVD risk factors (blood pressure (BP), arterial stiffness, biomarkers), 2) CVD incidence before and after retirement and 3) CVD recurrence after a first event **(PMID: 29534180)**.

Through these cohorts, they have contributed greatly to the impact of PSW on BP and CVD. Indeed, they have shown that men exposed to a cumulative job strain have higher systolic BP after 7.5 years of follow-up, an effect comparable to the magnitude observed for the effect of a sedentary behavior **(PMID: 16809603)**. In a subsample of subjects (N=2357), job strain and effort-reward imbalance were associated with short- and mid-term increases in ambulatory BP, and with a

higher prevalence of masked hypertension **(PMID: 20639388)**. In untreated participants with masked hypertension, 20% remained with the condition after a 5-year follow-up **(PMID: 24455208)**. In addition, among workers treated for hypertension, PSW exposure increased the prevalence of uncontrolled hypertension **(PMID: 28486615)**. They further showed the impact of long working hours on the prevalence of masked and sustained hypertension **(PMID: 31852264)**. Finally, in a separate quasi-experimental study, they showed that a preventive intervention targeting PSW had a beneficial effect on BP level and the prevalence of hypertension **(PMID: 33903279)**.

The group has also studied the adverse effects of PSW and long working hours on CVD events. In the post myocardial infarction cohort, PSW as well as longer working hours were independently associated with an increased risk of recurrent coronary heart disease with a magnitude comparable to that of current smoking **(PMID: 17925517; PMID: 21705691; PMID: 33795035)**.

After these major contributions to the field, they are now evaluating the impact of these factors on the incidence of coronary heart disease after 18 years of follow-up, using the PROQ study cohort.

INVITED PAPER

The ISH Kyoto meeting update

HIROSHI ITOH

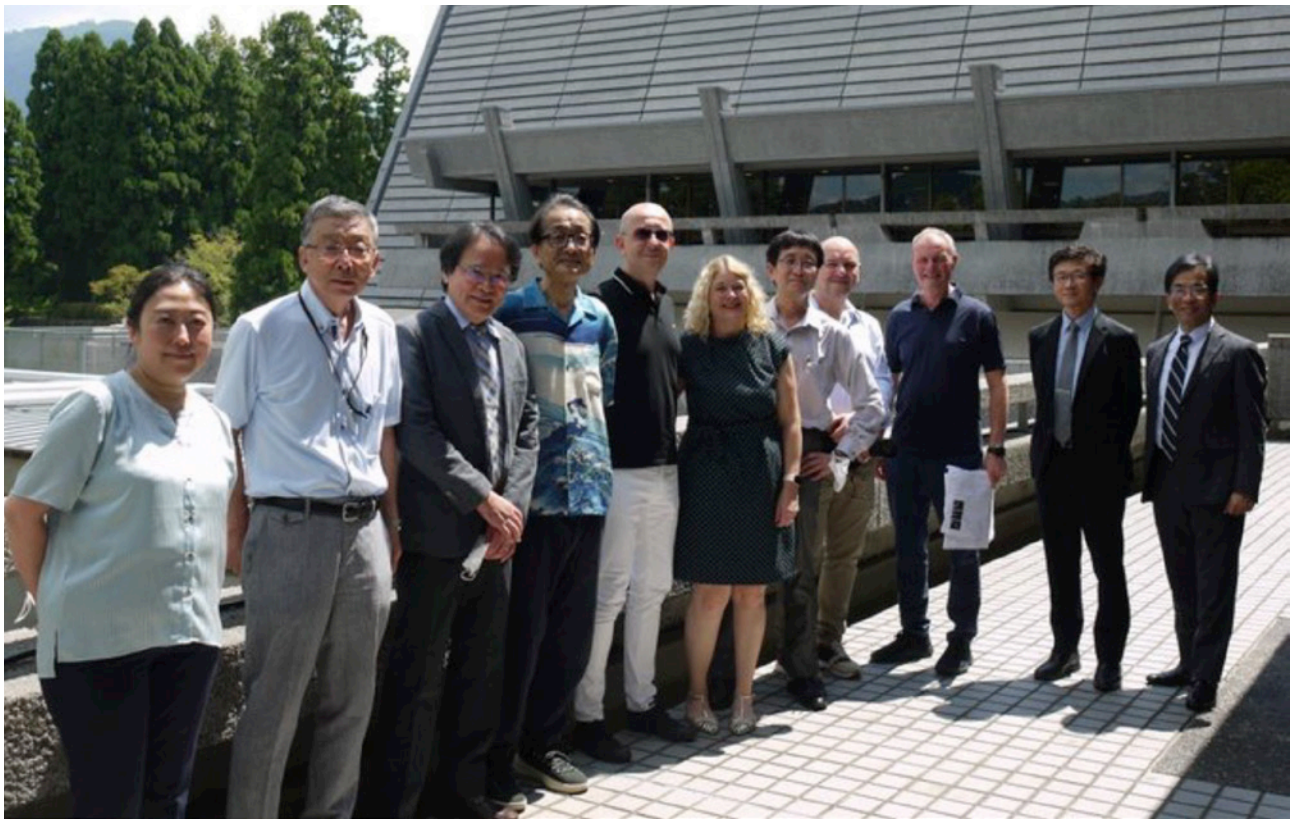
President, ISH2022 Kyoto scientific meeting

Vice President, ISH

There are just a month to go until ISH2022 KYOTO! The congress will be a hybrid event due to the ongoing COVID-19 situation, and members of the Local Committee are getting ready to welcome everyone there.

On August 19, members of the ISH Executive Committee—ISH President Prof. Maciej Tomaszewski, Secretary Prof. Bryan Williams, and Treasurer Prof. Fadi Charchar — made a site visit to the Kyoto International Conference Center where the congress will be held. It was also confirmed that there would be absolutely no problem with entry into Japan from the UK and Australia, and with the holding of an academic conference in Kyoto. Participants will be welcomed with lots of entertainment, including the Opening Ceremony and Gala Dinner, so please do not miss this opportunity to join us at the congress.

Finally, Japan is starting to ease the border control measures in September. Japan's government announced the plan to end the 72 hour pre-arrival COVID-19 test requirement for inbound travelers who have been fully vaccinated three times. There



might be other changes on the border control in September. Please visit our official website frequently to get the latest information.

October is one of the best months to visit the beautiful city of Kyoto because of the mild climate: little rain, neither too hot, nor too cold. We really hope to meet as many participants as possible in Kyoto.

Current information on entry into Japan, visa procedures, and ERFS applications is available on our website (https://www.ish2022.org/wp-content/uploads/2022/07/Immigration_Flowchart_2022.07.29.pdf). Please be sure to check it out.

Flow to Enter Japan

You are required to submit the documents below to the Japanese Consulate to apply for a visa.

- ERFS (Entrants, Returnees Follow-up System)
- Letter of Guarantee
- Invitation Letter
- Itinerary in Japan

1st STEP

Please make a registration to the ISH 2022 and create your My-Page.

2nd STEP

Please enter your details in the VISA Document Service System of the ISH 2022. (The system is scheduled to open in early August. We will inform you of the details via your My-Page.)

3rd STEP

The Japanese Society of Hypertension will email you the documents mentioned above later.

4th STEP

After receiving the documents, please submit them with your visa application form to the Japanese Consulate.

Restrictions on entry into Japan from the U.S. and Canada have also been eased (https://www.evisa.mofa.go.jp/index).

We are currently in the final stages of putting the program together. As already announced via social media and our website, the following people have been confirmed as Special Invited Speakers.

The program is built out a schedule full of exciting sessions on the latest developments in the field of hypertension. Now you can find the speakers of more than 100 attractive sessions on our website.

https://www.ish2022.org/scientific-information/scientific-program/

Please check it out and register for the ISH2022 Kyoto!

All of us here in the Local Committee look forward to seeing everyone at ISH2022 in Kyoto!


The Wisdom
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INVITED PAPER

When good intentions go wrong: Paracetamol formulations contain hidden sodium

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There are likely millions of people worldwide taking paracetamol on a daily basis. Paracetamol is one of the most commonly used over-the-counter painkillers used to treat aches, pains, or as part of cold and flu remedies. In the United Kingdom alone, there were in 2014 some 42 million paracetamol-containing medicines prescribed with a further 200 million packs sold over the counter.[1] This equates to about 6,300 tons of paracetamol sold each year in the UK with the figure for France close to 10,000 tons. Some paracetamol formulations contain large quantities of sodium, namely those that are typically indicated as 'fast-acting' or 'fizzy' and by taking these medications regularly, people are unknowingly increasing their risk for raised blood pressure and cardiovascular disease.[2]

In a recent paper by Zeng and colleagues in the European Heart Journal,[3] the authors compared the risks of incident cardiovascular disease and all-cause deaths among people who started to take sodium-containing paracetamol to those who started to take paracetamol, but without sodium. They used an electronic medical record database of approximately 17 million patients in the United Kingdom, and focused on people with hypertension and those without. In people with hypertension (N=151,398) and without (N=147,299) they consistently found that the use of sodium-containing paracetamol was associated with increased risks of cardiovascular disease and all-cause deaths, with the hazard ratio being 1.59 (95%CI 1.32-1.92) in those with hypertension and 1.45 (1.18-1.79) in those without hypertension. Risks across different cardiovascular outcomes, including myocardial infarction and stroke, were found in both those with and without hypertension.

It is important to realise that these paracetamol formulations contained a high amount of sodium, approximately 390 to 440 mg of sodium per tablet. If a person takes a full dose of paracetamol regiment, this would lead to over 3000 mg of additional sodium consumed per day – far exceeding the WHO daily limit of 2000 mg.[4]

For some time now, a reduction in salt intake has been considered a 'best buy'. Multiple national and international blood pressure guidelines, as well as the World Health Organisation, recommend that daily sodium intake should not exceed 2000 mg (~1 teaspoon of salt).[4] In turn, many government and non-governmental organisations advocate strongly for actions to reduce population sodium intake, with some interventions targeting public education, and industry reformulation of packaged foods among others. Most recently a global call to action was again published by the World Hypertension League and the International Society of Hypertension.[5] This is with good reason. The Global Burden of Disease study showed excess sodium intake to be among the leading dietary risks estimated to cause 3 million deaths around the world every year.[6] And a large, cluster-randomised trial recently showed that by lowering sodium intake (using a potassium-containing salt substitute with 25% less sodium chloride) not only lower blood pressure but also lower rates of stroke, major cardiovascular events and all-cause deaths.[7]

It therefore seems rather counterintuitive that millions of people are consuming large amounts of sodium unknowingly, while the World Health Organisation and many other organisations are

strongly calling for actions and awareness to lower sodium or salt intake. Note, that it is not only paracetamol formulations that contain sodium. This is also relevant to many other effervescent, dispersible and soluble fast-acting medications and vitamin pills that contain large quantities of hidden sodium, mostly being available over the counter (Table). For example, a single 5g sachet of effervescent antacids contain about 850 mg of sodium, and fizzy vitamins approximately 280 mg of sodium. In a study done in France, more than 1 in 4 of the general population who underwent medical check-ups had consumed 'fizzy' tablets in the past 30 days.[8] Nine in 10 of these were instances of self-medication, with paracetamol, aspirin, vitamins and betaine accounting for 95% of tablets used.[8]

What is also striking is that the paper by Zeng et al.[3] is not the first to demonstrate this. Their findings are highly aligned with previous similar papers, most notably a report done in 2013 by George and colleagues.[9] In following 1.3 million patients over 7.2 years that included 61,000 patients with an incident cardiovascular event and matched controls, they reported odds ratios for cardiovascular events consistent with those reported by Zeng and colleagues. There was also in the report an odds ratio of 7.18 (6.74 to 7.65) for hypertension in individuals exposed to sodium-containing drugs.[9]

With global calls for action to reduce salt intake, similarly these findings should not remain hidden. In an accompanying editorial,[2] we highlight that there is an immediate need to protect consumers against the risk of hidden sodium in over-the-counter medications. Perhaps the best approach is to require the mandatory labelling of all medications containing significant quantities of sodium with a front-of-pack warning label. Similar to general calls for action to reduce salt intake,[5] programs are required that raise public and practitioner awareness of the hidden sodium in medications, to educate about the need to avoid effervescent, dispersible, and soluble medicines in all but essential circumstances.

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Table. Sodium content of several over-the-counter medicines[10]

Medication		Amount of sodium (mg)
Antacids	(e.g. Alka-Seltzer), single sachet of powder or a tablet (weighing 5g)	850
Heartburn relief	(e.g. Eno, per 5g dose)	843
Soluble pain killers	(per tablet)	up to 500
	(Panadol soluble 500mg tablet)	425
Urinary alkalinisers	(sachet of Ural (4g)	644
	(sachet of Citravesent)	396
Fizzy vitamins	(Berocca effervescent tablet)	271–287
	(Redoxon effervescent tablet)	312

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AFRICAN VOICES

Introduction

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In this issue of Hypertension News, we continue with our African Voices section. This time three papers are presented, one discussing the history of ISH activities in Africa and two covering research topics on the prevalence and management of hypertension and associated risk factors.

We start with a paper by Robert Fagard, Emeritus at University of Leuven, Belgium. He gives a background on the activities that led to establishment of what is currently known as the ISH Regional Advisory Groups (RAGs), including one for Africa. The paper is focused on his decade-long role in ISH activities in Africa, during which teaching seminars were organised for medical doctors involved in the management and/or research in hypertension and hypertension-related domains. These seminars were carried out in Mozambique, Cameroon, Nigeria and the Democratic Republic of the Congo. Despite the challenges experienced in organising the seminars, the gains made by implementing ISH activities under Robert Fagard's leadership are still evident. With this work, Robert Fagard and the team that assisted him laid the foundation for the current activities of the Africa RAG, including the ISH African School of Hypertension.

The second paper is from Universidade Eduardo Mondlane, Mozambique. Here, Neusa Jessen and Albertino Damasceno discuss the burden of hypertension in Mozambique, a country with poverty disparities between regions and an under-resourced health system. The paper shows an increase in hypertension prevalence over the years, from 2005 and recently a high prevalence of hypertension in adolescents and youth. The paper highlights low awareness levels as one of the major concerns and the contribution of May Measurement Month (MMM) to the improvement in screening for hypertension in Mozambique.

Lastly, Tiny Masupe from the University of Botswana presents findings from a collaborative study carried out in a South African township. This study assessed yearly monitoring for disease risk factors and estimated the prevalence and determinants of disease complications among type 2 diabetes and hypertension patients attending the chronic disease management programmes. It was found that a significant proportion of patients had at least one disease complication. Overall, yearly monitoring for disease risk factors was poor, while blood pressure and weight were the best monitored risk factors.

The current state of hypertension prevalence and management in some African countries emphasises the need for continued efforts to provide education and training to those involved in hypertension management and/or research. Indeed, initiatives of the ISH, such as the Africa ISH RAG and MMM have and continue to make a significant contribution to overcoming some of the challenges in alleviating the burden of hypertension in Africa.

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AFRICAN VOICES

My 10 years of ISH activities in Africa – 2005 to 2015

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When I joined the ISH Scientific Council in 2000, I was very much surprised if not somewhat shocked by the discussion at my first Council meeting that the Society was going through some identity crisis, particularly with regard to the prefix 'International' and more specifically the apparent neglect of low and middle income countries (LMICs), which led to the foundation of the 'ISH Strategic Planning Group' in 2001. This think-tank proposed a number of recommendations to enhance the Society's contribution to antihypertensive and cardiovascular care in LMICs (Hypertension News, opus 5, 2004). Subsequently ISH founded the 'ISH LMIC Strategic Initiatives Working Group', the name of which was soon simplified to 'ISH LMIC Committee' (LMICC). At the Council meeting of 2004, and to my surprise, I was asked to chair this committee. Needless to say that the change of the emphasis from planning to practice would become the more difficult and demanding part of the whole enterprise but the sustained support of consecutive ISH presidents and council members has been of great help and encouragement throughout my 10 years of activities in LMICs. Because problems in LMICs differ from country to country or from region to region, four regional subcommittees were created, one of which concerned Africa. For practical purposes, I was mainly responsible for initiatives in Africa. An extensive 'Mission Statement' with immediately attainable goals was drafted and published in Hypertension News, opus 5, 2004. It is of note that the name of the LMICC has in the mean time been changed to 'Regional Advisory Groups' (RAGs) with subgroup 'RAG-Af' for Africa.

The major goal of the LMICC was to organise teaching seminars and workshops in LMICs. During my decade of activities in Africa, a total of seven ISH teaching seminars have been organised. The seminars were meant for medical doctors up to the age of 50 and residing in Africa, who were involved in the management and/or research in hypertension and hypertension-related domains. As summarized in the Table, seminars have been held in Maputo (Mozambique), Douala (Cameroon), Abuja (Nigeria) and Kinshasa (D.R. Congo). I am particularly grateful to my good friends and local co-organisers A. Damasceno, D. Lemogoum, B. Onwubere and J.R. M'Buyamba-Kabangu, who were responsible for the local organisation and for identifying potential candidates for attendance as well from their own country as from neighboring countries. Furthermore, the International Forum for Hypertension Control and Prevention in Africa (IFHA) was involved in all of the seminars. During two days a mixed European/African faculty of usually eight experts in hypertension lectured on various aspects of hypertension and related topics. These subjects were presented and discussed in general and with implications for Africa. Two additional lectures were given with an eye on research, that is 'How to set up an epidemiological study?' and 'How to set up an intervention trial?'. The World Health Organisation (WHO) delegated S. Mendis for the first cycle of four seminars to present and discuss WHO recommendations for LMICs. Finally young investigators participating in the seminar presented abstracts on hypertension research in Africa, based on a call for abstracts, followed by discussion with the international faculty. The language of the seminars was alternatively English and French. The number of registered participants ranged from 28 to 77. Approximately half of them were citizens from the host country and the others were residents from a total of 18 other African

Maputo 2006.

Douala 2008.

Abuja 2009.

Kinshasa 2010.

countries. Detailed reports of several of the seminars have been published in the Journal of Hypertension (2007,25:1521;2008,26:2244;2010,28:635) or Hypertension News (2010,opus22; 2011, opus28; 2013, opus33).

It may be clear from the Table that the organisation of the seminars was not cheap. The costs in EUR or USD in the Table are an approximation of the total costs, after converting the payments in various currencies, including local currencies, to EUR or USD. The costs comprised local organisational costs, accomodation costs of participants and faculty, and travel costs of participants and African faculty. It is of note that reliable and safe travel between and within African countries was quite expensive. As written in an original ISH document with regard to activities in LMICs, it was clear from the start 'that the ability of ISH to attain their ambitious goals would require funding and that, with its limited financial means, the Society must generate new resources from outside sources to fund these initiatives which are currently considered a central element in the ISH mission.' Apart from the input of ISH in the course of the years, approximately one third of the costs, I was happy to obtain support from WHO, the World Heart Federation, the European and Belgian Societies of Hypertension, the International Society of Nephrology, the University of Leuven, local African societies and organisations and from a number of corporate sponsors, by means of a financial contribution and/or by payment of travel costs of European speakers. I would have loved to end my term as chair of the LMICC with an eight seminar in Kinshasa in 2015 to complete the second cycle of four seminars, but regrettably the organisation had to be cancelled because of insufficient external support, highlighting the importance of support from outside sources.

Unfortunately, one should also be prepared for 'adverse events' and disappointments; a summary of some of them may be informative. To be sure that international flights and air travel within African countries would be reliable and safe, flights were arranged as much as possible by a travel agency in Leuven. It was therefore quite disappointing that tickets issued abroad were not accepted in Nigeria for Nigerian participants in the

first seminar in Mozambique, so that new tickets had to be bought locally, at double the cost... At another seminar abroad Nigerian participants had to change planes in Johannesburg, for which they had to leave the airport for an overnight stay in a nearby hotel. However, this was not allowed because they did not have the required visa for South Africa; the airport closed for the night and they had to return home the same day without attending the seminar. At one of the early seminars local expenses were unexpectedly high and in fact partly redundant. This experience prompted me to work out a set of rules and regulations for the organisation of the seminars, including a detailed and strict budget proposal. One pharmaceutical company supported the seminars by a gift of 100 excellent stethoscopes to be offered to participants. It was quite frustrating that a few of these valuable stethoscopes had to be handed over to a customs officer before being allowed to enter the country. At several seminars unregistered participants showed up; they were of course welcome to attend but caused problems for logistics, catering and costs.

I would like to finish this report with some of the other goals for LMICs as outlined in the original Mission Statement. The low number of members from LMICs was of great concern to ISH, at least partly due to the high cost of membership and mandatory subscription to the Journal of Hypertension. In 2006 an agreement was signed with the publisher to enable residents from low income HINARI countries to pay a modest membership fee and have free on-line access to the journal. Another aim was to support meetings on hypertension by other organisations and societies in LMICs and include active participation by ISH members, which happened in a number of meetings in Africa.

I hope that this report of my experiences, most of them excellent and rewarding, some of them a bit sad and disappointing, may be of help for the future organisation of ISH activities in LMICs, particularly in Africa.

Table. Details on the seven seminars organised by the ISH Low and Middle Income Countries Committee in Africa in the period 2005-2015.

Site	Date	Local organiser	Number of registered participants (from host country)	Number of lectures/ abstracts	Costs (x 1000)	Language
Maputo, Mozambique	21-22/09/2006	Damasceno A.	28 (13)	14/11	35 EUR	English
Douala, Cameroon	13-14/03/2008	Lemogoum D.	50 (30)	15/13	52 EUR	French
Abuja, Nigeria	24-25/09/2009	Onwubere B.	44 (26)	17/26	85 USD	English
Kinshasa, D.R. Congo	06-07/05/2010	M'Buyamba-Kabangu J.R.	77 (67)	17/18	90 USD	French
Maputo, Mozambique	06-07/10/2011	Damasceno A.	70 (51)	19/18	57 USD	English
Douala, Cameroon	25-26/10/2012	Lemogoum D.	33 (18)	16/13	54 EUR	French
Abuja, Nigeria	25-26/10/2013	Onwubere B.	50 (47)	16/17	74 USD	English

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AFRICAN VOICES

The high and increasing burden of hypertension in low resource settings – the case of Mozambique

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Hypertension remains the single most important attributable risk factor for global mortality. In sub-Saharan Africa (SSA) hypertension was found to be the main risk factor for several important public health problems including heart failure[1] and stroke.[2] Even so, the availability of reliable data remains scanty among SSA countries, particularly high quality and follow up studies using the same methodology. As such, it is of utmost importance that such studies are conducted, for a better characterization of the problem, evaluation of trends and comparisons with other countries. The World Health Organization (WHO) provides the STEPwise approach to Noncommunicable Disease (NCD) Surveillance (STEPS), a surveillance tool with standardized questions and protocols that allows countries to collect internationally comparable data.[3]

Mozambique is a low-income SSA country with poverty disparities between regions within the country (the north and rural areas perform worst economically) and a weak health system which is still overburdened by communicable diseases. Even so, the population is growing fast, life expectancy is increasing and the country is going through a process of rapid urbanization and associated dietary and lifestyles changes. Hence, risk factors for hypertension, other chronic conditions and related complications are increasing. Monitoring the trends of the prevalence of hypertension in the country and implementing strategies to curb its rise, must be a priority.

Two surveys were conducted in Mozambique, both based in the WHO-STEPS methodology and using a representative sample of the population.[4]

As shown in Figure 1, in a 10 years period, the prevalence [95% Confidence Interval (95% CI)] of hypertension (for the age group 25-64 years old) increased significantly from 33.1% (28.2-38.0) to 38.9% (35.9-41.9), p=0.048. On the other hand, no significant change was observed in the proportion [% (95%CI)] of hypertensive patients aware of their condition [14.8 (10.5 -19.1) in 2005 and 14.5 (11.2-17.8) in 2014/15; p=0.914], treated [51.9 (42.8-61.0) in 2005 and 50.1 (42.1-58.0) in 2014/15; p=0.770] and controlled [39.9 (28.2-51.6) in 2005 and 44.5 (32.8-56.3) in 2014/15; p=0.587], which remained very low.

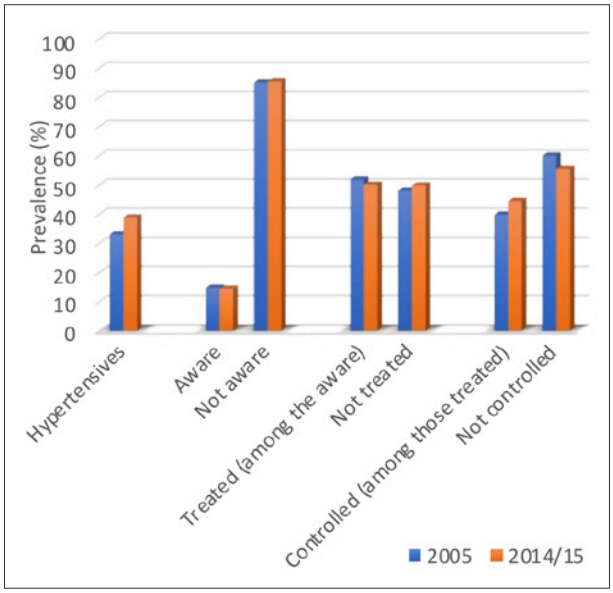

Figure 1. Changes in the prevalence of hypertension, awareness (and proportion of those not aware), treatment (and proportion of those not on treatment) and control of hypertension (and proportion of those not controlled) among the Mozambican population aged 25 to 64 years, in 2005 and 2014/15.

Of not, in the same period, there was a right shift in the mean blood pressure (BP) of the Mozambican population, with a significant increase of 4.3 mmHg in the mean diastolic blood pressure and a nonsignificant increase of 2.5 mmHg in the mean SBP.[4]

The last STEPS survey (2014/15) also raised, for the first time in the country, information regarding adolescents and young adults aged 15 to 24 years old, showing a high prevalence of hypertension in this fraction of the population [13.1% (95% CI: 9.8– 16.4)].

Importantly, as clearly shown in the Figure 1, the proportion of the Mozambican population not aware of own hypertensive condition is impressively high, highlighting the huge burden of undiagnosed hypertensives in this population. The fragile health system of the country is not prepared to face the weight of hypertension and related complications. There are significant deficits, from lack of sphygmomanometers in many health facilities to weak preparation of health professionals to deal with these conditions. And, although experiences from more developed countries show that universal health coverage is crucial to enhance hypertension care, Mozambique is still far from reaching this sustainable development goal (SDG target 3.8). Also, the silent nature of hypertension contributes to its disregard, particularly by people facing extreme poverty and low access to health care.

To increase awareness of hypertension, a paradigm change with task-shifting for greater and meaningful involvement of communities, should be pursued. In this regard, in 2017 the Mozambican Heart Association (AMOCOR) adhered to the May Measurement Month (MMM) project, a global initiative of the International Society of Hypertension to increase awareness of high BP. With this initiative, we have conducted the largest hypertension screening ever done in the country. In a cross-sectional survey, trained volunteers screened 4454 adults throughout the country and found 1371 hypertensives, most of them with uncontrolled BP.[5] This mass opportunistic BP screening acts as an inexpensive alternative to increase awareness of hypertension and also helps in expanding patient education regarding high BP.

Prevention and control of hypertension can contribute substantially to the achievement of the SDG target 3.4 on non-communicable diseases and should be a focus of greater attention in this developing country.

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AFRICAN VOICES

Prevalence of disease complications and risk factor monitoring among diabetes and hypertension patients attending chronic disease management programmes in a South African Township

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According to WHO data, approximately 27.4% of men and 26.1% of women in South Africa have hypertension[1], though a higher prevalence of up to 60% has been reported[2]. Studies have estimated a high prevalence of diabetes complications in South Africa including any grade of retinopathy (55.4%), proliferative and pre-proliferative retinopathy (15.6%), cataracts (7.9%), peripheral neuropathy (27.6%), absent foot pulses (8.2%), and amputations (1.4 %)[3]. Diabetic retinopathy was the most common complication[4].

South Africa has implemented several policies to guide self-management programmes for quality chronic disease care. One such policy was the establishment of chronic disease management programmes (CDMPs) called "clubs," aimed at equipping patients with the necessary knowledge and self-management skills to reduce disease progression and complications[5]. In these clubs, stable patients get access to medication, receive monthly blood pressure and glucose monitoring, and health education on self-management of lifestyle disease risk factors. However, the effectiveness of these clubs remains unclear in terms of chronic disease monitoring and halting the progress to complications.

We conducted a cross-sectional survey combined with a ten-year retrospective patient records analysis (2009-2018), to assess yearly monitoring for disease risk factors and estimate the prevalence and determinants of disease complications among Type -2- diabetes and Hypertension patients attending CDMPs in a peri-urban township in Cape Town, between 2018 and 2019. The study consisted of 379 patients aged between 18-74 years; diagnosed with T2D/ HTN for at least six months, living in Khayelitsha and attending the CDMP at the selected facility for at least six months.

Most patients (n=372; 98%) had HTN, with 159 patients (42.0%) having both T2D/HTN. Majority were female (n=308; 81.3%); mean age was 55 (+/-10.4 years). Two fifths (n=160; 42.2%) had no or primary level education, and over half were unemployed (n=210; 55%). Nine in ten (n=336; 88.6%) had a BMI ≥ 25. A fifth (n=73; 19.3%) had consumed alcohol while 48 (12.7%) had used tobacco products in the last 12 months. Nearly half (n=173; 45.6%) scored above 75% on the T2D/HTN knowledge questionnaire, and 294 (78%) reported good to complete control over their T2D/HTN.

Of the 372 available medical records, 361 (97.0%) were eligible for review. Most patients (n=351; 97.2%) were prescribed antihypertensive medication in 2009, increasing yearly to 358 (99.1%) by 2018. There were 56 (35.0%) T2D patients prescribed chronic diabetes medication and/or insulin in 2009, increasing yearly to 150 (94.3%) by 2018. Risk factor monitoring was best for weight (86.6%) and blood pressure (87.7%). Patient's annual weight monitoring increased from 11.9% in 2009 to 86.6% in 2018, and blood pressure monitoring increased from 21.2% in 2009 to 87.7% in 2018. Annual advice on foot care was 1.7% in 2010 (vs. 3.9% in 2018) and eye screening (0% in 2009 vs. 2.0% in 2018) [figure 1].

Overall, complications were reported by 172 (45.4%) of patients. Nearly one quarter (n=84; 22%) of patients reported one complication, 84(22.2%) reported two complications, and 35(9.2%) reported three or more complications. There were 73 (20.2%) patients with a complication documented in their medical records. Medically recorded complications ranged from 11.1% (1 complication) to 4.2% with 3 or more complications.

The most common complications reported by participants were eye problems (n=125; 33%) and poor circulation (n=104; 27.4%), while the least reported was amputation (n=3; 0.8%). From the medical records, peripheral neuropathy (n=62; 16.4%) was the most prevalent complication, while amputation (n=4; 1.1%) was least prevalent.

Self-reported occurrence of complications was positively associated with age, female gender and having tertiary education, Perceived illness control was negatively associated with occurrence of medically recorded complications. Diabetes knowledge showed a weak positive association with the occurrence of medically recorded complications.

Figure 1: Annual risk factor monitoring (medical records audit 2009-2018)

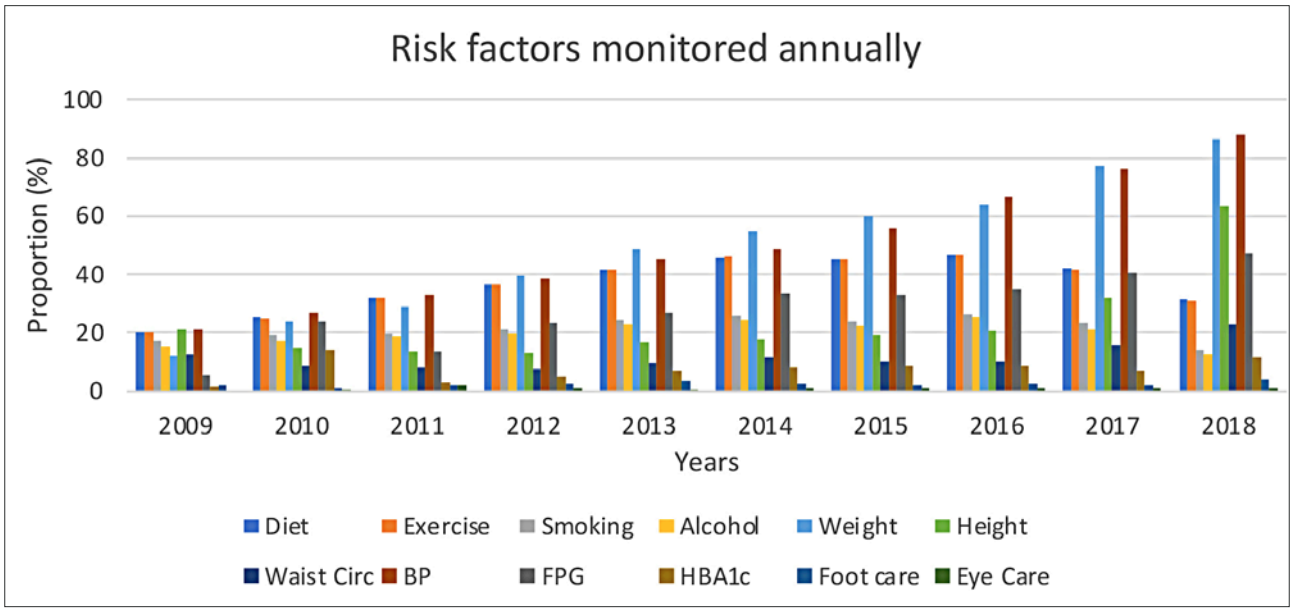

Table 1: Proportion of self-reported and medically recorded complications

Number of complications	Self-reported (n=379) n (%)	Medically recorded (n=361) n (%)
0	207 (54.6)	288 (79.7)
1	84 (22.2)	40 (11.1)
2	53 (13.9)	18 (5.0)
≥ 3	35 (9.2)	15 (4.2)

In conclusion, a significant proportion (45%) of patients had at least one disease complication while medically one fifth (20%) had medically recorded complications. There was overall, poor yearly monitoring for disease risk factors in the CDMPs especially foot and eye care. Blood pressure and weight were the best monitored risk factors. However, nearly 90% of the patients were overweight/obese. To provide optimal care, CDMPs should make patient self-management a core of their strategies, strengthen and evaluate risk factor monitoring and effectively address identified risk factors such as obesity.

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EARLY CAREER RESEARCHERS

Introduction

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I am thrilled to present these three papers discussing very distinct areas of hypertension. I am sure you'll agree that these showcase the high standard of work being carried out by early career investigators in this community.

Matías G. Zanuzzi from Hospital Privado Universitario de Córdoba, Argentina presents an interesting article on hypertension in HIV. He highlights how cardiometabolic disease is becoming increasingly common in people living with HIV due to the increased lifespan which is linked to early diagnosis and use of lifesaving treatment therapies. He presents data on the atypical circadian blood pressure patterns in these patients and highlights the potential importance of routine ambulatory blood pressure monitoring. His work contributes to a greater understanding of the complexities of blood pressure in HIV patients to work towards increasing their healthy life years.

With high blood pressure is a leading cause of chronic kidney disease, Kaori Hayashi from Keio University School of Medicine, Tokyo, Japan explores a novel hypertension treatment strategy based on DNA methylation in the kidneys. Karori's work suggests that assessing DNA methylation in the kidneys or blood could be used as a novel marker for hypertension-related kidney damage and to predict future renal function. Her work offers the potential for targeted preventive strategies in patients with high blood pressure who have poor kidney prognosis.

Finally, Akram Abolbaghaei from University of Ottawa, Canada provides a comprehensive introduction to the field of extracellular vesicles. Against the backdrop of his own research on protein composition of extracelluar vesicles in pregnancy with type 1 diabetes, he discussed the in vascular complications associated with type 1 diabetes and the role of large extracellular vesicles and the potential for them to be used as biomarkers of vascular health.

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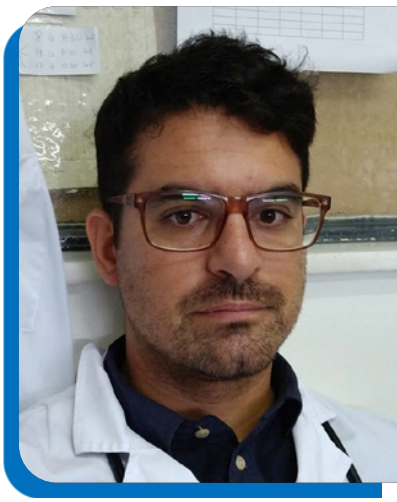
EARLY CAREER RESEARCHERS

Isolated Nocturnal Hypertension in People Living with HIV



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The increased life expectancy of people living with HIV (PLHIV) resulting from the widespread use of highly active antiretroviral therapy (HAART) has resulted in a shift in the morbidity and mortality pattern of PLHIV from AIDS-related opportunistic infections towards age-related chronic diseases, including hypertension (HTN), other cardiometabolic risk factors and consequential cardiovascular diseases (CVDs).[1]

Hypertension, the leading risk factor for mortality worldwide, is a growing problem in HIV-infected adults. In our study, the prevalence of clinic HTN was 33.5%, increasing up to 44% after the 24h ambulatory blood pressure monitoring (ABPM)[2]. In addition to better estimating the prevalence of hypertension, the use of ABPM offers the possibility of identifying different blood pressure (BP) phenotypes. In most of the studies that have performed ABPM in HIV-infected patients, only altered patterns of the circadian rhythm of BP, such as non-Dipper pattern, were reported. In our population, this pattern was present in 51.6% of the patients.

Although previous research has shown that altered BP patterns were associated with target organ damage and cardiovascular outcomes, many authors have demonstrated the advantage of nocturnal hypertension over the non-Dipper pattern[3]. Isolated nocturnal hypertension (INH) is a phenotype that can be identified only by using ABPM, but not by clinical BP measurements. It is characterized by elevated nocturnal BP in the presence of normal daytime BP and, when this condition is accompanied by normal clinical BP values, it can be considered a subtype of masked hypertension.

There are several potential mechanisms responsible for nocturnal hypertension in PLHIV. HIV infected patients have high levels of psychological stress and stigma, associated with sleep disorders. Autonomic dysfunction with a predominance of the sympathetic system. Some endocrine abnormalities associated with HIV, such as hypercortisolism and hyperaldosteronism. Mitochondrial toxicity, oxidative stress, lipodystrophy and insulin resistance associated with certain HAART regimens may lead to a higher prevalence of these phenotypes. In addition, even in HIV infection virologically suppressed with HAART, the incomplete immune restoration is related to greater immune activation that favors systemic inflammation, promoting vascular stiffness and atherosclerosis[4].

In our study, the prevalence of isolated nocturnal hypertension was 16.7%, a phenotype that represented 56.3% of patients with masked hypertension. Although these results were similar to other publications, the prevalence of HNA seems to be conditioned by race. In a study of HIV adults[5], African Americans had higher sleep BP and a higher prevalence of sleep masked hypertension compared with whites (58% vs 24%; p= 0.021). This can be explained by the salt sensitivity mechanism already known in the black race, that was also demonstrated in HIV-infected patients[6]. This mechanism was responsible for BP modulation and, consequently, higher nocturnal BP values with a greater proportion of non-Dipper pattern.

The diagnosis of INH is important, not only because it is at least twice as likely to develop sustained hypertension compared to those with normal blood pressure, but also because of its association with a worse cardiovascular prognosis[7]. Despite its importance, there are some controversies. On the one hand, the long-term and short-term reproducibility of isolated nocturnal hypertension is poor in the only two investigations exploring this issue. On the other hand, it seems that chronotherapy represents the best treatment which provides appropriate reduction in nocturnal BP, as well as conversion from unfavorable BP patterns to physiological BP pattern[8].

In summary, hypertension is common in HIV-infected patients and is likely due to a combination of traditional risk factors, HIV-specific factors, and HAART. The routine use of ABPM would have a particular clinical relevance among HIV infected patients, in whom an accurate diagnosis of hypertension would modify their CV risk.

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EARLY CAREER RESEARCHERS

Kidney DNA methylation in hypertension

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Chronic kidney disease (CKD) is increasing worldwide, mainly due to an increase in hypertension and diabetes, which lead to hypertensive nephrosclerosis and diabetic kidney disease, respectively. Accumulating evidence has suggested that epigenetic mechanisms are involved in the pathogenesis of lifestyle-related diseases such as diabetes and hypertension as well as cancers. DNA methylation is one of the epigenetic mechanisms regulating gene expression. Recent reports have demonstrated that DNA methylation status may be a promising factor both as a marker and as a novel therapeutic target for kidney damage. This short review summarizes recent advances in altered DNA methylation, focusing on hypertension-related kidney damage, and discusses future expectations.

Recent epigenome-wide analysis has revealed that DNA methylation in blood cells is associated with kidney function. A meta-analysis of these studies showed that eGFR was associated with changes in DNA methylation of pathways related to hemostasis and blood cell migration, and the urinary albumin/creatinine ratio was associated with changes in DNA methylation of pathways related to immune cell activation and response[1]. Just under half of the patients analyzed in this meta-analysis had hypertension, suggesting an association of DNA methylation changes with hypertension-related kidney damage.

In addition, kidney DNA methylation are related to kidney function, which is evaluated by analyzing kidney biopsy samples[2]. Moreover, a recent study using samples obtained during kidney transplantation showed that kidney CpG hypermethylation in pretransplantation specimens predicted chronic injury, particularly fibrosis and glomerulosclerosis, 1 year after transplantation[3]. These results indicate that kidney DNA methylation may become a novel marker for evaluating kidney damage.

We have recently reported that altered DNA methylation in the kidney is associated with DNA damage[4]. Then, we tried to evaluate kidney DNA damage and the expression of DNA methylation modulators using urine-derived cells in patients with hypertension and diabetes[5]. As a result, DNA damage in glomerular podocytes is increased in patients with hypertension and diabetes compared with patients with hypertension alone. On the other hand, DNA damage in proximal tubular epithelial cells was increased in patients with hypertension, with increased expression of the DNA methyltransferases DNMT1, DNMT3A, and DNMT3B and the demethyltransferase TET1-3, suggesting that hypertension increases DNA damage in proximal tubular cells, which may activate DNA methylation and demethylation modifications. Based on these results, we expect that the evaluation of DNA damage and the expression of DNA methylation modulators using a noninvasive method such as the analysis of urine-derived cells may be useful to evaluate kidney damage.

Hypertension-associated kidney damage is a major contributor to the increase in CKD, and early prediction of renal prognosis would lead to earlier initiation of renal protective therapy and management of complications, which could improve prognosis. The DNA methylation status in blood or kidney samples may reflect not only current renal function but also future renal function. Therefore, the analysis of DNA methylation in blood or kidney samples may lead to novel treatment strategies, including novel therapeutic targets and prognostic markers, for hypertension-associated renal damage. The mechanisms determining the sites of DNA methylation changes and their involvement in detailed pathological conditions remain unknown, and further research advances are expected.

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EARLY CAREER RESEARCHERS

Proteome of large extracellular vesicle in type 1 diabetes

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Type 1 diabetes (T1D) is a chronic autoimmune disease affecting almost 35 million people that is associated with significant cardiovascular risk[1]. Despite significant progress in the understanding of the pathophysiology of this disease, the molecular alterations that mediate the initiation and progression of cardiovascular disease in diabetes are not well understood and early markers are lacking. Therefore, it is important to develop biomarkers for early detection of injury and identify key molecular signalling processes driving the cardiovascular complications of T1D.

In recent years, attention have been targeted to the rapidly evolving research area of extracellular vesicles (EVs) as vehicles of intercellular communication. EVs are membrane-enclosed entities lacking replicative capacity that are released into the extracellular environment and involved in cell signaling[2,3]. They contain diverse content from their cell of origin including miRNA, mRNA and membrane/cytosolic protein[1,2]. They can be measured in biological samples such as urine, blood/plasma, ascites, sputum etc.[2]. A subclass of large EVs historically termed microparticles/microvesicles are ~100-1000 nm in size and shed from the surface of cellular membranes under stress conditions [2]. Because EV studies typically use size as the primary descriptor and do not directly verify subcellular origin, recent guidelines suggest that ~100-1000 nm vesicles should be referred to as "medium/large EVs" (L-EVs, historically termed microparticles) and ~20-100 nm vesicles as "small EVs" (S-EVs, historically termed exosomes)[4].

Accumulating evidence indicates that L-EVs are present in blood at low levels under physiological circumstances and at higher levels in various pathological states such as cardiovascular and metabolic disorders[2]. In particular, in both type 1 and 2 diabetic patients, studies have consistently observed elevated levels of circulating L-EVs (particularly endothelial EVs)[5]. These findings have also been replicated in both animal and cellular models that mimic high glucose or diabetic conditions[6]. In addition to the levels of L-EVs being altered in hyperglycemic conditions, both *in vivo* and *in vitro* studies have also suggested that the content of L-EVs can be affected under similar conditions. Extensive research has been conducted into the effect of high glucose and diabetic conditions on the molecular composition of L-EVs. Understanding how the content and function of L-EVs change in such environments may provide new insights into the etiology of diabetic complications.

The unbiased assessment of protein changes in diabetes could lead to the identification of dysregulated signaling responsible for diabetic complications. In this regard, Do Nascimento de Oliveira and colleagues previously conducted a proteomic study to identify candidate biomarkers associated with T1D and investigate the differential expression of serum proteins in plasma of patients with T1D[7]. T1D was associated with the upregulation of six proteins including prothrombin, alpha-2-macroglobulin, apolipoprotein A-II, β2 glycoprotein I, Ig alpha-2 chain C region and alpha-1-microglobulin and down-regulation of two proteins (complement C4 and pregnancy zone protein)[7]. Such proteomic profiling of plasma is a powerful tool for the identification of altered biochemical pathways and biomarkers of disease states. However a limitation is the complexity of the protein composition and uncertainty regarding origin of differentially expressed proteins[9]. Assessment of EV protein composition

may therefore provide greater insights given their ability to reflect the (patho) physiological status of their cell of origin.

In this regard, Casu and colleagues have conducted a study on patients with T1D to uncover the correlation of circulating EVs cargo with key clinical features. They identified a total of 181 differentially expressed EV proteins and 15 differentially expressed EV phosphoproteins. Gene Ontology analysis revealed enrichment in proteins associated with platelets, neutrophils, immune response functions, prion disease and neurodegenerative diseases. Downregulated EV proteins were involved in regulation of monocyte differentiation and MHC class II signaling[8]. While these observations require confirmation, analysis of proteomic signatures of EVs may aid in understanding of pathobiology of T1D and its complications.

We recently conducted a study to quantify circulating L-EVs in pregnant women with T1D and to examine associations between EV levels, continuous glucose measures, and pregnancy outcomes[1]. In this study we observed that high levels of circulating endothelial or platelet EVs at baseline were associated with increased risk of neonatal intensive care unit admission and hyperbilirubinemia. The data suggest that circulating EV levels may be a biomarker of vascular health and predictor of adverse outcomes in T1D in pregnant women. However, assessing key molecular pathways impacted by diabetes in pregnancy may better inform pathogenic mechanisms. Several proteomics studies have been conducted to identify EV protein composition in non-pregnant individuals with T1D, however, no studies have looked at this in pregnancy.

I am actively working to address this knowledge gap, assessing the protein composition of circulating of L-EVs in well-controlled vs poorly-controlled glucose in pregnancy. We anticipate the identification of novel molecular alterations associated with poor glucose control. Since the vast majority of L-EVs are formed from stressed cells, assessing L-EVs protein may provide greater focus on proteins that are altered by high glucose-induced stress. The long term goal is to discover novel pathways associated with the pathogenesis of vascular injury in pregnant women with T1D.

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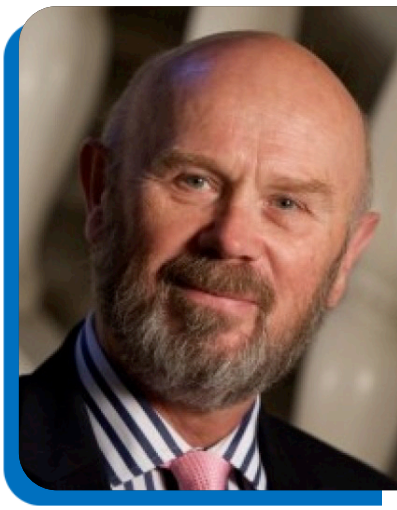
MMM REPORT

May Measurement Month 2022 breaks its country record



NEIL POULTER

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May Measurement Month (MMM), the annual global screening campaign that helps people to get their blood pressure (BP) checked, is celebrating a record-breaking number of countries participating in 2022.

MMM is now in its fifth year of screenings and this year 91 countries have participated, with four of them, Azerbaijan, Guinea-Bissau, Singapore and Uzbekistan, taking part for the very first time. With COVID-19 restrictions having been eased in most territories, the global MMM team is looking forward to this huge number of countries helping them to reach more people than ever. Home screening options, which were introduced last year during restrictions, will also now a permanent part of the campaign.

Screenings and data collection will continue until August, to allow countries who are still navigating restrictions to be able to contribute. MMM hopes that when all results are submitted the number of people screened will be one of the biggest yet.

This year MMM is also working with the European Heart Journal on a study from smaller countries who have collectively secured over 2000 participants across their MMM campaigns, which will be published in September.

MMM's collaboration with AF-SCREEN this year has recruited countries to begin atrial fibrillation screenings alongside blood pressure readings. This important sub-study will include results from 15 countries including Australia, China, Georgia, Nepal, Portugal and Poland.

Prof. Neil Poulter, CI of the MMM Campaign said "Although regular cardiovascular check-ups may happen in the UK, systematic blood pressure screening is not carried out in many countries. That's why May Measurement Month is so important. It gets into the press, people learn how to measure blood pressure, nurses and medical students get trained up, and it raises the profile of the whole condition. Hopefully with the data that we generate, we can persuade governments, and those who make healthcare decisions, to improve screening and management of raised blood pressure, and ultimately to prevent it."

For more information about how you can support, visit www.maymeasure.org

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MEANWHILE IN ‘HYPERTENSION MEWS’…

It is indeed an awfully hot summer in Sweden.
Don Pudro in a washbasin

Photo by Ms Li Winther, Stockholm
from the Lindholm family.

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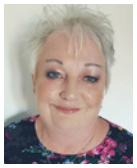

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