



# International Society of Hypertension HYPERTENSION NEWS

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## FROM THE EDITOR

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### Learning the Ropes. First out: meta-analyses

**Lars H. Lindholm**  
Editor, Hypertension News



#### Dear Member,

In this issue of Hypertension News (Opus 55), we introduce a new section called "**Learning the ropes**". As the first topic we address meta-analyses (pages 8-13). Today, the number of new, randomised, controlled trials in hypertension is limited, so we often fall back on meta-analyses in our discussions and guidelines. Meta-analyses are, however, not easy to make and interpret and you have to be very careful when doing so. I believe it was Franz Messerli who first said that "*a meta-analysis is like a bouillabaisse, no matter how much fresh seafood is added, one rotten fish will make it stink*". Stuart Spencer, however, countered with "*a spoonful of port may make a poor French wine drinkable*". In my interpretation, one really bad trial may totally ruin a meta-analysis, but one really good trial may lift a weak analysis.

We have invited Nadia Khan, Canada and Mattias Brunström together with Bo Carlberg, Sweden – all learned in the field of meta-analyses - to give us two papers from different perspectives, to which I have added a (maybe provocative) example of how difficult it can be when discussing beta-blockers as first-line treatment of hypertension. The new section is introduced by Thomas Kahan from our Editorial Team. We hope that these papers will help you to better understand some of the difficulties involved when making and interpreting meta-analyses.

In the previous issue of the ISH Newsletter (Opus 54), we started a new section called "News, Old News, and Fake News", with a first paper by Stephan Rössner entitled: *It ain't over until the fat lady sings*". We know that many of you opened and liked it. Hence we are now happy to publish a second paper (page 14) by the same author entitled "**I eat what I like and suffer thereafter**". Stephen Rössner begins his text: "*Martin Luther's health has been discussed extensively by psychiatrists and clinicians over the years – he clearly had a complex psychiatric history of neuroticism and, most likely, a manic-depressive condition, while also suffering from a somatic condition.....*"

The May Measurement Month project is now getting ready for its third, hopefully successful year. The project has so far reached 2.7 million

people and has identified over half a million people with uncontrolled hypertension. On page 16 you will find an update on this impressive undertaking by ISH.

The Deputy Editor, Dylan Burger has worked hard improving Hypertension News' distribution data and he has done very well indeed! In his text on page 5, you can see that the number of people who accessed the Newsletter has gone up from 1,385 (June 2018 issue) to a stunning 3,436 (November 2018 issue)! In the table, you can also see how this was achieved. Needless to say, we are delighted and want to thank everyone who has helped. Moreover, in this issue (page 22) there is a more personal "chat" on the use of Twitter in a medical context, by Anastasia Mihailidou.

Finally, it was a sad day, some months ago, when Ms Helen Horsfield told us that she was leaving our Secretariat to move away from London with her husband and son (see the President's thanks below). Helen has meant a lot, not only for Hypertension News but also for the whole Society. A couple of months later, Ms Charlotte Swindall told us that she was leaving too, for a year of traveling in Oceania. Both of them are brilliant ladies and we owe them a lot of thanks for their dedicated work. My work as an editor of Hypertension News has certainly increased after they left.

Have a good read.

Lars H Lindholm, Editor

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## MILLION THANKS TO HELEN

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*"Goodbyes make you think. They make you realize what you've had, what you've lost, and what you've taken for granted."* – Ritu Ghatourey

It is with a heavy heart that I am saying goodbye to Helen Horsfield, who has been at the helm of the ISH Secretariat for so many years. In fact, she started working with the ISH when joining Hampton Medical Conferences in September 2006 – right before the ISH Meeting in Fukuoka – and continued handling our affairs when the ISH moved business to the Conference Collective in April 2014.

Thus, for over 12 years we have gotten used to Helen's friendly face and rapid perfect responses to the ISH Council and members alike. She had indeed become the face of the Society! But with her family moving, we understand the personal circumstances that have resulted in her departure, and therefore I can only wish her all of the very best for the future.

Helen, you became a friend to many over the years - please know very well that you will be dearly missed!

Alta Schutte  
President of ISH



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## Alta Schutte

### ISH President 2018 - 2020

With January already a faint memory, I am delighted to say that the Society is taking the new year head on! The Council gained great momentum at the recent Council and ancillary meetings held on 1-3 February 2019 in London, and it is therefore my pleasure to share with you some of the great new initiatives.



- Members who attended my inaugural presentation as ISH President at the General Meeting in September 2018 in Beijing, or those who read the previous issue of Hypertension News, will remember that one of the main priorities for my term as ISH President is to establish **Worldwide Hypertension Guidelines**. It is particularly important to me that these new guidelines are relevant and widely applicable – *also* in lower and middle income countries. I am thus very excited to announce that the first meeting of the ISH Guidelines Committee also took place in London, lead by ISH Secretary, Thomas Unger. More details about these developments are in the *Secretary's Voice* section in this issue of Hypertension News.
- The Council Meeting kicked off with a spirited strategic session, lead by Richard Wainford, where all Council members were invited to put their heads together to identify short and long term goals for the Society. These will be shared with you in coming months, but an important outflow of this session was that the Council identified the need to redefine the Society's Vision and Mission to remain highly relevant. I am therefore pleased to share with you these updates:
  - ▶ **VISION:** Leading the drive towards the global elimination of raised blood pressure and its complications
  - ▶ **MISSION:** To reduce the global burden of raised blood pressure
- Serving as the **Membership** Chair of the Society from 2014-2018, issues related to membership remain close to my heart. Members come first, and it was therefore once again wonderful to see that during 2018 our membership numbers continued the upward trajectory seen in past years! All categories of membership expanded – from our Research Fellows in the New Investigator Network to Emerging Leaders and Professional members. Some important new additions include:
  - ▶ Implementation of the **Health Professional Affiliate** membership category. We now invite nurses, community health workers, pharmacists and related professionals to join the ISH Membership at a significantly reduced fee. Please refer to our website to join: <http://ish-world.com/membership/join.htm>. An important outflow of this category is anticipated for implementation later in 2019, namely online training modules on accurate measurement of blood pressure and management of hypertension.
  - ▶ I am pleased to mention that the Council approved the implementation of the new "**Fellow of the International Society of Hypertension**" (**FISH**). We wish to recognise and honour members of the Society who have distinguished themselves through excellence in clinical practice or research in the field of hypertension. FISH status will be a symbol of excellence, and will represent recognition by the ISH of our members' scientific and professional accomplishments in the field of hypertension. Members will be invited during 2019 to apply online. I am greatly looking forward to inaugurating our new Fellows of the ISH at the upcoming **Joint ESH-ISH Meeting** to be held in **Glasgow, Scotland from 29 May to 1 June 2020**. Please save the date!
- An important segment of the Council meeting was dedicated to updating (and modernising) the **ISH Constitution**. Please keep an eye out for upcoming emails where the Council would appreciate our membership's vote to approve these updates.
- With May fast approaching, the **May Measurement Month (MMM19)** team, lead by Neil Poulter, is actively preparing to involve even more countries and individuals in the coming months. The successes have been tremendous thus far, and the MMM network is an extremely valuable

component of the ISH. For more information, please refer to the piece on MMM19 in this issue of Hypertension News.

I trust that you are also enthused by these latest developments. I wish you all a productive 2019, and am looking forward to getting in touch with many of you during the coming months. And lastly, please do not hesitate to contact me with any ideas or suggestions ([secretariat@ish-world.com](mailto:secretariat@ish-world.com)).

With my very best wishes,



Alta Schutte

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## THE SECRETARY'S VOICE

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### Thomas Unger ISH Secretary

Last September, while still in Beijing at the ISH Biennial Meeting, Alta Schutte, the new President of ISH, asked me to become Secretary of the Society. I was not really craving for a new occupation but after the task of organizing the Beijing meeting was fulfilled, I considered this a new challenge and agreed not really knowing what it meant. Now, after half a year or so, I know better: It's quite a job, keeping you busy almost every day - including weekends. And I have learned to appreciate the tremendous efforts of my predecessor, Maciej Tomaszewski, as Secretary of the Society. Sure enough, when things are dark it only gets worse: right after the ISH Beijing 2018 congress, ISH lost its "secretariat", Helen Horsfield. She was extremely helpful in writing all the protocols, strategically reminding everybody of his or her duties within the Society, keeping track with the officers and members, especially the young investigators, being accessible whenever needed, in short: keeping the Society going. It took some time for Conference Collective, the Secretariat of ISH, to replace Helen. But since most things in life have two sides, the good one is that one learns again to do things by oneself without relying too much on others. So it happened to me.



Immediately after taking up office, I was confronted with two major tasks:

- ▶ Amendment of the ISH constitution
- ▶ Preparing ISH Hypertension Guidelines

The constitution of the Society was created years ago, during Lars Lindholm's presidency, from initial by-laws. It is now outdated in some respects. These relate mainly to the use of electronics in the voting procedures and a lack of clarity concerning the diverse rights and obligations of the different bodies of governance. Maciej Tomaszewski and Helen Horsfield had already begun to work on the amendments, I took over with Maciej's help. In recent weeks the Council has accepted the changes, which, after critical review by an attorney, will then be sent out to the members of the society for approval.

An even more challenging task is the creation of the new ISH Hypertension Guidelines. One may ask why ISH should come up with its own Hypertension Guidelines when there are abundant regional or national Guidelines

already present all over the world? This was indeed an issue that fuelled a lot of discussions. In the end it became clear that there is a need, not to compete with the more or less extensive, sophisticated Hypertension Guidelines already existing, but to create something special in line with the unique, global mission of ISH. An ISH Guidelines Committee was formed and has started its activities in high spirits after a first very productive face-to-face meeting in London. The Committee recognized that short, concise Hypertension Guidelines that – without being oversimplified - can be applied not only in the wealthier parts of the world but also in less affluent countries would be a welcomed addition. They will contain optimal as well as minimal requirements and simple recommendations on how to deal with the 'killer number one' in diagnosis and treatment that are still missing in other works. As the Chair of this Committee, I'm looking forward to yet another demanding challenge! However, with so many experienced, dedicated 'guideliners' on board, I'm sure this endeavour will be a success and will be an important cornerstone in our global fight against hypertension with all its disastrous sequelae.

Thomas Unger - [t.unger@maastrichtuniversity.nl](mailto:t.unger@maastrichtuniversity.nl)

## "DDD": DYLAN'S DISTRIBUTION DATA

### Dylan Burger

Deputy Editor, Hypertension News, Chair of ISH Communications Committee  
University of Ottawa, Canada



As highlighted in the previous issue, Hypertension News is in the midst of a dramatic expansion in readership. This is thanks in large part to the quality of the contributions that we are receiving as well as significant effort from ISH membership to help promote our flagship newsletter.

Beginning with this issue, the editorial board has asked that I track readership metrics in a section titled "Dylan's Distribution Data". The goal of this is two-fold: first, it will provide a transparent reference point for readers and contributors to know the reach of Hypertension News, second, it will provide a motivation to ensure consistent quality and continued growth from one issue to the next.

Below you will find the distribution data for this month, which represents a dramatic increase compared with the June issue. I would draw your attention particularly to the amount of content accessed through digital object identifiers (DOIs). In March 2018, Hypertension News began registering its content to DOIs through CrossRef. The aim of this initiative was to assist in referencing of our content and to increase visibility of all contributions to Hypertension News. As evidenced in this latest report, we are beginning to see the fruits of this enterprise. In the past 4 months Hypertension News has been accessed a total of 1793 times through DOIs (compared with 237 for the previous issue).

### Dylan's Distribution Data (November 2018-March 2019)

Total Estimated Readership	3436
Accessed via Twitter	262
Accessed via Facebook	222
Accessed via DOI	1793
Accessed via Web Site	1159

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## Weather and cardiovascular disease

**Thomas Kahan**

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There is seasonal variation in cardiovascular mortality with an increased risk for an acute coronary event during wintertime [1], and seasonal variations and ambient temperature are associated with the level of blood pressure [2,3]. Thus, seasonality of cardiovascular disease may be important to account for in studies. Whether cardiovascular disease is associated with other meteorological parameters than temperature and snow is, however, not well studied. A recent study by Mohammad and collaborators [4] now adds to our understanding on this.

This study [4] used information from the SWEDEHEART registry, a nationwide Swedish registry including all patients admitted to Swedish coronary care or intensive care units with symptoms suggestive of an acute coronary syndrome, and data from the Swedish Meteorological and Hydrological Institute, collecting data from 132 weather stations across the country. Information on air temperature, wind, duration of sunshine, air pressure, humidity, and precipitation was used. The study collected data from 1998 to 2013 (inclusive) and obtained data for 274 029 patients with an acute myocardial infarction and matched meteorological information at the time of the event (and 7 days before) in the same area as the hospitalization took place for the individual patient.

The authors show that the risk of an acute myocardial infarction was inversely related to temperature, with a 1 standard deviation (7.4 degrees centigrade) increase being associated with a 2.8% (95% confidence interval 3.3–2.3%;  $P < 0.001$ ) reduced risk of a coronary event [4]. Furthermore, low atmospheric air pressure, high wind velocity, and shorter duration of sunshine were also associated with higher risk of an acute myocardial infarction, whereas wind velocity was directly related to a coronary event.

Sudden plaque rupture in a coronary artery with subsequent thrombosis causes most acute myocardial infarctions. This acute event differs from hypertension, a condition with slow progression and generally no acute onset, although this may be the case in certain hypertensive emergencies. Hypertension is a risk factor for acute coronary disease. However, the association to stroke and to heart failure is stronger than to myocardial infarction. Thus it would be of interest to study how seasonal variations and weather conditions associate also with stroke and heart failure. High quality national event registries for both stroke and for heart failure are available (in Sweden and in other countries) and would make such analyses feasible.

Finally, the study by Mohammad and collaborators [4] also nicely show how large registries and available existing databases can be linked and used to study complex issues to provide new knowledge, complementary to other traditional study designs.

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## Thomas Kahan

### Hypertension News Team

It is my pleasure to introduce a new section to Hypertension News, which we have named *Learning the ropes*. To learn the ropes means to find out how to do something, learning how a particular task or job is done, to acquire an expertise. The idiom most probably is of nautical origin, where basic skills of handling the ropes on sailing ships were essential. The phrase has been known in standard English since the early 19th century, if not longer. We hope that this section will provide you with brief overviews and increase your knowledge on various topics relevant to accomplish your preclinical and/or clinical hypertension related work. Our aim is to have a translational touch. This is important, as translational research is added value for all of us, and – most importantly – to the benefit of our patients.



Much of the evidence in practised medicine is based on scientific studies. However, the results from studies addressing the same questions sometimes yield different results. There may be many reasons for this, but the ultimate challenge is to evaluate the collected results and make the right conclusions. Differences in study design may be important. Thus, treatment effects can not be safely estimated from observational data in many cardiovascular conditions, as association is not the same as causation. Also, results from observational data and uncontrolled studies may be subject to bias and confounding influence, and may be misleading [1,2]. This generally requires the findings from observational studies to be confirmed by properly designed randomized controlled studies. Having said that, however, randomized trials may be of a limited role when establishing the effectiveness of procedural interventions, where there are considerable barriers to conducting and implementing randomized controlled studies [3].

A systematic literature overview and meta-analysis is one way to strengthen the findings obtained from individual studies, in particular if those studies were of limited size or inconclusive, or if the studies yielded conflicting results. Whether studies with different design can be combined or not in such analyses is a matter of debate. Meta-analyses are sometimes considered to provide the strongest level of evidence, while others consider them misleading [4,5]. Thus, we considered it appropriate to start this new section *Learning the ropes* with three contributions on the potential difficulties in designing, performing, and interpreting meta-analyses; and more specifically in the context of blood pressure lowering therapy.

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## Should All Studies Swim in the Same Pool?

Mattias Brunström & Bo Carlberg

Umeå, Sweden

Meta-analyses have become increasingly popular since they were introduced in medical literature during the 80s and 90s, with publication rates increasing exponentially over time. Now, detailed instructions on how to design, conduct, and report meta-analyses are readily available, most notably from the Cochrane Collaboration. (1) The most important step in the meta-analysis process is the underlying systematic review of the published literature. An accurately performed systematic review ensures that all available evidence is considered and critically appraised before it is analyzed, which is essential for the meta-analysis to be valid.



The meta-analysis itself is a statistical method for pooling results from different studies. Instead of simply calculating the average treatment effect across studies, each study is assigned a weight corresponding roughly to its number of participants and events. This, the simplest form of meta-analysis, is often called fixed-effects model because it does not take differences between trials into account. When included studies differ to some extent, the overall estimate needs to be adjusted for between-study variability, requiring more sophisticated models. A variety of such models is available, commonly referred to as random-effects models.

The real challenge is when multiple studies, with different patient populations and interventions, are available within the scope of the proposed research question. Due to the portfolio of available drug classes, several agents within each class, several doses for each agent, the wide range of co-morbidities, and the extraordinary change in population blood pressure over time, evaluation of antihypertensive treatment is probably one of the most complex situations where meta-analysis could be applied. Nevertheless, it is one of the most important situations to be evaluated systematically, because the array of available studies invite to selective citing of studies supporting specific notions.

When deciding how to analyze data, a critical question is if the included studies best answer the proposed question together, or subdivided to some extent. Some authors have used the approach of randomized controlled trials, where the primary analysis contains all study participants, and subgroup analyses are performed to explore possible interactions. However, randomized controlled trials and meta-analyses differ on one very important point. All study participants in a trial are recruited to answer the same question, fulfilling the same eligibility criteria, and receiving the same intervention or control. Studies included in a meta-analysis are likely to have asked different research questions, having different eligibility criteria, interventions, controls, and follow-up. Whereas participants in trials are "pooled by design", trials in meta-analyses are not.

Thus, before trials are pooled in a meta-analysis, analysts need to carefully consider potential clinical heterogeneity between studies, as well as possible modifiers of treatment effect. Are trials with different drugs or drug classes included in the analysis; if so, is it possible that they differ with respect to the effect on blood pressure or cardiovascular events? How the answers to these questions affect the statistical analysis plan depends on the research question, but readers should be aware that when trials are pooled it is assumed that differences are negligible.

Once trials have been pooled in a meta-analysis, it cannot be fully accounted for by subgroup/interaction analyses. This is because the power to detect clinically important interactions in meta-analyses is extremely poor, especially when subgroups include few trials or when heterogeneity is present within subgroups. Thus, negative subgroup/interaction analyses should be interpreted with great caution, and not necessarily as "no difference between subgroups" if such an interaction is suspected from a clinical or pathophysiological point of view.(1)

For systematic reviews of antihypertensive treatment at different blood pressure levels, different analytical

For systematic reviews of antihypertensive treatment at different blood pressure levels, different analytical



strategies have resulted in very different conclusions, depending on how co-morbidities have been handled. For example, some reviews have included heart failure trials and trials in the acute phase after myocardial infarction.(2,3) In such trials, patients generally have low blood pressure due to failure of the left ventricle. At the same time, several antihypertensive drug classes (such as inhibitors of the renin-angiotensin system, beta-blockers and diuretics) have important effects not related to blood pressure lowering, affecting cardiovascular mortality and morbidity. Thus, what appears to be a consistent effect of blood pressure lowering across blood pressure levels is actually an effect of blood pressure lowering in the upper end of the blood pressure spectrum and an effect of heart failure treatment in the lower end of the spectrum, which happens to be statistically similar in terms of effect size.

Even if heart failure trials are excluded from the analyses, different systematic reviews come to different conclusions about the effect of treatment at different blood pressure levels, largely dependent on how analyses are pooled or sub-grouped. For example, one analysis, pooling primary and secondary preventive trials, found treatment effect to be similar across blood pressure levels. (4) Other analyses, splitting primary and secondary preventive trials, have found attenuated treatment effect at lower blood pressure levels in primary prevention, as well as differences between primary and secondary preventive trials. (5)

In the end, which analysis to trust depends on whether one can accept the assumption that treatment effects are similar across the pooled trials. We hope that this paper has illustrated some of the potential problems with broad analytical approaches, missing differences between subgroups. In the end, who likes it when the pool is too crowded?

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## The Devil is in the Details

**Nadia Khan**

**Professor of Medicine, University of British Columbia, Canada,  
Centre for Health Evaluation and Outcomes Sciences.**



Meta-Analyses and systematic reviews have been traditionally placed at the top of the hierarchy for evidence pyramid because they increase the power to detect differences, provide greater precision of treatment effects and can investigate consistency of effect across groups. As such, over the past decade there has been an explosion of meta-analyses – with almost 18,000 meta-analyses published in 2017 alone. However, this enthusiasm for meta-analyses must be tempered with cautious optimism.

As eloquently discussed in the accompanying paper by Drs. Brunström and Carlberg, some important methodological decisions in designing and executing meta-analysis rely on personal judgement and expertise and therefore can introduce personal bias and strongly influence conclusions (1). Authors and consumers of meta-analyses need to be aware of these potential sources of bias arising in the selection of patient populations, trials and outcomes when designing and interpreting findings from meta-analyses (2). Here we will illustrate the influence of study selection and outcomes with three recent examples of meta-analyses purporting to investigate the same question, “What are the optimal blood pressure targets for high risk persons with hypertension?”

The first meta-analysis published in 2018 by the Cochrane Group compared blood pressure targets ( $\leq 135/85$  mmHg) with standard blood pressure targets ( $\leq 140$  to  $160/90$  to  $100$  mmHg) in people with hypertension and a history of cardiovascular disease (3). The Cochrane Group updated this meta-analysis in response to multiple guidelines commenting on blood pressure targets in high-risk individuals. Although guideline recommendations refer to high-risk individuals (4), the authors restricted their analysis to only patients with established cardiovascular disease defined as those with a history of myocardial infarction, angina, stroke, peripheral arterial disease. Although angina was included, other cardiovascular risk equivalents were not: diabetes and chronic kidney disease (5) for example. The Cochrane Group analyzed patients regardless of age or baseline blood pressure. Based on these criteria, the authors included evidence from six RCTs (9,484 patients) (AASK 2002; ACCORD BP 2010; HOT 1998; Past BP 2016; SPRINT 2015; SPS3 2013) (6-11) with only small subsets of individual patient data being drawn from each of these trials with the exception of including the majority of patient data from the SPS3 study (11). Perhaps not surprising, the pooling of these small groups, even among trials that did not pre-specify CVD subgroups, yielded no significant differences in reduction of total mortality or total cardiovascular events with more intensive blood pressure lowering ( $\leq 135/85$  mmHg) compared with more relaxed BP targets ( $\leq 140$  to  $160/90$  to  $100$  mmHg).

The second meta-analysis was published in 2017 as the basis for the 2017 American Association of Family Physicians hypertension guidelines recommendations for target blood pressures in the elderly (12). This meta-analysis also aimed to investigate intensive vs. less intensive blood pressure lowering but restricted to patients 60 years or older and further stratified by baseline blood pressure ( $< 160$  mmHg SBP and  $\geq 160$  mmHg). In contrast to the Cochrane study, this meta-analysis included patients with cardiac disease but excluded patients with prior cerebrovascular disease. The outcomes examined included total mortality, stroke, and cardiac events (narrowly defined as myocardial infarction or sudden cardiac death). These outcomes also differ from the Cochrane review and did not include heart failure, arguably one of the most salient endpoints in the management of hypertension. Six RCTs (41,491 patients) were included: ACCORD BP 2010, Cardio-Sis 2009, HOT 1998, SPRINT 2015, JATOS 2008, VALISH 2010 (7, 8, 10, 13-15). The target SBP of less than 140 mmHg was not significantly different from a less strict target for mortality (RR: 0.93, 95%CI 0.75-1.14), stroke 0.86 (0.64-1.07) or cardiac events (0.91, 95%CI: 0.77-1.04). Heterogeneity was generally low within these pooled comparisons.

In a meta analysis conducted by the ACC/AHA guideline group (16), the authors included 15 RCTs and specifically 9 trials evaluating SBP target  $<130$  mmHg for the intensive target: SPS3, SPRINT, MDRD 2005, AASK

2006, REIN-2 2005, Asayama K et al. 2012, Schrier RW et al. 2014, Cardio-Sis 2009, and ACCORD 2010 (7, 10, 11, 13, 17-21). This patient population included high-risk patients with diabetes, chronic kidney disease, stroke and cardiovascular disease. This meta-analysis evaluated a broader number of endpoints including: total mortality, cardiovascular mortality, composite major cardiovascular events, myocardial infarction, stroke, heart failure, and renal outcomes. Here, intensive BP lowering was associated with significant reductions in major cardiovascular events (RR: 0.84; 95% CI: 0.73 to 0.99) and stroke (RR: 0.82; 95% CI: 0.70 to 0.96) but not total mortality or heart failure.

From these three meta-analyses, which conclusion is true? There have been at least 8 systematic reviews and meta-analyses published on this topic in the last few years and most of the differences in conclusions arise from the variability in selection of studies and outcomes. Certainly, authors and readers will have differing opinions on the appropriateness of combining different RCTs and patient populations. As the entirety of the available data on blood pressure targets are diverse, differences in non-random selection of studies and outcomes, the starting point of a meta-analysis, can significantly influence the conclusions. Although when selection is too broad, the risk of increased statistical and clinical heterogeneity increases. When selecting too narrowly, the heightened power of a meta-analysis is attenuated, diminishing the probability of detecting differences that exist. Although one may argue that narrow comparability is essential to avoid comparing apples with oranges, one of the methodological advantages of meta-analysis over large single RCTs is the ability to address a broader question and formally assess generalizability. Michael Borenstein (22) stated meta-analysis ask "questions about fruit, for which both apples and oranges (and indeed pears and melons) contribute valuable information." A number of solutions may help to mitigate issues of selection and outcome reporting bias including appropriately ensuring relevant patient populations are included, registering meta analysis protocols, inclusion of primary endpoints from the primary RCTs, and robust sensitivity analyses to examine narrow subgroups after broader examination (1, 22). Indeed, the devil is in the details.

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## Beta Blockers As First Drugs in HT Treatment An example of difficulties when making and interpreting meta-analyses.

Lars H. Lindholm

Editor, Hypertension News



Frans Messerli and co-workers were the first to challenge beta-blockers as acceptable first-line treatment for elderly hypertensives (1). They did so in 1998 in a meta-analysis that included only two (!) studies which reported events. A Swedish group followed in 2004-5 (2,3) with two more comprehensive meta-analyses. This gave rise to an intensive debate in the medical community as well as a "media storm", since treatment with a beta-blocker reduced the risk of stroke by only 19% in comparison with placebo or no treatment, about half of that expected from previous trials. Moreover, in comparison with other blood pressure lowering drugs, the risk of stroke was 16% higher (!) for beta-blockers.

In 2006, a Canadian group looking at a combination of cardiovascular events (death, stroke, and MI) found beta-blockers to be inferior to all other therapies for elderly (60+) hypertensives (4), similar to the Swedish finding for stroke (3). The Canadians, however, didn't find any difference in effect for younger (<60) patients. A contributing factor to this difference was that the Canadians included the results of the Captopril Prevention Project (CAPPP,) comprising 10,985 men and women aged 25-66 years from Sweden and Finland (mean follow-up 6.1 years), who were randomised to "conventional treatment" (a diuretic and/or a beta-blocker) or an ACE-inhibitor (5). Patients in CAPPP were younger (mean age 51.5 years) than those in previous large hypertension trials in Scandinavia. In the Canadian analysis of younger patients, CAPPP accounted for about half of the events (4). The CAPPP findings were excluded from the Swedish meta-analysis, since the percentage of patients who received a beta-blocker was unknown, as stated in the paper (3).

Randomisation in CAPPP had been made by sealed envelopes and there was unfortunately an imbalance at baseline, as low-risk patients were more likely to get "conventional treatment" than an ACE-inhibitor. Systolic blood pressure at baseline was 2-3 mm Hg higher in the ACE-inhibitor group and there were more patients with diabetes mellitus in that group (5). The relative risk of stroke in the ACE-inhibitor group was 25% higher in the patients treated with an ACE-inhibitor than in those receiving "conventional" treatment, RR 1,25 (95% CI 1,01-1,55). This is hardly surprising, if one considers the difference in systolic blood pressure at baseline and during the trial.

Needless to say, the findings of CAPPP were criticised and Sir Richard Peto, FRS, at Oxford wrote in The Lancet (6): "*differences between the two treatment groups in pre-randomisation height, weight, systolic, and diastolic blood pressure (with respective p-values of  $10^{-4}$   $10^{-3}$   $10^{-8}$   $10^{-18}$  respectively), show that the process of randomisation by sealed, numbered envelopes was frequently violated*". Also, "*the present report cannot be taken as coming from a properly randomised trial*".

So, **what** should one believe? Well, I leave that to the readers of Hypertension News to decide. Just remember that stroke is uncommon in younger patients (only 10,2% of all strokes in Sweden in 2005 and 2006 were in patients below 60), which makes comparisons difficult! Personally, I avoid using the findings of C(R)APPP!

In conclusion. First, when interpreting a meta-analysis, make sure that the trials included are the right ones! Second, if beta-blockers are less effective, have side-effects, and cost about the same as other blood pressure lowering drugs, why use them as first-line treatment of hypertension, unless there is a compelling indication?

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## NEWS, OLD NEWS, FAKE NEWS.

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***"I eat what I like and suffer thereafter"***

**Martin Luther (1483 – 1546)**

**Stephan Rössner, Professor Emeritus Apple Bay Obesity Research Centre, Bromma, Sweden**

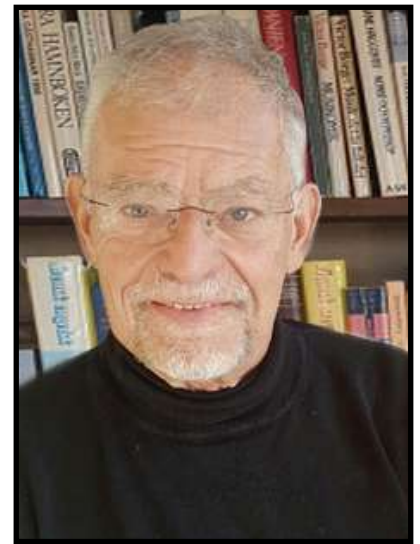
Martin Luther's health has been discussed extensively by psychiatrist and clinicians over the years – he clearly had a complex psychiatric history of neuroticism and, most likely, a manic-depressive condition, while also suffering from a somatic condition.

Luther was born in 1483 in Eisleben in Germany and began his study in Erfurt in 1501. He admitted that he enjoyed the life of a student more than the studies themselves, engaging heavily in eating and drinking and even referred to the University as 'a pub and a brothel'(1) He woke everyday at 4 o'clock for a day filled with 'mechanical learning and tiring spiritual exercises'1. Here, academics taught Luther to be critical towards even the greatest philosophers and to test matters through his own experience. Luther resisted the concept that the Bible was the only tool for spiritual development and believed that common sense would not necessarily lead man to God.

In 1505 Luther was accepted into a monastery, however the early years were not easy as he was ostracized by his fellow monks who forced him to execute undesirable tasks as they despised the academic and learned young man. The University eventually reacted to this treatment of their scholar and had him admitted into proper ranks of the Order. Luther could now begin his career, where he eventually met his academic goals and became a Professor of Theology in 1512. Luther's critical approach to his work resulted in the famous '95 Theses' that he nailed on the church door of Wittenberg in 1517. This endeavor angered the Pope and caused Luther and his wife to live in constant fear of being imprisoned by the papal revenge system.

Despite this threat to his personal safety, Luther was also at risk due to his poor health throughout his life. At the age of only 20 years old, Luther developed a leg ulcer that never healed and it is believed he suffered from angina pectoris from 1527, however it is difficult now to evaluate the severity of his chest pains. Numerous paintings depict Luther becoming increasingly obese over time and it is likely that he suffered from high blood pressure, certainly experiencing continuous headaches and epilepsy or possibly Ménière's disease(1). In 1525 he had his first kidney stone, he suffered from continuous severe constipation, had bleeding haemorrhoids and suffered from insomnia. All of these medical problems began in the early 1520s, which he interpreted as provocations from Satan. Due to the early onset of his health problems, it is surprising that Luther managed to produce 124 publications, including a translation of the entire Bible from Hebrew into German and numerous religious publications.

In 1525, Luther married Katharina von Bora, who had been a nun. She had escaped from a cloister with eleven other nuns. Luther worked hard to find them work or a partner as their families did not want them back. With



him, came the change that a clergyman could be a married man, no longer living a celibate life. During the critical years of conflict with the Pope and the political system, Luther lived a simple life, his marriage was happy and Luther changed his dietary habits for the better. The family was always poor, but Katharina made ends meet by cultivating her garden, caring for a pig sty, and renting out rooms in their home to tenants and students.

From a historical perspective, it is interesting to note the treatment that the doctors at the time recommended for his constipation: Luther was ordered to consume six large spoons of butter daily, which likely promoted his obesity more than cured his haemorrhoids. It is obvious that he did not care too much about the advice he received from the medical profession and stoically concluded that he would be prepared to pay the price for his enjoyment of food. In 1533, Luther had his first attack of gout and began to develop psychiatric symptoms including bitterness, depression and aggression. Of course, we have no data on weight and height from Luther, but we can guess from paintings and his writing that he suffered considerable abdominal obesity, which will also fit with the symptoms suggesting a metabolic syndrome. His death mask also suggests a man with considerable weight problems. With time, he developed a cataract, arthritis and an ear infection, which ruptured one of his tympani. In December 1544, his more severe symptoms of angina pectoris started. It remains an enigma that this man under such demanding conditions could be so academically and theologically productive.

With time Luther's writing and mood became increasingly aggressive and his later texts are extremely antisemitic. Luther had never intended to leave Catholicism; what he disliked was the papal management with the letters of indulgence and the ensuing business, which the popes were involved in. A main reason for the later separation from the Catholic Church was Luther's negative attitude towards the indulgences. These letters promised that any sinner, who could contribute money for the completion of St Peter's Basilica in Rome, would be forgiven. Luther objected, wrote his 95 theses and nailed them on the wall of the castle church door on 31 October 1517, a date which today is regarded as the start of the Protestant Reformation.

Martin Luther worked till the end of his life and he delivered his last sermon only three days before his death. In 1546 on February 17 he woke up in the evening with severe chest pains. He confirmed his religious beliefs to his two companions who were present, had a stroke which made it impossible to speak and died the following day. With his massive medical history and the complete lack of any effective treatment, apart from a strict diet, to which he would not adhere, it is amazing that Martin Luther reached the age of 63.

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## May Measurement Month gets set for its third successful year

May Measurement Month (MMM) continues to build on its success. After measuring the blood pressure of over 1.2 million people across 80 countries in 2017, the 2018 campaign saw over 1.5 million people screened across 89 countries. This means we have now reached over **2.7 million people** since MMM began and have identified over half a million people with uncontrolled hypertension. As the **largest ever synchronised standardised multinational screening of any cardiovascular risk factor**, we are going a long way to meet our objectives to raise global awareness of the issues surrounding raised blood pressure.

Having had the global analysis of MMM17 published on the eve of World Hypertension Day 2018 in a paper in [The Lancet Global Health](#), we are pleased to confirm the publication of 39 national papers from top contributing MMM17 countries in the European Heart Journal Supplement. Countries that screened over 2,500 people were invited to contribute to the Supplement. Hard copies of this Supplement will be sent to 35,000 cardiologists around the world before May 2019. We expect to follow these publications with the global MMM18 publication in a top level journal before the 2019 campaign begins (currently undergoing review).

Professor Alta Schutte, President of the International Society of Hypertension, stated: ***"ISH is delighted to see May Measurement Month go from strength to strength on such a global scale. We hope its success will encourage more people to join the generous volunteers who have made this happen."***

Thank you to the numerous organisations around the world, including national hypertension and cardiac societies, who have driven May Measurement Month over the past 2 years. We hope you will continue to support this programme into its third year. If you have not already signed up for MMM19 and would like to, it's not too late and we have a bank of resources to help you in setting up your MMM, which are available to download from the [MMM website](#). Even if you are only able to run a small campaign you will be contributing important data to help improve and save lives. If you would like to know more about how to get involved, please contact the MMM Project Manager: [manager@maymeasure.com](mailto:manager@maymeasure.com)

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## The Dobney Hypertension Centre

Markus Schlaich

### Dobney Hypertension Centre, School of Medicine - Royal Perth Hospital Unit, Perth, Australia

Markus Schlaich, the current Treasurer, Chair of Corporate Liaison and Co-Chair of the North Asia, South-East Asia and Oceania Regional Advisory Group (RAG) of the ISH, is the inaugural Dobney Chair in Clinic Research which has been established in 2014 by a collaboration between the Royal Perth Hospital (RPH) Medical Research Foundation (MRF), The University of Western Australia (UWA) and the WA Department of Health. The appointment recognises the extraordinary contribution made to the MRF and medical research by the late Mr Ray Dobney. Well-known for its research and clinical teaching, the UWA Medical School is ranked 39th in the world by the 2018 *Academic Ranking of World Universities* in clinical medicine and just celebrated its 60th anniversary. To complement the ongoing work in cardio-metabolic and diabetic medicine, clinical nutrition, geriatrics and stroke medicine he was appointed due to his extensive experience as a Renal Physician and ESH certified Hypertension Specialist to direct the Hypertension Services at RPH and further strengthen the field both clinically and academically. The clinical service of the Dobney Hypertension Centre (DHC) was recognised as an ESH Hypertension Centre of Excellence in 2016, one of only a few outside of Europe. In conjunction with an extensive research program these efforts will continue the legacy set by some of the greats in the field including the former ISH president Professor Lawrie Beilin (2002-2004).



### Clinical Services at the Royal Perth Hospital

As a state-wide service the Dobney Hypertension Centre acts as a tertiary referral centre for the largest state in Australia covering an area of 2.5 million square kilometres, around 10 times the size of the UK (242,495 km<sup>2</sup>) with ~ 2 million people in its direct catchment area. The sheer size of WA renders management of patients in remote areas a real challenge and telemedicine has been an integral part of clinical care for many years. The iconic *Royal Flying Doctor Service of Australia* continues to set the standards in the field. The centre manages all



Prof Markus Schlaich and Prof Lawrie Beilin in front of the University Club

aspects of clinical hypertension with a specific focus on difficult to control and resistant hypertension. All relevant disciplines required for thorough diagnostic work-up and management including nephrology, cardiology, endocrinology and radiology are key stakeholders in the Dobney Hypertension Centre and work collaboratively to achieve best outcomes for each patient.

Understanding the close and bi-directional links between hypertension and cardiovascular, metabolic and other risk factors, we work closely with dietitians, exercise physiologists, psychologists and other allied health disciplines. Obesity related hypertension is very common in Australia and collaborations with bariatric surgeons allows us to use these options if deemed appropriate. We also routinely screen for obstructive sleep apnea which is highly prevalent in the patient cohorts we see in our clinics, as well as assessing central BP and pulse wave velocity. A large ambulatory BP monitoring service complements our diagnostic work up and is used to ensure optimal management of patients.

### Clinical research

Clinical research is a key component of the Centre's work and the close proximity between the Royal Perth Hospital and the MRF building where the dedicated clinical research laboratories are housed enables and facilitates translational research. The research arm of the DHC comprises two fully equipped cath-lab style clinical research rooms for semi-invasive tests and procedures, 2 clinical rooms for non-invasive testing and 5 clinical consulting rooms. Adjacent to these are 2 "wet-labs" for direct

processing of patient samples obtained from research studies and a large array of molecular biology techniques. This is complemented by an animal facility on the campus, primarily for small animal research.

A major aim of the DHC is to bring together scientists and clinicians from various backgrounds and with complementary expertise and skills to address the most relevant questions related to human health. We do this through scientific discussions, seminars, collaborative grant applications as well as provision of our own expertise to other groups who may be able to utilise our specific research techniques for their own research. The core DHC research team currently consists of members from 8 countries including 6 research fellows (3 clinicians, 3 scientists), 5 research officers, one administrative staff, and 9 MD/PhD/Masters students.

Scientifically, the DHC's interest focus on 3 major areas including hypertension, cardio-metabolic risk factors, and autonomic/sympathetic function as depicted in more detail below.

HYPERTENSION	CARDIO-METABOLIC RISK FACTORS	AUTONOMIC FUNCTION
<ul style="list-style-type: none"> <li>Resistant hypertension</li> <li>Interventional approaches</li> <li>Obesity related hypertension</li> <li>Renal hypertension (CKD, RAS, FMD)</li> <li>Pregnancy related HTN</li> <li>Hypertensive urgencies / emergencies</li> </ul>	<ul style="list-style-type: none"> <li>CKD / ESRD</li> <li>Metabolic Syndrome / T2DM</li> <li>OSA (Obstructive Sleep Apnea)</li> <li>Pre-eclampsia</li> <li>PCOS (Polycystic Ovary Syndrome)</li> <li>Salt / Inflammation</li> </ul>	<ul style="list-style-type: none"> <li>Stress (Takosubo) cardiomyopathy</li> <li>POTS Syndrome</li> <li>Diabetic autonomic neuropathy</li> <li>Orthostatic intolerance</li> <li>Sympathetic regulation of SGLT-2</li> <li>Sympathetic hyperinnervation</li> </ul>

CKD: chronic kidney disease; RAS: renal artery stenosis; FMD: fibromuscular dysplasia; ESRD: end stage renal disease; T2DM: type 2 diabetes; POTS: postural orthostatic tachycardia syndrome; SGLT-2: sodium glucose transporter 2.



Some key members of the DHC team (from left): Ms Justine Chan, A/Prof Vance Matthews, Ms Anu Joyson, Ms Derrin Brockman, Dr Revathy Carnagarin, Prof Markus Schlaich, Mr Kearney Tan, Ms Alice Rothwell, Dr Jan Ho.

## Research Highlights

Improving management of patients with resistant hypertension has been a key area of our research for the last decade. Given our interest in the role of the sympathetic nervous system, in particular the renal nerves, in the development of hypertension we have been deeply involved in the development and assessment of catheter-based **renal denervation (RDN)** as a novel interventional approach for this and other conditions. The hype triggered by our first-in human studies in 2009 (1) was dampened by results from the Symplicity HTN-3 study which reported no additional effect of RDN beyond that of a sham control, but has now been rectified by data from 3 appropriately designed sham-controlled studies clearly

demonstrating a significant BP lowering effect, as recently summarized (2). While further and larger studies are currently being conducted it is likely that RDN will become an integral part of modern hypertension management.

We have also explored other avenues of targeting central sympathetic outflow in hypertension and beyond. The **carotid body** is a peripheral chemosensor strategically positioned between the internal and external carotid arteries and amongst others governs cerebral blood flow and senses oxygen levels. Once activated, the carotid body via afferent signalling from sensory nerve fibres stimulates central integrative nuclei which in turn increase central sympathetic outflow thereby contributing to rise in BP. Data from our first-in-man study targeting the carotid body and its sensory fibres via a transvenous ultrasound ablation approach are promising and demonstrate a significant 24h BP reduction.

Obesity and its metabolic and cardiovascular consequences represent a large burden on general health

worldwide. Aside from hypertension being frequently associated with obesity, we have been struck by the substantial cardio- and reno-protective effects conferred by **SGLT-2 inhibitors** with a 38% relative risk reduction in death from cardiovascular (CV) causes. Interestingly, sudden cardiac death and hospitalization for heart failure were the major drivers of CV risk reduction, raising the possibility that SGLT-2 induced antagonism of increased sympathetic nervous system (SNS) activation may be an important underlying mechanism. Indeed, our own A/Prof Vance Matthews was able to demonstrate in human proximal tubular cells and a mouse model of obesity that SNS activation through increased release of noradrenaline (NA) up-regulates SGLT-2 expression and promotes translocation to the cell membrane and that pharmacologic inhibition of SGLT-2 reduces sympathetic innervation both in the kidney and the heart (3). These findings are indeed indicative of a sympatho-inhibitory action of SGLT-2 inhibition. In a translational approach we now aim to further investigate the apparent crosstalk between the SNS and SGLT-2 regulation in relevant animal models and in patients with T2DM. Unravelling the mechanisms of SGLT-2 inhibitor induced cardio-renal protection will have wide ranging implications beyond diabetes.

Other currently ongoing studies address the role of the immune system and its inhibition for human hypertension, the role of the SNS in polycystic ovary syndrome and pre-eclampsia associated cardiovascular and metabolic disturbances, the effect of specific targeting of renal sympathetic nerves in loin-pain-haematuria syndrome, investigation of the central pathways involved in regulating sympathetic outflow using functional MRI imaging, and several others. We are also a site for several national and international randomized controlled clinical trials.

As always, it is the people who make a real difference and we would be pleased to hear from anyone with a passion for clinical research who would be interested in joining us in our efforts to combat the large burden that cardiovascular and metabolic disease puts on the global community.

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## First things first: Accurate blood pressure (BP) measurement for hypertension diagnosis and management

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### Conventional office BP measurement

In the last 100 years the evolution of clinical hypertension has been an excellent model for evidence-based medicine. Sixty-one prospective observational outcome studies including one million adults with 12.7 million person-years at risk and 56,000 cardiovascular deaths during follow-up have shown that BP is strongly and directly related to cardiovascular and total mortality. More importantly, 122 interventional randomized outcome trials, in which 350,000 subjects participated, demonstrated the benefits of drug-induced BP lowering in reducing the risk of fatal and nonfatal cardiovascular events. This enormous database of mega-trials, on which the current management of hypertension is based, has been almost exclusively derived from conventional upper-arm cuff-based office BP measurements, initially using manual auscultatory devices and more recently using automated oscillometric ones.

Despite the indisputable value of the conventional office BP measurement in defining and managing hypertension worldwide, this method has major deficiencies which seriously undermine the accurate BP measurement and the reliable diagnosis of hypertension. These shortcomings are mainly related to (i) unstandardized methodology (rest period, posture, talking, number of measurements) resulting in poor reproducibility of office BP, (ii) observer error and bias with the auscultatory method, and (iv) the white-coat and masked hypertension phenomena which are common in both untreated and treated individuals.

### Out-of-office BP measurement

Out-of-office BP evaluation using 24-hour ambulatory or self-home BP monitoring (i) provides multiple measurements in the usual environment of each individual, (ii) avoids the white-coat and masked hypertension phenomena, (iii) is more reproducible and (iv) more closely related to cardiovascular risk than the office measurements. Current guidelines on both sides of the Atlantic recommend treatment decisions in hypertension to be based on out-of-office BP measurements in most untreated and treated hypertensives.

### Automated attended and unattended office BP

The development of automated oscillometric BP monitors has been essential for ambulatory and home BP monitoring and is being increasingly used for office measurement. Automated office BP avoids the observer-related issues and requires less training than the auscultatory measurement. Unattended automated office BP (several measurements taken automatically while the patient remains alone in the examination room) is the most standardized office BP measurement method, as it avoids the observer issues and talking during measurements and ensures triplicate (usually) measurements. However, a special device and additional space and time is required, and the BP threshold for diagnosing hypertension is rather uncertain and lower than with the conventional office measurement.

### Accuracy of automated BP monitors

The accuracy of automated BP monitors (for office, ambulatory or home use) needs to be verified using an established validation protocol. Moreover, an automated device which is accurate in adults may not be accurate in special populations (e.g. children and pregnancy). Unfortunately, only one in five of the BP monitors available on the market has proven accuracy. There are several on-going initiatives by scientific societies to inform doctors and patients by listing properly validated devices. The American Medical Association and the American Heart Association, as well as an international group of BP measurement experts (STRIDE-BP organization) are currently developing internet resources with accurate devices lists.

## Conclusions

The accurate measurement of BP is essential for the diagnosis and management of hypertension. With recent hypertension guidelines recommending lower BP targets with treatment, the need for accurate BP evaluation has become even more important. The hierarchy of using the currently available BP measurement methods is presented in the table. Out-of-office BP measurement (ambulatory or home) should be the basis for hypertension diagnosis and management. Office BP measurement should be used as a screening test in most cases. International initiatives are urgently needed to optimize office, home and ambulatory BP measurement in clinical practice.

## References

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	Method	Advantages	Limitations	Threshold (mmHg)	Clinical Utility
1	24-hour ambulatory BP	<ul style="list-style-type: none"> <li>• Prognostic ability superior to office BP</li> <li>• More reproducible than office BP</li> <li>• Night-time BP sleep evaluation</li> </ul>	<ul style="list-style-type: none"> <li>• Limited availability in primary care</li> <li>• High cost of devices</li> <li>• Intolerable by some patients particularly for repeated use</li> </ul>	130/80	<ul style="list-style-type: none"> <li>• Recommended method for treatment decisions (preferred for diagnosis) <sup>#</sup></li> </ul>
2	Self-home BP	<ul style="list-style-type: none"> <li>• Prognostic ability superior to office BP</li> <li>• More reproducible than office BP</li> <li>• Wide availability</li> <li>• Preferred by patients</li> <li>• Improves compliance with treatment - hypertension control</li> </ul>	<ul style="list-style-type: none"> <li>• Many devices not validated for accuracy</li> <li>• Possible misreporting of BP readings by patients (avoided with automated memory, or mobile/PC link)</li> <li>• Some patients self-modify treatment</li> </ul>	135/85	<ul style="list-style-type: none"> <li>• Recommended method for treatment decisions (preferred for long-term follow-up) <sup>#</sup></li> </ul>
3	Automated unattended office BP	<ul style="list-style-type: none"> <li>• Most standardized office BP</li> <li>• Avoids several issues of office BP</li> </ul>	<ul style="list-style-type: none"> <li>• Requires special device and additional space and time</li> <li>• Uncertain BP threshold</li> </ul>	135/85 (?)	<ul style="list-style-type: none"> <li>• Probably the best screening method <sup>*</sup></li> </ul>
4	Automated attended office BP	<ul style="list-style-type: none"> <li>• Strong prognostic data</li> <li>• Avoids most observer-related issues</li> </ul>	<ul style="list-style-type: none"> <li>• Usually inadequately standardized</li> </ul>	140/90	<ul style="list-style-type: none"> <li>• Most applicable screening method for wide use <sup>*</sup></li> </ul>
5	Auscultatory office BP	<ul style="list-style-type: none"> <li>• Strong prognostic data</li> <li>• Wide availability</li> <li>• Low-cost devices</li> </ul>	<ul style="list-style-type: none"> <li>• Poorly standardized and subject to observer error and bias</li> </ul>	Higher than 140/90	<ul style="list-style-type: none"> <li>• Screening method when automated devices are not available or have questionable accuracy <sup>*</sup></li> </ul>
6	Pharmacy BP	<ul style="list-style-type: none"> <li>• Access to treated and undiagnosed hypertensives.</li> <li>• Useful in collaborative approaches aiming to improve BP control</li> </ul>	<ul style="list-style-type: none"> <li>• Poorly standardized</li> <li>• Limited evidence on threshold values, reproducibility and clinical relevance</li> </ul>	135/85 (?)	<ul style="list-style-type: none"> <li>• Low cost screening method</li> <li>• Monitoring of BP control in treated hypertensives <sup>*</sup></li> </ul>
7	Public space kiosk BP	<ul style="list-style-type: none"> <li>• Access to undiagnosed hypertensives</li> </ul>	<ul style="list-style-type: none"> <li>• No evidence on threshold values, reproducibility and clinical relevance</li> </ul>	?	<ul style="list-style-type: none"> <li>• Low cost massive screening in general population <sup>*</sup></li> </ul>

<sup>#</sup> Ideally perform both home and ambulatory BP monitoring as these methods are complementary and their reproducibility is imperfect.

<sup>\*</sup> Requires confirmation by out-of-office BP measurement (ambulatory or home).

## More than the number of followers

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There have been several articles recently published about the impact of social media for academia (1,2). The message is consistent - engagement on social media, Twitter specifically, is the most efficient platform to engage in scholarly discussion, have research achievements recognised, form networks and develop collaborations.

By sharing my personal experience with Twitter, I hope to engage those colleagues who continue to be skeptical about the social media platform. The best analogy I can offer is that Twitter can amplify life's "sliding doors" moments towards opportunity, collaborations and friendships. While some individuals focus on self-promotion and their number of followers or "likes", Twitter has a major role in science communication; not only peer review, but also engaging our community. The flow of information and interactions is faster and greater than traditional channels and it has transformed the world into a supportive network, without boundaries of distance or status.

While many who interact with me on Twitter will be surprised to hear this, I was exactly like the sceptics and against engaging in social media until two years ago. I am still a novice, but following a seminar I heard by the founder of Wiki-doc, Dr Michael Gibson, on how social media will change academia, I began to engage and it was the best decision I have made. It certainly has enhanced my career by providing me with collaborations that would never have developed through traditional channels. It has connected me with leaders in diverse specialties and led to wonderful friendships across the world.

Initially my interactions with Twitter were limited, but I quickly noticed that in addition to the personal opinions, there were discussion threads for case presentations or journal articles. Wanting to maintain professional interaction I didn't interact in these online discussions for the first year as I had heard the warnings to "be careful what you post since it cannot be removed". One day there was a discussion thread and I bravely added my comment. The response from the group was so uplifting and encouraging. It was a new experience for me to have people that I had never met, not only interested in what I had to say but also congratulatory. It was empowering and restored my confidence that my knowledge and viewpoint were valued. I found my network and friendships growing and recognition for my content expertise. Being supported in this manner allowed me to share my sense of humour, which had been hidden in my professional interactions. Having previously been referred to as "an enigma" or "falling between the cracks" as well as been exposed to academic bias by a former institution and isolation by colleagues, I found Twitter provided me strength in the knowledge that I was not alone in having experienced bias. I felt supported and not abandoned. There have been some challenges, but overall it has been a very positive experience with a faster pace and rewarding method of learning. In a traditional academic path, I would still be struggling to receive recognition. Unlike my other colleagues, I did not have a sponsor or local support.

The impact of social media is also personal – it has provided me with friendships not only for exchange of scientific content, but also with a community. I feel part of a team, supporting and encouraging each other, including the #DropAndGiveMe20 family for promoting less sitting and more activity. In academia, we are now asked about identifying the impact our research has in addition to the scholarly publications. There is now discussion that this should also include the influence on Twitter (**Figure 1** provides an example). There were 150 people who "liked" my message to support awareness for heart disease in women, with 30 people sending my message out to their followers, resulting in it reaching over 19,400 people. Further, the opportunities that have arisen entirely as a result of my activity on Twitter include: Member of ISH Women In Hypertension and Communications Committees; Scientific Committee Member of the National College of French Cardiologists; Invited Speaker to European Society of Cardiology & Session Chair: *How to measure blood pressure*; 15th Asian-Pacific Congress of Hypertension (APCH) 2019 Organising Committee as Social Media Chair; Collaborations across the world. (**see figure 2**)

## References

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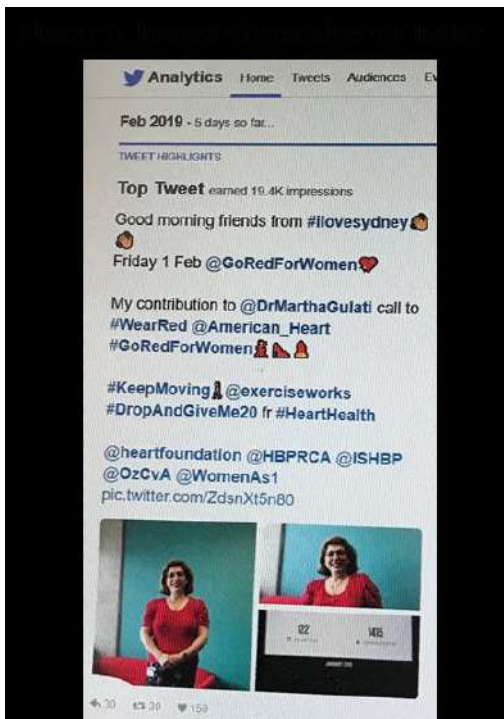


Figure 1



Figure 2: Global Collaborations which resulted from engaging on Twitter

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## APSH/ISH SUMMER SCHOOL JULY 2019.

The APSH/ISH Summer School is an interactive training program with lectures by ISH and APSH faculty, interactive discussion and research presentations by scholars. The Summer School in 2019 will be held July 22 to July 26 in Ayutthaya, in the Central Plains of Thailand, 85 km north of Bangkok. The venue is The Krungsri River Hotel.

Participants in general will be under the age of 35 and nationals of the Asia Pacific region. They also should be people who will become future leaders in their field. In general, they will have completed all or most of their clinical training. The clinical field in which a person has trained may be in Cardiology, Nephrology, Neurology, Endocrinology or Internal Medicine. In addition to the clinical strand, some participants may be more actively involved in epidemiology, health practice or delivery of health care, with a focus on Hypertension and / or cardiovascular disease.

People who wish to attend are invited to contact their country's Hypertension Society to let them know of their interest. Nominations will be made by each Society to APSH. This opportunity applies particularly to members of ISH and their students

There is no Registration Fee. Accommodation and maintenance at the Summer School will be provided by the Host Society, supported by a grant from ISH. The participant and/or their nominating Society will be responsible for their travel to the summer school location.





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