On May 6, 2020, the International Society of Hypertension (ISH) has released new guidelines entitled “2020 ISH Global Hypertensive Practice Guidelines” which were published online concomitantly in the Journal of Hypertension and Hypertension. These guidelines follow those published by ISH in conjunction with the American Society of Hypertension (ASH) published in the Journal of Hypertension and Journal of Clinical Hypertension in 2014.

What is new, what is different from other clinical guidelines published in recent years?

New guidelines always have to justify their existence. Normally they do this by extracting most recent evidence from the literature exceeding or correcting earlier evidence on which their respective predecessors are based. One could also say, they reflect the evidence-based state of the art of a given time, period, and shape recommendations from current evidence. Since they want to be detailed and to exhaust the literature in a more or less comprehensive fashion, they tend to become quite voluminous which impairs readability and practical use. In addition, these guidelines, e.g. the recent ESH/ESC or ACC/AHA or Japanese hypertension guidelines, come from affluent regions of the world and predominantly subserve populations in high income settings or countries (HIC) where resources and facilities of medical care are abundant, but they tend to ignore the situation in less affluent settings, not only in low- and middle income countries (LMIC) but also in their own countries.

The new ISH hypertension guidelines are quite different in this respect, and this relates to their novelty. In the introduction of the ISH guidelines the authors state:

“...the adoption of guidelines from high income regions are sometimes impractical as low resource settings are confronted with a substantial number of obstacles including severe lack of trained healthcare professionals, unreliable electricity in rural clinics, low access to basic office BP devices and limited ability to conduct basic recommended diagnostic procedures and poor access to affordable high-quality medications. In both low and high income regions, the ambiguities of latest guidelines are often met with confusion among healthcare providers, anxiety among patients, and they resulted in a call for global harmonization. Guidelines from high income regions may thus not fit global purpose.”
In view of the fact that recent blood pressure trends show a clear shift of the highest blood pressures from high-income to low-income regions with an estimated 349 million with hypertension in HICs and 1.04 billion in LMICs in 2010, it becomes clear that a globally acting society like ISH with the mission “to reduce the global burden of raised blood pressure” has to act by providing recommendations not only for HICs but also for low resource settings. And this is the major thrust of the new ISH guidelines.

To achieve this goal, the ISH guidelines committee decided for three major structural elements of the document:

1. not to review the current evidence again since this had been done by recent guidelines such as ESC/ESH- or ACC/AHA guidelines, but extract the evidence-based content from recently published guidelines and tailor them to the needs of both, high and low resource settings,

2. advise on essential and optimal standards of diagnostics and care and

3. make the guideline concise, simplified and easy to use by clinicians, nurses and community health workers.

What is essential, what optimal?

In the ISH guidelines this is defined as follows:

“Optimal care refers to evidence-based standard of care articulated in recent guidelines and summarized here, whereas essential standards recognize that optimal standards would not always be possible. Hence essential standards refer to minimum standards of care. To allow specification of essential standards of care for low resource settings, the Committee was often confronted with the limitation or absence in clinical evidence, and thus applied expert opinion.”

This may be regarded as betrayal of the holy grail of evidence-based medicine, but it was felt to be an inevitable compromise.

Whereas most sections of the new ISH guidelines follow the principle of dividing the recommendations in essential (green) and optimal (blue) this was not always possible, for instance in the sections on cardiovascular risk factors or comorbidities. Also, the authors were aware of the fact that even

“some recommended essential standards may not be feasible in low income settings, e.g. out-of-office blood pressure measurement, multiple visits for the diagnosis of hypertension of single pill combination therapy”. But these limitations had to be accepted. Thus, under ‘essential’ recommendations, one often finds a remark as to feasibility, for instance when it comes to hypertension diagnosis: “Confirm office blood pressure with ABPM or home measurement if possible”. Likewise, with respect to drug treatment: “If systematic, stepwise drug combination according to the recommended scheme (as under optimal conditions) is not available: Use any available drug to lower blood pressure.”

The strict, almost continuous division between recommendations concerning essential versus optimal standards is certainly the hallmark and major raison d’être of our new ISH guidelines. However, there are several other features which differentiate them from previous ones.

In contrast to previous guidelines, definition and grading of hypertension have been simplified: “Normal Blood Pressure” is defined as up to <130/85 mm Hg followed by “High-normal Blood Pressure” up to 139/89 mmHg, followed by “Grade 1 Hypertension” (140-159/90-99 mmHg) and “Grade 2 Hypertension” (>160/100 mmHg).

The threshold of hypertension concurs with the one in the ESC/ESH guidelines but differs from the ACC/AHA guidelines in that “Hypertension” is defined from 140/90 mmHg and above versus ACC/AHA: 130/80 mmHg. Grade 1 Hypertension in the ISH guidelines thus corresponds to Grade 2 Hypertension in the ACC/AHA guidelines. In addition, in the new ISH guidelines there is no category of “Elevated blood pressure” as in ACC/AHA guidelines, and no category of “Optimal blood pressure” and “Grade 3 hypertension” as in the ESC/ESH guidelines. This simplifies the issue substantially and facilitates understanding of document.

Concerning drug treatment, the division into essential and optimal impacts mainly the essential part: Regarding optimal standards, treatment decisions and targets are pretty well aligned with the European- and to a certain degree also with the US guidelines, the difference comes again with the recommendations concerning ‘essential’ conditions: While under optimal conditions, blood pressure should generally be lowered to <130/80
mmHg except in frail elderly patients, the essential recommendations go for a general blood pressure reduction of 20/10 mmHg, ideally to 140/90 mmHg (again individualized in the elderly based on frailty). This takes care of circumstances of poor drug availability, where blood pressure lowering as such is primordial to reduce cardiometabolic risk, whereas well defined, evidence-related blood pressure targets are less important.

In addition: If under ‘essential’ conditions in Grade 1 hypertensives blood pressure cannot be controlled after 3-6 months of lifestyle intervention, the guidelines recommend to start drug treatment in those aged 50-80 years. This aspect of triage may fuel discussions, but it merely recognizes the fact that under essential conditions, i.e. limited drug availability in this case, a practical choice has to be made.

As outlined in a joined editorial in *Hypertension* and *Journal of Hypertension* by the respective editors, Anna Dominiczak and Giuseppe Mancia, there is another facet in the drug treatment section which distinguishes the new ISH guidelines from the previous European ones: Instead of going from the initial dual combination directly to triple drug treatment, there is an intermediate step in the ISH guidelines to increase the dose of the initial dual drug combination from low to high. The authors remark that this would provide physicians with a greater treatment flexibility giving them a major treatment advantage worldwide. Although this applies mainly to treatment in the realm of optimal conditions, the recent listing of single pill antihypertensive combination therapy in the Essential Medicines list of the World Health Organization, is likely to increase the availability of combination pills also in low resource settings.
Further elements of novelty in the ISH guidelines include a detailed section on treatment adherence and how to monitor it as well as the introduction of stress avoidance and stress-reducing measures including the avoidance of air pollution wherever possible. New is also a detailed section on factors which may exacerbate or induce hypertension as well as a section featuring uncommon- besides common comorbidities and their management.

The specific influence of ethnicity and race on hypertension in different regions of the globe is given a special section with region-specific treatment recommendations.

A final section with two comprehensive figures called “Hypertension management at a glance” constitutes a further novelty of the ISH Guidelines compared to previous ones.

This section also strictly follows the scheme of optimal versus essential summarizing the content of the forgoing pages. Thus, if the reader has no time or is unwilling to go through the whole document, he or she can obtain a concentrated message regarding essential and optimal conditions in a nutshell on two pages.

The guideline document closes with a detailed compilation of resources ranging from previous guidelines from Europe, USA, Japan, China, Latin America, recent guidelines on metabolic disorders, and specific sources of support for low resource settings to listings of validated electronic blood pressure devices and blood pressure management in pediatric populations. These sources of information serve the purpose of the new ISH Guidelines to provide hands-on, practical, and usable information around hypertension and related diseases.

A final note on the authors and reviewers of the ISH guidelines. Since the Council of the ISH include respected scientists from across the globe, the decision was made to make this an in-house writing effort. However, perhaps the most important aspect was to send a first draft of the guidelines to 12 external reviewers covering low to high resource settings, and upon revisions sending it out to another round of 12 external reviewers – with a specific focus to include those with expertise in LMICs. The reviews were comprehensive and contributed immensely to the final version of the published ISH guidelines.

In the introduction, the authors state:

“Although challenging to implement, these guidelines may aid in local initiatives to motivate policy changes and serve as an instrument to drive local improvements in standards of care. Every effort should be made to achieve essential standards of care to reduce hypertension-induced cardiovascular morbidity and mortality”.

This represents a further aspect of the ISH guidelines, differentiating them from previous ones and reflecting again the global mission of the Society.