

Validation protocols for blood pressure measuring devices: The impact of the European Society of Hypertension International Protocol (ESH-IP) and the development of a Universal Standard

Short title: Blood pressure monitors validation

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Abstract

In the last three decades protocols for the validation of blood pressure (BP) measuring devices have been developed by the US Association for the Advancement of Medical Instrumentation (AAMI), the British Hypertension Society, the German Hypertension League, the European Society of Hypertension (ESH) Working Group on BP Monitoring and the International Organization for Standardization (ISO). The ESH International Protocol (ESH-IP) required much smaller sample size than the other protocols, aiming to reduce the time, resources and cost of validation studies and thereby increase the number of validated devices. Given its specifications, the ESH-IP was adequate for 'high and 'low accuracy' devices, yet assessment of 'moderate accuracy' devices had high uncertainty with resultant high rate of device failure. Thus, devices validated using the ESH-IP should be considered to be as accurate as those validated with the previous AAMI or BHS protocols. However, the ESH-IP did not allow subgroup evaluation (arm sizes, special populations, etc). The mission of the ESH-IP to promote the concept of validation has been well achieved, as almost double studies have been published using it than all the other protocols together. However, the maintenance of different validation protocols is confusing and therefore experts from AAMI, ESH-IP and ISO have now developed the AAMI/ESH/ISO Universal Standard (ISO 81060-2:2018) as the recommended 21st-century procedure for worldwide application. The ESH Working Group has published a practical guide for using the Universal Standard. It is in the interests of all scientific bodies to propagate the Universal Standard and ensure its wide implementation.

Keywords: accuracy, blood pressure measurement, device, monitor, protocol, standard, validation

In this issue of the *Blood Pressure Monitoring* journal Alpert et al recommended that validation studies of blood pressure (BP) measuring devices using the *European Society of Hypertension International Protocol* (ESH-IP) [1,2] should no longer be accepted for publication in scientific journals [3]. As we transition to a new Universal Standard for the validation of BP measuring devices, which is replacing not only ESH-IP but also all other previous validation protocols (**Table 1**), it is an opportunity to overview the contribution that the ESH-IP has made to the accuracy of BP measurement over the past two decades.

History of validation protocols

The accuracy of the BP measuring devices is an important prerequisite for the reliable evaluation of BP and thereby the diagnosis and management of hypertension. In the last three decades several organizations, such as the United States Association for the Advancement of Medical Instrumentation (AAMI), the British Hypertension Society (BHS), the German Hypertension League (DHL), the European Society of Hypertension Working Group on BP Monitoring (ESH) and the International Organization for Standardization (ISO) have developed protocols for the validation of BP measuring devices (**Table 1**) [4].

These protocols have been devised by prestigious organizations and experts around the world and have important similarities and differences. All share a common objective, namely the standardisation of the validation procedure with the establishment of minimum standards of accuracy.

Rationale, accuracy and mission of the ESH International Protocol (ESH-IP)

The most important difference among the established validation protocols (**Table 1**) is the sample size required, with the ESH-IP requiring 33 subjects compared to 85 with the other protocols [4,5]. The rationale for a considerable reduction in the sample size was to facilitate the widespread application in more centres with a resultant increase in the number of devices subjected to independent validation [4]. The small sample size stipulation resulted in lower cost with fewer resources needed, which are important considerations for manufacturers who wish to continuously

develop the technology of the BP measuring devices. Moreover, it was probably also attractive for scientists to conduct and publish more studies using the ESH-IP, including repeated testing of the same monitor by different investigators. On the other hand, a larger sample size increases the study power and accuracy and allows subgroup evaluation, for example, for different arm and cuff sizes, age groups, or special populations (children, pregnancy, etc), which was not possible to do meaningfully within a 33-subject ESH-IP validation [4,5].

It is important to note that the ESH-IP was not necessarily easier to pass than the other protocols requiring larger samples. On the contrary, the revised ESH-IP 2010 [2,4,5] has proved itself to be the most stringent protocol used in the validation of BP measuring devices. First, as it is noted in a recent AAMI/ESH/ISO Collaboration Statement [5], the revised ESH-IP [2] and the ANSI/AAMI/ISO [6] allow for a similar tolerable error of 10-mmHg with frequency of 12-18%. Second, study power calculations performed by an experienced US NIH biostatistician collaborating with the AAMI [5], showed that the sample size of the ESH-IP is (i) adequate for 'high accuracy' devices, (ii) adequate for 'low accuracy' devices, but (iii) inadequate for 'moderate accuracy' devices as they have an unacceptably high chance to fail [5]. Thus, using the ESH-IP accurate devices passed and inaccurate ones failed, and moderate accuracy devices were more likely to fail rather than pass [5]. This analysis performed in the US for AAMI suggests that the devices which passed the ESH-IP are as accurate as any of those passing the other validation protocols (**Table 1**). Third, the ESH-IP validation results are reproducible, as shown in a recent publication reporting on the ESH-IP procedure performed independently by two different validation centres and teams that tested the same device [7]. This study showed good inter-center reproducibility with very similar validation results. This important characteristic of any evaluation procedure, particularly for validation protocols, must be established for any validation protocol to avoid contradictory results when evaluating the same devices in different centers and to allow for valid comparison among different devices.

The mission of the ESH-IP, which was to expand the validation procedure and increase the number of devices subjected to independent validation, has been well achieved. Since the publication of the

first version of the ESH-IP in 2002 up to March 2019 a total of 200 validation studies (PubMed) using the ESH-IP have been published versus 115 using the AAMI and/or ISO protocol, and 103 using the BHS protocol (**Fig. 1**). This steep rise in the number of validation studies published in the last decade using the ESH-IP, has increased international awareness of the importance of using monitors validated with an established protocol, and thereby had indisputable benefits for scientists and the public.

A Universal Standard for 21st century validations

The presence of several different validation protocols for BP measuring devices (**Table 1**) has resulted in confusion not only for physicians and researchers, but also for patients and for manufacturers who may be uncertain as to which protocol to use. The presence of multiple protocols also weakened efforts to influence regulatory authorities to make the validation of devices a mandatory requirement for marketing. Thus, it was decided that a universal standard for the validation of BP monitors, which would be acceptable for global use, would be in the best interest of the scientific community and the public.

In 2016 experts from AAMI, ESH-IP and the ISO came together and reviewed all the methodological, statistical and clinical aspects of the existing validation protocols over the last 30 years and agreed on the principles for developing a universal standard that would have worldwide application [5]. The aims of this universal standard are to (i) provide more accurate and more detailed information on the performance of BP measuring devices, (ii) allow arm-size stratification and evaluation of patient subgroups and special populations, and (iii) strengthen the case for regulatory authorities to make mandatory for all devices to undergo independent clinical validation for marketing.

The AAMI/ESH/ISO Universal Standard (ISO 81060-2:2018) has been recently published [8,9]. It is now up to the scientific community to implement it internationally and to abandon all other validation procedures in a progressive and orderly manner. To allow completion and publication of ongoing validation studies using any of the previous protocols (AAMI, BHS, ESH, ISO), we have recommended that the Universal Standard should be implemented as the mandatory international

standard for BP measuring devices 1 year after the date of its publication, at the beginning of 2020 [9].

Unfortunately, and despite the efforts by several organizations worldwide, only few of the BP measuring devices currently available on the market have been subjected to independent validation using any of the established protocols [4]. Thus, work reporting data on the accuracy of BP monitors using any of the earlier validation protocols (**Table 1**), or any other procedure for the assessment of BP measurement accuracy, may still be considered for publication in a scientific journal if the peer reviewers and the editors judge these data as being valid and the information provided as important for the scientific community and the public. This accepted, however it will be in the interests of all scientific bodies to propagate the routine use of the AAMI/ESH/ISO Universal Standard (ISO 81060-2:2018) [8,9] as the recommended 21st-century standard. Efforts should be made by all contributing organizations to ensure its wide implementation, abandoning all previous protocols for future work. The ESH Working Group on BP Monitoring has recently published detailed recommendations and practical guidance for investigators performing validation studies according to the AAMI/ESH/ISO Universal Standard (ISO 81060-2:2018) [9], with the purpose of ensuring that its stipulations are meticulously implemented, and that complete data are reported. We expect that this new Universal Standard will become widely used worldwide and enhance efforts to standardize the validation and regulatory oversight of BP measuring devices.

Whereas we uphold the adoption and implementation of the new Universal Standard and support efforts by international bodies to ensure its widespread use, we acknowledge the contribution made to device accuracy by previous protocols. Until data on the accuracy of devices using the new Universal Standard become plentiful, it is scientifically correct to recognise devices validated by previous protocols, including the ESH IP, as being accurate.

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TABLE 1.

History of validation protocols (modified with permission from reference [4]).

Protocol	Organization	Publication
AAMI	US Association for the Advancement of Medical Instrumentation	1987, 1992, 2002
BHS	British Hypertension Society	1990, 1993
DHL	German Hypertension League (Deutsche Hochdruckliga)	1999
ESH-IP	European Society of Hypertension International Protocol	2002, 2010
ISO	International Organization for Standardization	2009
ANSI/AAMI/ISO	American National Standards Institute/Association for the Advancement of Medical Instrumentation/International Organization for Standardization	2009, 2013
AAMI/ESH/ISO (ISO 81060-2:2018)	Association for the Advancement of Medical Instrumentation/ European Society of Hypertension/ International Organization for Standardization	2018

FIGURE 1.

Cumulative graph of published validation studies from 2002 to March 2019 performed using the European Society of Hypertension International Protocol (ESH-IP), the British Hypertension Society (BHS) protocol and the US Association for the Advancement of Medical Instrumentation (AAMI) and/or the International Organization for Standardization (ISO) standard (modified from reference [4]).

