

## ORIGINAL ARTICLES

## Method of Blood Pressure Measurement in Neonates and Infants: A Systematic Review and Analysis

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**Objectives** To determine the recommended blood pressure (BP) measurement methods in neonates after systematically analyzing the literature regarding proper BP cuff size and measurement location and method. **Study design** A literature search was conducted in MEDLINE, PubMed, Embase, Cochrane Library, and CINAHL from 1946 to 2017 on BP in neonates <3 months of age (PROSPERO ID CRD42018092886). Study data were extracted and analyzed with separate analysis of Bland-Altman studies comparing measurement methods. **Results** Of 3587 nonduplicate publications identified, 34 were appropriate for inclusion in the analysis. Four studies evaluating BP cuff size support a recommendation for a cuff width to arm circumference ratio of approximately 0.5. Studies investigating measurement location identified the upper arm as the most accurate and least variable location for oscillometric BP measurement. Analysis of studies using Bland-Altman methods for comparison of intra-arterial to oscillometric BP measurement show that the 2 methods correlate best for mean arterial pressure, whereas systolic BP by the oscillometric method tends to overestimate intra-arterial systolic BP. Compared with intra-arterial methods, systolic BP, diastolic BP, and mean arterial pressure by oscillometric methods are less accurate and precise, especially in neonates with a mean arterial pressure <30 mm Hg.

**Conclusions** Proper BP measurement is critical in neonates with naturally lower BP and attention to BP cuff size, location, and method of measurement are essential. With decreasing use of intra-arterial catheters for long-term BP monitoring in neonates, further studies are urgently needed to validate and develop oscillometric methodology with enhanced accuracy. (*J Pediatr 2020;221:23-31*).

roper measurement of blood pressure (BP) in neonates and infants can be technically challenging. BP values may reflect perfusion, fluid status, cardiac, and endocrine function as well as overall level of illness. In neonates, especially those born prematurely, BP values change rapidly over the first days of life as the neonate hemodynamically adapts to an extrauterine environment.<sup>1</sup> Unfortunately, the literature to guide clinicians and researchers on proper BP measurement methods in neonates is limited.

Currently, the gold standard method of BP measurement in neonates is through an in-dwelling intra-arterial catheter. The method is associated with technical difficulties such as dampening of the waveform, air bubbles, and the need to calibrate the system regularly, as well as complications such as ischemia and thrombosis.<sup>2</sup> Advances in the design of noninvasive BP monitoring, including oscillometric devices, has resulted in their increasing use in neonatal intensive care units (NICUs). Oscillometric devices detect the amplitude of pulsations within the artery. The cuff is inflated above the systolic pressure then as the cuff gradually deflates, the arterial pulsations increase in amplitude to a maximal extent which is determined to be the mean arterial pressure (MAP).<sup>3</sup> Using estimates of pulse pressure and computational algorithms specific to each device manufacturer, systolic BP (SBP) and diastolic BP (DBP) are calculated. In practice, intra-arterial monitoring is reserved for

BP	Blood pressure
DBP	Diastolic BP
MAP	Mean arterial pressure
NICU	Neonatal intensive care unit
SBP	Systolic BP

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0022-3476/\$ - see front matter. © 2020 Elsevier Inc. All rights reserved. https://doi.org/10.1016/j.jpeds.2020.02.072 BP measurement in unstable critically ill neonates and oscillometric methods are used for the majority of neonates in the NICU.

A consensus document for a universal standard for BP device validation was published with collaboration of the Association for the Advancement of Medical Instrumentation, the European Society of Hypertension, and the International Organization for Standardization.<sup>4</sup> They recommend that  $\geq$ 85 subjects are required for a device validation study with a minimum of 35 participants for BP studies in special populations.<sup>4</sup> Many of the currently published neonatal studies would not fulfill this criterion. Another key recommendation is that the mean BP difference between the test and approved comparator is  $\leq$ 5 mm Hg with an SD of  $\leq$ 8 mm Hg.<sup>4</sup> In neonates with expected BP values in the 30- to 50-mm Hg range, these large differences are unacceptable for clinical care and research. Given the uniqueness of the neonatal population, the accuracy of BP devices, efficacy of measurement techniques, and interpretation of measured values all need special consideration.

In 2015, the International Neonatal Consortium was established to collaborate to advance the regulatory science of medicines and devices for neonates.<sup>5</sup> Within this collaboration are representatives from industry, regulatory agencies, academic and clinical communities, professional societies, and patient groups. A hemodynamic adaptation workgroup was established in the fall of 2016 with the goals to establish an international consensus on observed ranges of BP in neonates, identify factors that influence neonatal BP, and provide recommendations for proper BP measurement methods in neonates. This report represents a systematic review and analysis of the international literature on methods of BP measurement in neonates <3 months of age, including proper cuff size, optimal location, and measurement method. The ultimate goal is to guide clinicians, researchers, and industry to conduct future clinical research studies in a consistent, evidence-based manner to improve the quality and applicability of future neonatal hemodynamic studies.

### **Methods**

A literature search was conducted by a professional librarian in MEDLINE, PubMed, Embase, the Cochrane Library, and CINAHL. The search terms were (blood pressure OR hypertension OR hypotension) AND (infant OR newborn OR neonate) AND infant [MeSH] AND (measurement OR normative) AND humans [MeSH]. Study design inclusion criteria were prospective or retrospective, cohort, case series, and randomized controlled trials. Study design exclusion criteria: absence of extractable data in letters, comments, papers, and reviews. The search included January 1946 to January 2017 and did not limit year of publication because some of the earliest studies provide evidence for correlation of intra-arterial and oscillometric methods as well as correct cuff size. Full details of the literature search are available in the **Appendix** (available at www.jpeds.com). The neonatal period was defined for term and preterm infants as day of birth through term plus 27 days.<sup>6</sup> Studies that included neonates with major congenital anomalies, such as cardiac defects, were excluded from consideration. Although 70 non-English-language articles were identified, all were reviewed except for 13 in languages including Bulgarian, Czech, Hungarian, and Russian because they were unable to be translated by workgroup members.

The first stage of data extraction by workgroup members included bibliographic details, study population including gestational age and postnatal age, study design and intervention, method of BP measurement, outcome measures, description of results, and study limitations. Agreement on the selection of studies to enter the second stage of data extraction was reached by the hemodynamic workgroup based on the quality of the available literature. This stage involved a more detailed consideration of the statistical methods described in the selected articles as well as extraction of study comparisons, sample size and setting, descriptive statistics including location and dispersion, statistical analysis method, effect estimate, and precision. Reporting of methods and results are in accordance with the PRISMA standard. The protocol for this review is registered on the PROSPERO website with ID CRD42018092886.

Only studies that were judged to have used appropriate statistical methods were considered in the analyses. This factor extends to study design, data analysis, and reporting of results. Results were not selected for extraction on the basis of statistical significance. Instead, all relevant results were extracted. There was no statistical synthesis of aggregate data and therefore no assessment of statistical heterogeneity was needed. Where possible, the bias and SD were calculated using simple algebra on the quantities given, for example, difference in mean or SD from 95% CIs.

One aspect of comparing the performance of a device to the gold standard method (intra-arterial) is assessing the agreement of measurements. This can be quantified by the bias and the limits of agreement.<sup>7</sup> The bias is estimated as the mean of the paired differences between intra-arterial and noninvasive measurements. The limits of agreement are at bias  $-1.96 \times$  SD and bias  $+1.96 \times$  SD, where SD is the SD of the paired differences. Because paired differences tend to follow a normal distribution, the expectation is that 95% of the differences will lie within the limits of agreement.

The Association for the Advancement of Medical Instrumentation protocol for BP device validation requires a mean BP difference of  $\leq 5$  mm Hg with an SD of  $\leq 8$  mm Hg and both the European Society of Hypertension and British Hypertension Society criteria included approximately 85% of readings to be <10 mm Hg difference from the standard method.<sup>8,9</sup> These differences are too large for neonates with a lower BP and the workgroup agreed that an acceptable bias in BP measurements between the reference method and comparator would be  $\pm 5$  mm Hg with SD of 5 mm Hg. These values define the limits of agreement (in millimeters of mercury) at -14.8 and 4.8, and at -4.8 and 14.8, depending on the direction of the bias.

### Results

The systematic search identified 5299 reports. After removing duplicates, 3587 titles and abstracts were reviewed by 11 members of the working group (**Figure 1**). 602 articles were reviewed and data extracted according to predefined criteria (in spreadsheet). A total of 401 were excluded leaving 201 for further consideration. These articles were identified as being pertinent to  $\geq 1$  of the 3 primary research questions of the working group; 34 were identified as relevant to the current research question.

### Cuff Size

Four studies investigated the relationship between cuff size of noninvasive oscillometric devices and invasive BP values (**Table I**; available at www.jpeds.com).<sup>10-13</sup> Lum and Jones repeatedly measured SBP in neonates 24-42 weeks of gestation using 3.50-, 4.75-, and 6.00-cm cuffs.<sup>10</sup> They found that BP measurements varied based on cuff size, with the most reliable measurements (as compared with umbilical arterial values) being obtained when a cuff width to arm circumference ratio of 0.5 was used. In a study by

Kimble et al of neonates born at 28-40 weeks of gestation, a significant increase in the mean error rate for MAP measurements occurred when the cuff width to arm circumference ratio was <0.45 or >0.7.11 Briassoulis compared cuffs by intra-arterial measurements in a population of neonates 27-33 weeks gestation using both the recommended cuff size (cuff width to arm circumference ratio of 0.41-0.59) and a cuff that was "one size above the recommended size.<sup>\*12</sup> For both cuff sizes, a significant percentage of measurements were >5 mm Hg different than the invasive BP measurements and the correlation between intra-arterial and oscillometric measures were not significantly different based on cuff size. In a population of preterm neonates with a mean gestational age at birth of 27.7  $\pm$  1.7 weeks, Sonesson and Broberger reported "reasonably accurate" MAP measurements with a cuff width to arm circumference ratio of 0.44-0.55 and an increased risk of overestimating the MAP when a lower cuff width to arm circumference ratio was used.<sup>13</sup> Findings from these studies, which are summarized in Table I, support that a cuff width to arm circumference ratio of approximately 0.5 should be used for



Figure 1. Flow diagram of systematic review literature search.

Table II. International Neonatal Consortium
recommendations for measurement of BP in neonates

Aspects	Recommendations
Cuff	Use a BP cuff with a cuff width to arm circumference ratio closest to 0.5 for noninvasive BP measurements obtained by the oscillometric method.
Location	Right upper arm BPs are the recommended location for oscillometric measurements. Calf BPs may be considered only in the first few days of life or if there is a contraindication to arm BP measurements. Right upper arm is preferred to the left in case of
Method	<ul> <li>coarctation of the thoracic aorta.</li> <li>Oscillometric devices may be used to screen for BP abnormalities, but if there are concerns with values that are too low, too high, or do not seem to correlate with the clinical condition of the infant, intra-arterial BP values should be obtained.</li> <li>When oscillometric devices are used, MAP should be compared to normative values as the most accurate BP value in these devices.</li> <li>Use oscillometric devices with caution in neonates with a MAP of &lt;30 mm Hg because they are less accurate in these infants.</li> <li>For both intra-arterial and oscillometric measurements, repeated measures of BP should be used for clinical decision making owing to BP</li> </ul>
Future research	<ul> <li>A standardized BP measurement protocol (including the above criteria) with adequate patient sample size should be used for all neonatal research studies that include BP as an outcome measure.</li> <li>Further research studies are needed to better define in which neonatal populations, oscillometric values closely approximate intra-arterial values and conversely, in which populations to use only intra-arterial methods for clinical decision making.</li> <li>Advancements in oscillometric device technology or other methods of circulatory assessment specific for neonates and infants could improve the accuracy of these noninvasive measurements with widespread clinical implications.</li> <li>As BP is used as a marker of blood volume and perfusion, additional research is needed to determine the biological implication of peripheral BP measures compared with other vascular markers such as central aortic pressure, cerebral blood flow and oxygenation, and vascular regulation in neonates.</li> </ul>

noninvasive BP measurements obtained by the oscillometric method (Table II and Figure 2).

### **Measurement Location**

Available studies evaluating measurement location BP differences are mostly small in size with a wide range of gestational ages and heterogeneous study protocols. Although 1 study compared umbilical with peripheral intra-arterial SBP and DBP values and found good correlation between the measurements, this older study had a small sample size and limited detail on the analysis conducted.<sup>14</sup> Two studies assessed lower limb oscillometric SBP, DBP, and MAP compared with umbilical intra-arterial measures in neonates between 27 and 40 weeks of gestation (**Table III**; available at www.jpeds.com).<sup>15,16</sup> Baker et al showed strong correlation of all BP measurements between the umbilical and lower limb locations, whereas Moniaci and Kraus showed only moderate correlation (4-6 mm Hg difference in many measures).<sup>15,16</sup> No study aimed to directly compare calf measurements with thigh measurements, but 2 studies commented on their observations. Rahiala and Tikanoja studied oscillometric BP in healthy neonates and found that thigh DBP was statistically lower than calves and arms.<sup>17</sup> Park and Lee also compared healthy neonate leg with arm oscillometric measures and found that all thigh measurements were 4-8 mm Hg higher than calves or arms.<sup>18</sup>

Six studies compared neonatal arm with calf oscillometric BP and found similar differences between the 2 locations (Table III). These studies show that mean calf SBP, DBP, and MAP are comparable with the mean arm BP in the first few days of life, but the SD of the measurements was often large and clinically significant.<sup>17-20</sup> In a study by Kunk and McCain, the difference in all BP and SD of the measurements were higher with more advanced postnatal age.<sup>19</sup> Calf BP has also been noted to have a wide variability of values at all ages. Crapanzano et al compared arm with calf BP over the first few years of life and found that in infants <6 months of age, all calf BP measures were slightly lower than arm pressures but by 6-9 months of age, the calf BP exceed arm pressures.<sup>21</sup> Given the level of evidence in the literature, we recommend measurements be taken in the right upper arm when using an oscillometric device and cannot endorse the routine use of calf BP measurements (Table II).

# Measurement Method Studies Using Bland-Altman Methods

We identified 18 articles in which the authors had applied Bland-Altman methods to quantify the bias and agreement between different methods of measuring BP, comparing direct (intraarterial) with indirect (oscillometric) methods.<sup>15,20,22-37</sup> Results extracted from those articles are presented in forest plots (**Figure 3**, A-C) showing the bias and limits of agreement for all of the comparisons reported in the articles. Some articles incorporated >1 analysis if several subgroups of neonates were analyzed separately.

In the majority of studies, the mean BP difference between intra-arterial and oscillometric measures was outside of the agreed upon acceptable bias of  $\pm 5$  mm Hg and SD  $\pm 5$  mm Hg. Analyses of MAP showed an almost equal distribution of analyses with positive (13 results) and negative bias (15 results). Twenty-four of 29 analyses (83%) demonstrated a mean BP difference within 5 mm Hg (**Figure 3**, A). Only 4 analyses for MAP had both mean BP difference of  $\pm 5$  mm Hg and dispersion within the predefined limits of agreement. Two of these analyses came from Baker et al that included 5-14 neonates of a wide gestational ages (25-40 weeks) and postnatal ages (1-12 days).<sup>15</sup> Similarly, the study by Yiallourou et al that met our limits of agreement included 10 neonates of 27-36 weeks gestational age and 1-4 days of life.<sup>35</sup> Unfortunately, other similar studies had BP measurement



Figure 2. A method to determine the proper BP cuff size in neonates and infants. The cuff bladder width should be approximately 50% of the infant mid-arm circumference. Illustration by Robert Pintilie.

differences that did not meet our bias and limits of agreement and therefore limit the conclusions we can make about BP methodology in these populations.<sup>20,24,26,29,31,32,34</sup> In studies that focused primarily on the first 1-5 days of life, almost all analyses showed that the oscillometric method gave BP values higher than by the intra-arterial method.<sup>20,24,26,28,33,35</sup> There were no obvious associations by gestational age at birth or birth weight.

There were fewer analyses that compared intra-arterial with oscillometric methods with SBP or DBP as the outcome. Thirteen of 17 analyses (76%) of SBP showed a mean BP difference within  $\pm 5$  mm Hg (**Figure 3**, B). The studies by Baker et al and Yiallourou et al were the only analyses to satisfy both the accepted mean BP difference and limits of agreement; all other studies were outside these limits.<sup>15,35</sup> Most analyses of SBP showed a negative mean BP difference comparing direct with indirect methods consistent with higher BP readings by the oscillometric method. In DBP analyses, 11 of 16 (69%) showed a mean BP difference within  $\pm 5$  mm Hg and only 4 analyses also had limits within our limits of agreement, similar to above (**Figure 3**, C).



**Figure 3.** Forest plot of studies using the Bland-Altman method for comparison of direct (intra-arterial) to indirect (oscillometric) methods of BP measurement in neonates. **A**, Analyses of MAP. **B**, Analyses of SBP. **C**, Analyses of DBP. Descending each figure, results, labelled by the first author, publication year, and any additional distinguishing feature are ordered by the magnitude of bias from positive to negative. Bias is represented by the midpoint of each horizontal bar, the end points of which are the lower and upper 95% limits of agreement. The *red vertical line* marks no bias, the *blue dashed vertical lines*, and the *green dashed vertical lines* mark the lower and upper limits of agreement (*blue* for studies with positive bias, *green* for negative bias).

The interpretation is limited somewhat by the heterogeneity of the study analyses. Patient numbers ranged from a low of 5 to a high of 87.<sup>15,22</sup> The number of paired BP comparisons ranged from 1 to >50 per patient.<sup>26</sup> In addition, study analyses were often subdivided by other clinical features such as birth weight,<sup>23,28</sup> location of measurement, or illness. One study included neonates 23-35 weeks gestational age over the first 7 days and found good correlation between direct and indirect BP readings except when infants had low BP.<sup>32</sup> When the MAP was <30 mm Hg, the oscillometric method gave significantly higher values than intra-arterial methods.

#### **Other Studies**

Seven additional studies were identified that did not use Bland-Altman methodology for analyses comparing intraarterial BP measurement with the oscillometric method (**Table IV**; available at www.jpeds.com). Some studies showed good correlation of the 2 measurement methods,<sup>38,39</sup> whereas others showed poor correlation or large SDs.<sup>12,40,41</sup> Chia et al showed that there was good agreement in the measured BP values when the MAP was >40 mm Hg.<sup>42</sup> When the MAP was <40 mm Hg, 69% of the oscillometric values were higher and in 34% the difference was ≥5 mm Hg. If the MAP was <30 mm Hg, then oscillometric values overestimated BP in 81% of readings and in 59% the difference was ≥5 mm Hg.<sup>42</sup> Diprose et al also showed in neonates weighing less than 1500 grams that oscillometric readings overestimated intraarterial pressures, with greater overestimation in those with the lowest BP measurements.<sup>40</sup>

The effect of a BP measurement protocol was studied in a cohort of 64 low birth weight neonates who were 7-42 days old by Nwankwo et al.<sup>43</sup> Measurements were taken by the

same individual ≥90 minutes after the neonates' last feed or medical intervention. An appropriate sized cuff was applied to the right upper arm and the neonate was left undisturbed for  $\geq$ 15 minutes or until the neonate was sleeping or in a quiet awake state. Three successive BP recordings were taken at 2minute intervals. The first measurements were significantly higher than third measurements. For both the prone and supine positions, the mean BP values obtained by routine nurse measurement were significantly higher and varied more widely than those obtained using the standard protocol (54.4 mm Hg vs 47.0 or 49.1 mm Hg; P < .003).<sup>43</sup> Several of the other identified studies commented on oscillometric device sensitivity to movement and state of infant arousal with greater variability of oscillometric readings compared with direct measurements.<sup>12,15,27,37</sup> Low et al concluded from their analysis of BP variability that a single reading could be misleading and others studies also used or recommended  $\geq$ 3 BP measurements for improved accuracy<sup>15,21,27,37</sup> (Table II).

### Discussion

The ideal BP measurement method is the one that provides the most accurate readings, with the least variability, and lowest potential for side effects or complications. The technique is even more important in neonates because expected MAP values are lower than older children and adults and may be in the 30-50 mm Hg range. Our systematic review of the literature identified some important measurement practices for accurate readings, but also some areas of uncertainty. Implementing a standardized BP measurement approach for both clinical care and research may help to improve the accuracy of values obtained, but also highlight areas where this hemodynamic marker does not correlate with the condition of the infant and where more research is needed.

The first step for noninvasive BP measurement in neonates is choosing the correct cuff size. Although the number of studies on this topic was small, the conclusions were consistent showing that a cuff size with a cuff width to arm circumference ratio of approximately 0.5 provides the most accurate BP values. The most concerning risk is that too small of a cuff size overestimates BP values compared with intra-arterial methods, which could lead to under-recognition of hypotension.<sup>11,13</sup> The recent American Academy of Pediatrics Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents also highlights the importance of proper measurement technique for children.<sup>44</sup> For children, they recommend a cuff size with a cuff width to arm circumference ratio of  $\geq 0.4$  and bladder length that covers 80%-100% of the upper arm circumference. They also highlight child size variability and the lack of appropriately sized BP cuffs in many pediatric settings.<sup>44</sup> Similar to older children, neonates vary in size and multiple BP cuffs need to be available in the NICU and the outpatient setting to match the proper cuff size to the size of the infant for accurate BP readings.

When using oscillometric devices for BP measurement in neonates, the right upper arm is the preferred location for mea-

surements. There are obviously scenarios in neonates where peripheral lines or devices preclude using the upper arm for BP measurements. However, calf BP values are more variable and may be less accurate than arm BP values.<sup>19,21</sup> Thigh BP values are not similar to arms or calves and should not be used in neonates. In addition, measured BP values should be compared with normative data for neonates of the same postmenstrual age and these norms are based on upper arm BP.<sup>45</sup> Moreover, the right upper arm is the preferred location for BP measurements in case of the presence of a coarctation of the thoracic aorta, which is consistent with the American Academy of Pediatrics guideline recommendation for children.44,46 Because the majority of thoracic coarctations are diagnosed in neonates and infants, measurement location is particularly important and an elevated BP in the right upper arm should be investigated with 4-limb BP, assessment of femoral pulses and/or echocardiography.<sup>47</sup>

Although oscillometric BP measurements are not as accurate or precise as direct intra-arterial measurements in neonates, it is not practical or safe for all neonates to have indwelling arterial catheters. It is reasonable to use oscillometric devices to screen for BP abnormalities (Table II). They should not replace direct measures when there is a clinical concern with values that are too low, too high, or not consistent with other features of the infant's condition, and where intra-arterial values are still needed. Oscillometric measurements should be interpreted with caution in neonates with a MAP of <30 mm Hg because the devices are less accurate in this range. It is also recommended that MAP be the primary assessed BP value to compare with normative data as this measurement is most similar to the intra-arterial value and the only measured value of oscillometric devices (Table II). Some of the differences in BP accuracy in studies may be due to the fact that each oscillometric device manufacturer uses a different computational algorithm for determining BP and several studies have shown differences between devices.<sup>20,48</sup>

A consistent BP measurement technique could be implemented through the use of a standard measurement protocol to improve quality of care. A survey of physicians in Nordic university hospitals reported that standardized procedures for noninvasive BP measurement in infants were lacking in 77% of hospital units.<sup>49</sup> In addition to using the proper cuff size and measurement location, the state of the infant is also an important consideration.<sup>43</sup> Infant BP is higher when awake and crying, when feeding or sucking, and when being held head up.<sup>50,51</sup> The standardized protocol for BP measurement studied by Nwankwo et al is in line with the findings of our systematic review.<sup>43</sup> For oscillometric BP measurements, an appropriate sized cuff should be applied to the right upper arm, the neonate allowed to settle and when the infant is asleep or quietly awake, up to 3 BP measurements should be taken. First BP readings are usually higher than subsequent readings, so second and third readings should be used if discrepant.<sup>43</sup> Unfortunately in practice, with routine nursing care, multiple BP measurements can occasionally result in quite different readings, leading to clinical uncertainty. A

study comparing a BP measurement by protocol with 3 readings 5 minutes apart compared with routine nursing care in full-term healthy newborns found no significant difference between measurement with a single BP reading done when infants were quiet or asleep.<sup>52</sup> However, in neonates in the NICU with rapidly changing BP and multiple factors affecting BP variability, repeated measures of BP should be used when the screening BP does not correlate with the condition of the infant and when management decisions will be based on the BP value. Although this is not always possible in the NICU, clinicians should be cautious in making clinical decisions on the basis of a single BP measurement (Table II).

We identified several limitations of our systematic review and analysis. Most of the studies included were single center, used convenience samples, and did not report power calculations which would support statistical testing. Included patients were often from a wide range of gestational ages, postnatal ages, and birth weights. Study protocols were not consistent and different analysis methods were used. Given the diversity of research settings and neonatal populations, clinical heterogeneity, and variability in BP devices used, statistical synthesis of the results was not deemed appropriate. The majority of studies reporting Bland-Altman comparisons were based on small numbers of neonates and the limits of agreement (between oscillometric and intra-arterial methods) were generally wider than can be safely recommended for clinical practice.

Although the strength and consistency of the evidence for BP cuff size and measurement location was moderate, there remains much uncertainty about the accuracy of oscillometric devices in neonates. Unfortunately, in some studies, BP was not measured and recorded in a standardized fashion. Future research studies need to use an evidence-informed measurement protocol to ensure that the values obtained are reliable (Table II). More studies are needed to define the neonatal populations where it is safe to trust the oscillometric device readings and in which populations intra-arterial BP readings are needed. There is also a need for improved normative BP data based on current measurement methods in neonates. It is important to remember that BP is a cardiovascular marker that needs to be assessed in the context of clinical status, with further research directed towards the biological implication of different vascular states in the neonate.

After systematic review and analysis of the medical literature, we have developed best evidence-based recommendations for proper measurement of BP in neonates that can be incorporated into a BP measurement protocol for use in clinical care and future research studies. ■

Acknowledgments available at www.jpeds.com.

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### Appendix

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Table I. I	mpact	of cuff size on BP	measurem	ents in newł	oorn i	nfants		
Articles	Year	Population	Sample size	No. of paired measures	BP	Cuff size (cm)	Reported difference between cuff and invasive measurement	Additional findings
Lum <sup>10</sup>	1977	Gestational age: 24-42 wk	26	26	SBP	3.5	Data not provided	r = 0.40, SBP <sub>cuff</sub> – SBP <sub>UAC</sub> = 2.56 (extremity circumference) – $13.72$ ; $P < .05$
				26	SBP	4.75	Data not provided	r = 0.71, SBP <sub>cuff</sub> – SBP <sub>UAC</sub> = 2.46 (extremity circumference) – 26.85: $P < .05$
				26	SBP	6.0	Data not provided	r = 0.66, SBP <sub>cuff</sub> – SBP <sub>UAC</sub> = 1.88 (extremity circumference) – $31.11: P < .05$
Kimble <sup>11</sup>	1981	Gestational age: 28-40 wk	17	250	MAP	$2.2 \times 5.9,$ $3.0 \times 6.8,$ $3.8 \times 10.2,$ $4.4 \times 11.2$	Mean $\pm$ SD: $-0.2\pm3.8$ torr (W:AC 0.45-0.70)	r = 0.853, regression line of $y = 0.822x + 7.480$ ( $x = UAC MAP$ , $y = cuff MAP$ )
Briassoulis <sup>12</sup>	1986	Gestational age: 27-33 wk	6	225	SBP	Recommended		Number of cuff size measurements with >3 mm Hg, >5 mm Hg, and >10 mm Hg difference between invasive measurement (respectively): 141 (63%); 73 (32%); 14 (6.3%)
				225	DBP	Recommended	Mean $\pm$ SEM: 0.76 $\pm$ 5.3 mm Hg (P < .05)	Number of cuff size measurements with >3 mm Hg, >5 mm Hg, and >10 mm Hg difference between invasive measurement (respectively): 149 (66%): 95 (42%): 16 (7.1%)
				185	Map	Recommended	$\begin{array}{l} \text{Mean} \pm \text{SEM:} -1.65 \pm 4.35 \text{ mm Hg} \\ (\textit{P} < .001) \end{array}$	Number of cuff size measurements with >3 mm Hg, >5 mm Hg, and >10 mm Hg difference between invasive measurement (respectively): 112 (60%): 62 (34%): 7 (3.8%)
				225	SBP	One size above recommended	$\begin{array}{l} \text{Mean} \pm \text{SEM:} -0.82 \pm 4.92 \text{ mm Hg} \\ (\textit{P} < .02) \end{array}$	Number of cuff size measurements with >3 mm Hg, >5 mm Hg, and >10 mm Hg difference between invasive measurement (respectively): 130 (58%); 66 (29%); 9 (4.0%)
				225	DBP	One size above recommended	Mean $\pm$ SEM: $-0.91 \pm 5.37$ mm Hg (P < .02)	Number of cuff size measurements with >3 mm Hg, >5 mm Hg, and >10 mm Hg difference between invasive measurement (respectively): 140 (62%): 93 (41%): 21 (9.3%)
				176	Map	One size above recommended	$\begin{array}{l} \text{Mean} \pm \text{SEM:} -1.73 \pm 4.82 \text{ mm Hg} \\ (\textit{P} < .001) \end{array}$	Number of cuff size measurements with >3 mm Hg, >5 mm Hg, and >10 mm Hg difference between invasive measurement (respectively): 93 (53%): 58 (33%): 10 (5.7%)
Sonesson <sup>13</sup>	1987	Mean gestational age at birth:	15	30	SBP	small (W:AC 0.33-0.42)	Mean $\pm$ SD difference: 6.9 $\pm$ 10.8 mm Hg	
		$27.7\pm1.7$ wk		30	DBP	Small	Mean $\pm$ SD 6.1 $\pm$ 5.4 mm Hg	
				30	MAP	Small	Mean $\pm$ SD 6.2 $\pm$ 7.2 mm Hg	
				30	SBP	Large cuff (W:AC 0.44-0.55)	Mean $\pm$ SD 0.7 $\pm$ 5.3 mm Hg	
				30 30	DBP MAP	large large	Mean $\pm$ SD 0.2 $\pm$ 2.7 mm Hg Mean $\pm$ SD –1.0 $\pm$ 2.3 mm Hg	

SEM, Standard error measurement; UAC, umbilical artery catheter; W:AC, width to arm circumference ratio.

Table III.	Compa	risons of BP differenc	e based	on measure	ment location											
Articles	Year	Population	Sample size	No. of paired measures	Measurement location	Postnatal age	Descriptive results (BP difference)	Estimate of effect (correlation)	Comments							
Butt <sup>14</sup>	1984	NICU; 26-39 wk gestational age; 740-3200 g	11	34	Umbilical (IA) vs peripheral artery (IA)	1-7 d	SBP U = $1.03 \times$ Per- $1.5 \text{ mm Hg}$ DBP U = $1.04 \times$ Per- $.61 \text{ mm Hg}$	SBP: r = 0.98 DBP: r = 0.97	Small sample size. Statistics unclear.							
Baker <sup>15</sup>	1984	NICU; 25-40 wk gestational age; BW 740-3500 g NICU; 28-40 wk gestational age; BW 1040-3730 g NICU; 27-42 wk gestational age	14	98	Umbilical (IA) vs L upper arm (Osc)	1-12 d	SBP: $2.5 \pm 2 \text{ mm Hg}$ DBP: $2.9 \pm 1.7 \text{ mm Hg}$ MAP: $2.0 \pm 2 \text{ mm Hg}$	SBP: $r = 0.99$ , $P < .00001$ DBP: $r = 0.97$ , $P < .00001$ MAP: $r = 0.99$ , $P < .00001$	Strong correlation. Small sample size.							
			5	50	Umbilical (IA) vs L leg (Osc)	1-12 d	SBP: $1.7 \pm 1.3$ mm Hg DBP: $1.6 \pm 1.3$ mm Hg MAP: $1.7 \pm 1.2$ mm Hg	SBP: $r = 0.98$ , $P < .00001$ DBP: $r = 0.98$ , $P < .00001$ MAP: $r = 0.98$ , $P < .00001$								
			17	425	L Upper arm (Osc) vs L leg (Osc)	1-12 d		SBP: $r = 0.99$ DBP: $r = 0.98$ MAP: $r = 0.98$								
Moniaci <sup>16</sup>	1997	NICU; 27-39 wk gestational age; BW 835-3990 g	20	60	Umbilical (IA) vs L calf (Osc)	Day 1	SBP: 0.6 mm Hg DBP: 4.2 mm Hg MAP: 3.5 mm Ha	SBP: $r = 0.69$ , $P = .00075$ DBP: $r = 0.47$ , $P = .03564$ MAP: $r = 0.64$ , $P = .00228$	Correlations were moderate.     Mean differences were     clinically large.							
						Day 2	SBP: 4.0 mm Hg DBP: 5.9 mm Hg MAP: 5.6 mm Hg	SBP: $r = 0.65$ , $P = .00203$ DBP: $r = 0.41$ , $P = .07316$								
						Day 3	SBP: 5.0 mm Hg DBP: 6.4 mm Hg MAP: 5.8 mm Hg	SBP: $r = 0.56$ , $P = .00037$ DBP: $r = 0.56$ . $P = .01081$ MAP: $r = 0.65$ . $P = .00208$								
Rahiala <sup>17</sup>	1997	Healthy; BW 2680-4140 g; mean gestational age 39 wk	36	108	R+L upper arm (Osc) vs R+L calf (Osc)	Days 2-5	SBP: $1.0 \pm 4.7$ mm Hg (range, -9.3 to +13.3 mm Hg)	MALT = 0.00.7 = .00200	Cardiac anomalies excluded. Thigh DBPs were significantly lower than calves and arms							
Park and Lee <sup>18</sup>	1989	Healthy; term; BW 2320-4580 g	219	657	R upper arm (Osc) vs calf or thigh (Osc)	Days 1-6	SBP: 1.1 $\pm$ 7.7 mm Hg DBP: $-0.01$ $\pm$ 6.3 mm Hg MAP: 0.9 $\pm$ 6.9 mm Hg		Thigh measures were abandoned part way through study.							
Kunk <sup>19</sup>	1996	NICU; 26-36 wk gestational age; BW 789-2443 g	65	1040	R or L upper arm (Osc) vs calf (Osc)	Day 1	SBP: $0.51 \pm 4.84$ mm Hg DBP: $0.42 \pm 3.68$ mm Hg MAP: $0.66 \pm 3.90$ mm Hg	P = NS P = NS P = NS	Excluded coarctation of aorta. Differences and SD increase with increasing days of age							
		DW 709-2443 g	5 700 2770 y	2 100 2 y	2.1.700 Z++0 y	54 700 2440 g	511 700 2440 g	2 100 2++0 y	DW 703 2443 g	100 2440 g			Day 3	SBP: $0.01 \pm 5.33$ mm Hg DBP: $0.39 \pm 3.39$ mm Hg MAP: $0.59 \pm 4.30$ mm Hg	P = NS P = NS P = NS P = NS	for all measures. Birth weight did not have a significant effect of BP
						Day 5	SBP: $1.77 \pm 5.55$ mm Hg DBP: $0.66 \pm 4.12$ mm Hg MAP: $0.83 \pm 4.59$ mm Hg	P = NS P = NS P = NS P = NS	difference. A priori sample size calculation							
						Day 7	SBP: $2.65 \pm 5.80$ mm Hg DBP: $1.34 \pm 4.41$ mm Hg MAP: $1.51 \pm 5.24$ mm Hg	P < .01 P = NS P = NS								
O'Shea <sup>20</sup>	2009	NICU; BW 560-4050 g	25	332	R+L upper arm (Osc) vs R+L leg (Osc)	1-3 d	All: 0.13 $\pm$ 9.97 mm Hg	All: r = 0.68, <i>P</i> < .001	Cardiac anomalies excluded. Moderate correlation. Large SD.							
									(continued)							

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### Table III. Continued

Articles	Year	Population	Sample size	No. of paired measures	Measurement location	Postnatal age	Descriptive results (BP difference)	Estimate of effect (correlation)	Comments
Crapanzano <sup>21</sup>	1996	Out-patient clinic; healthy	17	34	R upper arm (Osc) vs R calf (Osc)	2 wk to <3 mo	SBP: 2.8 $\pm$ 13.4 mm Hg DBP: 0.9 $\pm$ 11.7 mm Hg MAP: 0.9 $\pm$ 13.9 mm Hg		Cardiac anomalies excluded. In young infants calf BP was slightly less than arm but at
			23	46	R Upper Arm (Osc) vs R Calf (Osc)	3 to <6 mo	SBP: 1.3 $\pm$ 11.7 mm Hg DBP: 5.5 $\pm$ 14.3 mm Hg MAP: 4.2 $\pm$ 15.9 mm Hg		6-9 months of age the calf pressures exceed arm pressures. Wide variability of calf BPs at all ages.

BW, Birth weight; IA, intra-arterial; L, left; Osc, oscillometric; Per, peripheral; R, right; U, umbilical.

Table IV. BP n	neasu	rement method comparis	son in non	-Bland-Altm	an studies			
Articles	Year	Population	Sample size	No. of paired measures	Measurement location	Postnatal age	Descriptive results (BP difference)	Estimate of effect (correlation)
Briassoulis <sup>12</sup>	1986	Preterm newborns gestational age: 27-33 wk BW: 750-2405 g	6	225 225 185	IA vs Osc 2 cuff sizes	Early days of life	Recommended cuff SBP: not reported DBP: 0.76 $\pm$ 5.3 mm Hg MAP: $-1.65 \pm$ 4.35 mm Hg	-
				225 225 176			Large cuff SBP: $-0.82 \pm 4.92$ mm Hg DBP: $-0.91 \pm 5.37$ mm Hg MAP: $-1.73 \pm 4.82$ mm Hg	
Sonneson <sup>13</sup>	1987	Gestational age: mean 27.7 $\pm$ 1.7 wk;	15	30	IA vs arm (Osc) 2 cuff sizes	NA	Small cuff SBP: 6.9 ± 10.8 mm Hg DBP: 6.1 ± 5.4 mm Hg MAP: 6.2 ± 7.2 mm Hg	-
		bw. <1400 y					Large cuff SBP: 0.2 ± 7.2 mm Hg DBP: 0.2 ± 2.7 mm Hg MAP: -1.0 + 2.3 mm Hg	
Alpert <sup>38</sup>	1996	NICU newborns BW:1.2 to >2.0 kg	35	154	Arm (Osc) vs IA	NA	SBP: 1.4 mm Hg DBP: 4.3 mm Ha	Good correlation between methods
Dellagrammaticas <sup>39</sup>	1981	NICU gestational age: 28-35 wk BW:1100-2460 g	10	126	IA vs arm (Osc)	1-7 d	Regression intercept SBP at 0.66 mm Hg DBP at 6.57 mm Hg MAP at 4.5 mm Hg	Regression coefficient: SBP: 0.88 DBP: 0.92 MAP: 0.93
Diprose <sup>40</sup>	1986	NICU gestational age <30 wk BW: 700-1470 g	12	417	IA vs arm (Osc)	1-10 d	_	Correlation coefficient SBP: 0.67 DBP: 0.49
Emery <sup>41</sup>	1992	NICU gestational age: 24-30 wk BW: 540-750 g	10	>30	IA vs arm (Osc)	3-18 d	Mean difference SBP: 1.34 mm Hg	Coefficient of variation Osc: 8%-15%
Chia <sup>42</sup>	1990	PICU; BW >1500 g;	28	273	IA MAP vs limb	Early days of life	Good agreement if MAP >40 mm Hg; if MAP <40 mm Hg in 34%, a 5 mm Hg overestimation	Interclass correlation SBP: rl: 0.646 DBP: rl: 0.761
		BW ≤1500 g	21	165				MAP n: 0.767 SBP n: 0.722 DBP: n: 0.760 MAP n: 0.787
Nwankwo <sup>43</sup>	1997	NICU gestational age: 26-37 wk BW: 901-2423 g	64	448	Arm (Osc) prone/supine protocol vs	7-42 d	Prone lower than supine by 2.1 mm Hg First BP higher than third by 3 mm Hg	All comparisons significant with <i>P</i> < .003 Higher variability with

Routine nursing higher by 5.3 to 7.4 mm Hg

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measurements (SD, 11.4 mm Hg)