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GUIDELINES, CLINICAL TRIALS, AND META-ANALYSIS (WILLIAM J. KOSTIS, SECTION EDITOR)

A Meta-analysis to Determine the Validity of Taking Blood Pressure Using the Indirect Cuff Method

Scott J. Dankel[1] · Minsoo Kang[2] · Takashi Abe[1] · Jeremy P. Loenneke[1]

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Abstract

Purpose of Review The purpose of this meta-analysis was to compare the magnitude of systematic bias (mean difference) and random error (standard deviation of mean difference) between the cuff method of indirect blood pressure and directly measured intra-arterial pressure.

Recent Findings Blood pressure is almost exclusively assessed using the indirect cuff method; however, numerous individual studies have questioned the validity relative to directly measured intra-arterial blood pressure.

Summary PubMed, SportsDiscus, and Scopus were searched through February 2018. Data were analyzed using a random effects model. A total of 62 studies met the inclusion criteria for quantitative analysis including 103 effect sizes for systolic and 114 effect sizes for diastolic blood pressure. Indirect measures of systolic blood pressure were underestimated (− 4.55 (95% CI = − 5.58 to − 3.53) mmHg), while diastolic blood pressure was overestimated (6.20 (95% CI = 5.09 to 7.31) mmHg). The random error (SD units) was 10.32 (95% CI = 9.29 to 11.36) for systolic and 7.92 (95% CI = 7.35 to 8.50) for diastolic blood pressure which corresponds to an estimation accuracy (95% confidence) of ± 20.2 mmHg for systolic blood pressure and ± 15.5 mmHg for diastolic blood pressure. These data indicate that it may be difficult to accurately estimate intra-arterial blood pressure using the cuff method. These results not only have implications for clinicians in diagnosing hypertension, but also may detail a potential underestimation of the association between blood pressure and numerous other health outcomes found in epidemiological studies.

Keywords Artery · Cardiovascular · Diastolic · Systolic · Hypertension

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These author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation

✉ Jeremy P. Loenneke
jploenne@olemiss.edu

Scott J. Dankel
sdankel@go.olemiss.edu

Minsoo Kang
kang@olemiss.edu

Takashi Abe
t12abe@gmail.com

[1] Department of Health, Exercise Science, and Recreation Management. Kevser Ermin Applied Physiology Laboratory, The University of Mississippi, 231 Turner Center, University, MS 38677, USA

[2] Department of Health, Exercise Science and Recreation Management, Health and Sports Analytics Laboratory, The University of Mississippi, University, MS, USA

Abbreviations

AAMI	American Association for the Advancement of Medical Instrumentation
BHS	British Hypertension Society
CI	Confidence interval
ES	Effect size

Introduction

The discovery of blood pressure itself was made in 1733 when Stephen Hales connected a glass tube to the artery of a horse and noticed that blood would repeatedly rise and fall up and down the glass tube [1]. Today, we attempt to indirectly quantify blood pressure by estimating the force that blood exerts on the vessel walls and this is done using either oscillometric or auscultatory methods (automatically or manually). Due to the overwhelming use of indirect blood pressure measurements to quantify blood pressure, it is imperative that these measurements are valid. If these measurements are not valid, the current prevalence of hypertension (approximately 29.1% among Americans ages 18 and over) may be incorrect, and the large sum (approximate 76%) of hypertensive individuals taking anti-hypertensive medication may be doing so inappropriately [2•]. Conversely, some individuals who are hypertensive may be misdiagnosed as normotensive, and failure to treat hypertension may be problematic given that it is associated with an increased risk (approximately 2–3-fold) of numerous cardiovascular-related outcomes (i.e., myocardial infarction, stroke, cardiac failure, sudden death) [3•]. Aside from implications for clinicians, the validity of the cuff method for taking blood pressure has implications in epidemiological research as the reported associations between blood pressure and various health outcomes may be substantially underestimated if a large degree of random error exists between the cuff method and directly measured arterial pressure.

Studies have been performed to validate the use of automated blood pressure machines to that of manual sphygmomanometry [4•, 5]; however, a more appropriate (although more invasive) assessment would be to assess the validity relative to that of directly measured intra-arterial pressure. While numerous studies have attempted to validate the indirect auscultatory and oscillometric blood pressure measurements to that of directly measured intra-arterial pressure (included in this analysis), an overwhelming number of these studies simply focus on correlations and mean differences between groups, neither of which provide information on the validity of the blood pressure measurement at the individual level. Mean differences may provide some indication of systematic bias as to whether the indirect measures of blood pressure consistently overestimate or underestimate directly measured blood pressure, while significant correlations indicate that individuals who have higher blood pressure values measured indirectly also have higher blood pressure values when measured directly. In order to assess the accuracy of these measurements on the individual level, one must consider limits of agreement to assess random error and this can easily be calculated by examining the standard deviation of the difference between measurements [6]. Support for the importance of assessing random error and systematic bias exists in that the American Association for the Advancement of Medical Instrumentation (AAMI) recommends that for a blood pressure machine to be deemed acceptable, it must have a systematic bias of less than 5 mmHg and a standard deviation of less than 8 mmHg (95% confidence interval of ± 16 mmHg). Given the prevalence of hypertension, coupled with the significant proportion of hypertensive individuals taking prescription medications [2], the purpose of this systematic review and meta-analysis was to quantify (1) the level of systematic bias between the indirect and direct blood pressure measurements and (2) the magnitude of random error that exists between direct and indirect blood pressure measurements.

Methods

The data bases of PubMed, SportsDiscus, and Scopus were searched through February 2018 using the following search terms: (1) "blood pressure" AND catheter AND validity; (2) "direct blood pressure"; (3) "indirect blood pressure"; and (4) direct and indirect comparison of blood pressure. All relevant articles were obtained and the reference lists were examined for more articles meeting the inclusion criteria which were as follows: (1) written in English, (2) performed in humans, (3) mean age ≥ 18 years, (4) includes a comparison between either systolic or diastolic blood pressure measured using the indirect (auscultatory or oscillometric) and direct (arterial catheter) method, (5) placement of the pressure cuff is around the arm, (6) individuals must be resting either seated or lying down, (7) there must be a way to obtain the standard deviation of the difference score between the direct and indirect methods, and (8) each individual must only have one observation contributing to the difference score calculation. A total of 62 studies [7–66, 67•, 68] met all the inclusionary criteria and were included in the computation of the meta-analysis. A flow chart detailing reasons for excluding studies is illustrated in Fig. 1. Details about each of the included studies are shown in Table 1.

All data were analyzed by an independent observer. If data were reported as standard errors, they were converted to standard deviations by using the appropriate formula (i.e., multiplying by the square root of the sample size). When means and variability statistics were not present in the text but were illustrated in graph form, a graph digitizer (Engauge Digitizer Software, version 10.4) was used to estimate the values. The standard deviation of the difference score between measurements was used when reported directly, but was often calculated by extracting the data with a graph digitizer and inputting the data into a statistical software. When correlation coefficients were given, the standard deviation of the difference between measurements was calculated using the formula: $SD_{difference}$ = square root $[(SD_{indirect\ measure})^2 + (SD_{direct\ measure})^2 - (2r \times SD_{indirect\ measure} \times SD_{direct\ measure})$.

All statistics were computed using SPSS version 25 (Armonk, NY, USA). Effect sizes were computed as the mean differences (systematic bias) and standard deviations of the mean differences (random error) for both systolic and diastolic blood pressure. That is, the effect sizes for systematic bias are mmHg units, and the effect sizes for random error are standard deviation units. A random effects model was used for the computation of overall effect sizes. For the analysis in which mean differences were used as the effect size, each of the

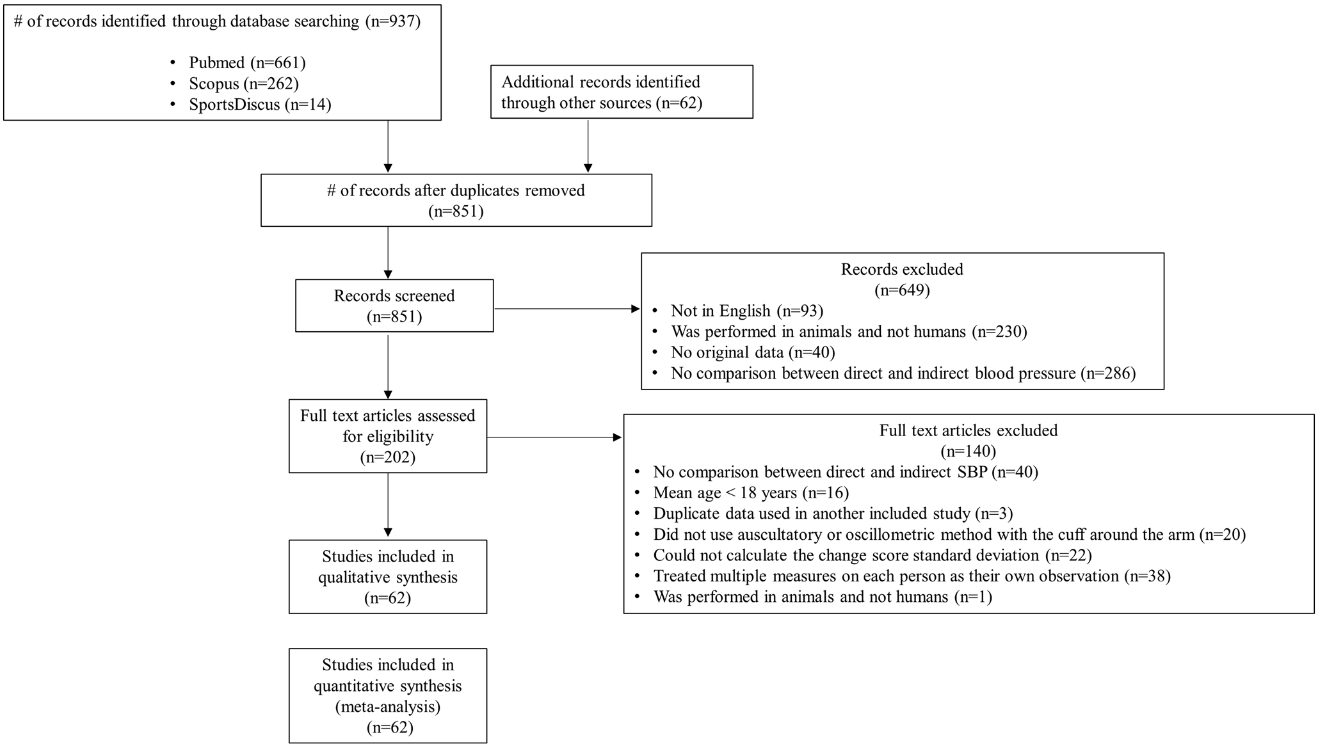

Fig. 1 Flow chart detailing search results and rationale for excluding studies

individual effect sizes was weighed by the inverse of the sample variance. For the analysis in which standard deviations were used as the effect size, each of the individual effect sizes were weighed based on the sample size. This was done because the dependent variable (i.e., the effect size) was the standard deviation and thus it would not be appropriate to weigh each study based on the level of variability as this would lower the estimated standard deviation by default. Both methods have been reported to be appropriate ways for weighing individual effect sizes [69].

Meta-regression was used to assess the influence of (1) mean age and (2) mean baseline blood pressure which were treated as continuous moderator variables. Additionally, homogeneity of effect size tests were used to assess the influence of the following categorical moderator variables: (1) body position (sitting, semi-recumbent, supine); (2) location of arterial catheter (brachial, aorta, radial, femoral); (3) cuff size used (arbitrary vs. based on arm circumference); (4) type of blood pressure determination (auscultatory vs. oscillometric); and (5) method of blood pressure determination (automatic vs. manual). Additionally, for diastolic blood pressure, an additional categorical moderator variable included the method of determination (Korotkoff phase 4, Korotkoff phase 5, oscillometric, not specified). Lastly, limits of agreement were calculated as 1.96 × the standard deviation of the difference score between the direct and indirect blood pressure measurements. The potential for publication bias was assessed using Egger's test. Sensitivity analyses were also performed to assess the influence of publication year on effect size estimates via meta-regression, and the one study removed method was used to assess changes in point estimates. Statistical significance level was set 0.05.

Results

A total of 62 studies met the inclusion criteria for quantitative analysis. A total of 103 effect sizes were extracted for systolic blood pressure, and 114 effect sizes were extracted for diastolic blood pressure.

Systolic Blood Pressure (Systematic Bias)

Effect sizes (in mmHg) and 95% confidence intervals for studies are shown in Fig. 2. The weighted mean effect size was − 4.55 ((95% confidence interval (CI) = − 5.58 to − 3.53); $Q = 1441.68$; df = 102; $p < 0.001$; $I^2 = 92.92$) indicting a significant underestimation of 4.55 mmHg when systolic blood pressure is measured using the indirect method. The only statistically significant moderator variables were the location of the intra-arterial measurement ($Q = 15.170$; df = 3; $p = 0.017$) and the cuff size used ($Q = 4.894$; df = 1; $p = 0.026$). Of the arteries measured, the effect sizes were as follows: brachial: − 3.58 (95% CI = − 5.10 to − 2.06); aorta: − 0.51 (95% CI = − 4.11 to 3.08); radial: − 6.97 (95% CI = − 8.88 to − 5.05); and

Table 1 Details on the included studies

Author	Number	Age	Artery	Indirect measure	SBP	DBP	Position
Araghi (2006) a	54	57	Radial	Oscillometric (HP 66)	146	70	N/A
Araghi (2006) b	54	58	Radial	Auscultatory (manual)	146	70	N/A
Arnold (1985) a	4	21	Brachial	Auscultatory (manual)	132.7	55.3	Supine
Arnold (1985) b	4	21	Brachial	Auscultatory (manual)	132.7	55.3	Supine
Arnold (1985) c	4	21	Brachial	Oscillometric (Dinamap 845)	132.7	55.3	Supine
Belmin (1995) a	24	89	Radial	Auscultatory (manual)	151.8	60.6	Recumbent
Belmin (1995) b	24	89	Radial	Oscillometric (Sentron-Bard)	151.8	60.6	Recumbent
Borow (1982)	30	60	Aorta	Oscillometric (Dinamap 845)	132.1	71.9	Supine
Bos (1992)	13	66	Brachial	Auscultatory (manual)	194	90	N/A
Bos (1992) a	19	63	Aorta	Auscultatory (manual)	145	71	N/A
Bos (1992) b	29	51	Brachial	Auscultatory (manual)	156	87	N/A
Breit (1974) a	30	N/A	Brachial	Auscultatory (manual)	122	72	Semi-recumbent
Breit (1974) b	30	N/A	Brachial	Auscultatory (manual)	122	72	Semi-recumbent
Breit (1974) c	30	N/A	Brachial	Auscultatory (manual)	122	72	Semi-recumbent
Breit (1974) d	30	N/A	Brachial	Auscultatory (manual)	122	72	Semi-recumbent
Brown (1994) a	28	N/A	Radial	Auscultatory (manual)	133	80	Seated
Brown (1994) b	28	N/A	Radial	Auscultatory (manual)	133	80	Seated
Burch (1973) a	10	41.2	Brachial	Auscultatory (manual)	133.7	71.7	Supine
Burch (1973) b	10	41.2	Brachial	Auscultatory (manual)	133.1	70.7	Supine
Burch (1973) c	10	41.2	Brachial	Auscultatory (manual)	131.9	70.1	Supine
Byra-Cook (1990)	50	44	Radial	Auscultatory (manual)	132.6	63.5	Supine
Fagher (1994) a	10	59	Brachial	Auscultatory (manual)	173	90	Supine
Fagher (1994) b	15	61	Brachial	Auscultatory (manual)	140	70	Supine
Finnie (1984) a	26	58	Radial	Oscillometric (manual)	137.2	67.2	N/A
Finnie (1984) b	26	58	Radial	Auscultatory (manual)	137.2	67.2	N/A
Finnie (1984) c	26	58	Radial	Auscultatory (manual)	137.2	67.2	N/A
Forsberg (1970) a	5	52.6	Brachial	Auscultatory (manual)	210	112	Supine
Forsberg (1970) b	47	52.6	Brachial	Auscultatory (manual)	171	102.1	Supine
Ganio (2011)	10	42	Radial	Auscultatory (Tango+)	126	68	Supine
Goldstein (1962)	8	34	Brachial	Auscultatory (manual)	145.1	37	N/A
Gould (1984) a	26	50	N/A	Auscultatory (Remler M2000)	168	89	Seated
Gould (1984) b	28	50	N/A	Auscultatory (manual)	162	88	Seated
Gravlee (1990) a	38	55	Brachial	Auscultatory (manual)	131	65	N/A
Gravlee (1990) b	38	55	Brachial	Oscillometric (Dinamap 845)	131	65	N/A
Henschel (1954)	11	24.5	Radial	Auscultatory (manual)	114	63	Supine
Holland (1964) a	47	44.3	Brachial	Auscultatory (manual)	160	88	N/A
Holland (1964) b	47	44.3	Brachial	Auscultatory (manual)	160	88	N/A
Horvath (2010)	55	66	Aorta	Oscillometric (arteriograph)	154	93	N/A
Hunyor (1978)	7	44	Brachial	Auscultatory (Electronic R & D)	171	96	N/A
Kaijser (1987) a	15	38.5	Brachial	Auscultatory (manual)	151	N/A	Seated
Kaijser (1987) b	15	38.5	Brachial	Auscultatory (manual)	151	N/A	Seated
Karlefors (1966)	38	N/A	Brachial	Auscultatory (manual)	148	85	Supine
Karvonen (1964) a	53	35	Radial	Auscultatory (manual)	145	75	N/A
Karvonen (1964) b	53	35	Radial	Auscultatory (manual)	145	75	N/A
Karvonen (1964) c	53	35	Radial	Auscultatory (manual)	145	75	N/A
Karvonen (1964) d	53	35	Radial	Auscultatory (manual)	145	75	N/A
Kirshon (1987) a	12	24.9	Radial	Auscultatory (manual)	156	88	N/A
Kirshon (1987) b	12	24.9	Radial	Auscultatory (Dinamap)	147	85	N/A
Kotte (1944)	28	N/A	Brachial	Auscultatory (manual)	149	71	Supine
Kuwajima (1990)	59	73.5	Brachial	Auscultatory (manual)	167.2	77.3	Recumbent
Lewis (1994) a	15	79	Radial	Auscultatory (manual)	160	70	Supine
Lewis (1994) b	21	76	Radial	Auscultatory (manual)	224	93	Supine
Manios (2007)	51	73.8	Radial	Oscillometric (SpaceLabs)	166.2	77.2	Supine
Manolio (1988)	14	48	Radial	Oscillometric (Dinamap 845)	138	65	Supine
Marks (2000) a	50	61.6	Radial	Auscultatory (manual)	N/A	N/A	Seated
Marks (2000) b	50	61.6	Radial	Auscultatory (manual)	N/A	N/A	Seated
Marks (2000) c	50	61.6	Radial	Auscultatory (manual)	N/A	N/A	Seated
Marks (2000) d	50	61.6	Radial	Auscultatory (manual)	N/A	N/A	Seated
McMahon (2012)	56	N/A	N/A	Oscillometric (various)	117	N/A	N/A
Melamed (2012)	49	62.1	N/A	Oscillometric (various)	120.3	64.9	N/A
Messerli (1985) a	11	74.8	Aorta	Auscultatory (manual)	172.9	74.5	N/A
Messerli (1985) b	13	77.6	Aorta	Auscultatory (manual)	180.5	77.9	N/A
Nagle (1966) a	2	48	Aorta	Auscultatory (manual)	136.4	85.4	Supine
Nagle (1966) b	2	48	Aorta	Auscultatory (manual)	148.7	93.4	Seated
Nielsen (1974) a	28	42	Brachial	Auscultatory (manual)	158.3	85.8	Supine

Table 1 (continued)

Author	Number	Age	Artery	Indirect measure	SBP	DBP	Position
Nielsen (1974) b	28	42	Brachial	Auscultatory (manual)	155.5	85.8	Supine
Nielsen (1974) c	21	52.6	Brachial	Auscultatory (manual)	176.8	93.6	Supine
Nielsen (1982) a	52	41	Brachial	Auscultatory (manual)	158	86.8	Supine
Nielsen (1982) b	59	51	Brachial	Auscultatory (manual)	182.8	97.6	Supine
Norman (1991) a	30	55.6	Radial	Auscultatory (manual)	129.8	60.9	Supine
Norman (1991) b	30	55.6	Radial	Auscultatory (manual)	129.8	60.9	Supine
Nystrom (1985) a	15	N/A	Radial	Oscillometric (Dinamap 845)	120.8	65.4	Supine
Nystrom (1985) b	18	N/A	Radial	Auscultatory (Infrasonde 4000)	126.5	67.6	Supine
O'Callaghan (1983) a	20	38	Radial	Auscultatory (manual)	172	90	Supine
O'Callaghan (1983) b	40	68	Radial	Auscultatory (manual)	180	81	Supine
Ochiai (1997) a	34	47.5	Brachial	Oscillometric (UA 510)	155.1	84.4	Supine
Ochiai (1997) b	34	47.5	Brachial	Auscultatory (UA 213)	155.1	84.4	Supine
Ochiai (1997) c	34	47.5	Brachial	Auscultatory (manual)	155.1	84.4	Supine
Oliner (1993)	19	76	Brachial	Auscultatory (manual)	201	81	N/A
Penny (1999) a	13	N/A	Radial	Auscultatory (manual)	N/A	N/A	Semi-recumbent
Penny (1999) b	13	N/A	Radial	Oscillometric (Dinamap XL)	N/A	N/A	Semi-recumbent
Penny (1999) c	13	N/A	Radial	Oscillometric (SpaceLabs)	N/A	N/A	Semi-recumbent
Raftery (1990) a	50	54	Brachial	Auscultatory (manual)	170.4	104	N/A
Raftery (1990) b	50	54	Brachial	Auscultatory (manual)	170.4	104	N/A
Rasmussen (1985)	27	32.4	Radial	Auscultatory (manual)	153.4	90	N/A
Roberts (1953) a	30	70	Brachial	Auscultatory (manual)	150	74.7	Recumbent
Roberts (1953) a	47	70	Brachial	Auscultatory (manual)	158.2	73.2	Recumbent
Roberts (1953) b	30	70	Brachial	Auscultatory (manual)	150	74.7	Recumbent
Roberts (1953) b	47	70	Brachial	Auscultatory (manual)	158.2	73.2	Recumbent
Rossen (2014)	22	66	Aorta	Oscillometric (arteriograph)	137.8	67.8	N/A
Russell (1989) a	53	62	Femoral	Auscultatory (manual)	147	73	N/A
Russell (1989) b	53	62	Femoral	Auscultatory (manual)	147	73	N/A
Saghiv (2016)	8	41.9	Brachial	Auscultatory (manual)	134	88	N/A
Sagiv (1995)	5	33	Brachial	Auscultatory (manual)	126	76	N/A
Sagiv (1999)	14	23	Brachial	Auscultatory (manual)	101	77	N/A
Simpson (1965) a	24	42.5	Brachial	Auscultatory (manual)	137.2	79	Supine
Simpson (1965) b	24	42.5	Brachial	Auscultatory (manual)	137.2	79	Supine
Simpson (1965) c	24	42.5	Brachial	Auscultatory (manual)	137.2	79	Supine
Simpson (1965) d	24	42.5	Brachial	Auscultatory (manual)	137.2	79	Supine
Spence (1978)	40	62.4	Radial	Auscultatory (manual)	187	87	Recumbent
Stolt (1993) a	20	20	Brachial	Auscultatory (manual)	145	76	Recumbent
Stolt (1993) b	58	50	Brachial	Auscultatory (manual)	137	76	Supine

femoral: − 9.70 (95% CI = − 15.89 to − 3.51). This indicates that measuring blood pressure in the aorta appears to limit the systematic bias in comparison to taking blood pressure in the radial artery. Additionally, with respect to the cuff size used, choosing one set cuff size for all individuals resulted in a lower systematic bias (effect size (ES): − 4.26 (95% CI = − 5.95 to − 2.57); Q = 4.89; df = 1; $p = 0.026$; $I^2 = 79.55$) when compared to choosing a pressure cuff based on arm circumference: (ES: − 7.31 (95% CI = − 9.41 to − 5.20)). Egger's test for publication bias was not statistically significant ($p = 0.718$).

Systolic Blood Pressure (Random Error)

Effect sizes and 95% confidence intervals are shown in Fig. 2. The weighted mean effect size was 10.32 ((95% CI = 9.29 to 11.36); $Q = 79{,}970.97$; df = 102; $p < 0.001$; $I^2 = 99.87$) indicating that the 95% limits of agreements were 20.2 mmHg (1.96 × 10.32). This details that, when an individual's systolic blood pressure is measured indirectly using the standard cuff method, the directly measured systolic blood pressure is likely to be somewhere within plus or minus 20.2 mmHg of the given value. When examining moderator variables, the only statistically significant moderator variable was the location of the intra-arterial measurement ($Q = 9.571$; df = 3; $p = 0.022$; $I^2 = 68.65$) indicating that the aorta resulted in the lowest degree of random error. Effect sizes for each artery were as follows: brachial: 9.41 (95% CI = 7.96 to 10.85); aorta: 6.94 (95% CI = 3.46 to 10.43); radial: 12.20 (95% CI = 10.41 to 13.99); and femoral: 11.83 (95% CI = 5.81 to 17.85). Egger's test for publication bias was statistically significant ($p = 0.012$) indicating the potential for publication bias.

Diastolic Blood Pressure (Systematic Bias)

Effect sizes and 95% confidence intervals are shown in Fig. 3. The weighted mean effect size was 6.20 ((95% CI = 5.09 to 7.31); $Q = 3194.57$; df = 113; $p < 0.001$; $I^2 =$

96.46) indicating a significant overestimation of 6.20 mmHg when diastolic blood pressure is measured using the indirect method. There were no significant moderator variables. Egger's test for publication bias was statistically significant ($p = 0.004$) indicating the potential for publication bias.

Diastolic Blood Pressure (Random Error)

Effect sizes and 95% confidence intervals are shown in Fig. 3. The weighted mean effect size was 7.92 ((95% CI = 7.35 to 8.50); $Q = 26{,}571.59$; df = 113; $p < 0.001$; $I^2 = 99.57$) indicating that the 95% limits of agreements were 15.5 mmHg (1.96 × 7.92). This details that, when an individual's diastolic blood pressure is measured indirectly using the standard cuff method, the directly measured diastolic blood pressure is likely to be somewhere within plus or minus 15.5 mmHg of the given value. When examining moderator variables, the only significant moderator was baseline diastolic blood pressure ($Q = 4.644$; df = 1; $p = 0.031$; $I^2 = 78.46$) indicating that each 10 mmHg increase in resting blood pressure resulted in a 0.5 standard deviation unit increase on the difference between measurements ($\beta = 0.049$ (95% CI = 0.004 to 0.940)). Egger's test for publication bias was statistically significant ($p = 0.017$) indicating the potential for publication bias.

Sensitivity Analyses

There was no significant effect of publication year for any of the effect size calculations ($p > 0.05$). Furthermore, when examining effect size changes using the one study removed method, point estimates remained relatively unchanged. The furthest departure from the reported effect sizes on both the higher and lower end of the estimate were as follows: systolic blood pressure mean (lowest = − 4.72, highest = − 4.35); systolic blood pressure standard deviation (lowest = 10.12, highest = 10.42); diastolic blood pressure mean (lowest = 6.04, highest = 6.40); and diastolic blood pressure standard deviation (lowest = 7.83, highest = 7.99). Collectively, these results demonstrate that the findings of the current study were not heavily influenced by a single study included in the analysis.

Discussion

The primary findings of this study were as follows: (1) indirect blood pressure measurements underestimate systolic blood pressure by an average of ~ 4.5 mmHg and overestimate diastolic blood pressure values by an average of ~ 6.2 mmHg; (2) the 95% confidence limits detailing the precision of the indirect blood pressure measure relative to the direct intra-arterial measure are ± 20.2 mmHg for systolic blood pressure and ± 15.5 mmHg for diastolic blood pressure. The results of this study bring into question the universal use of oscillometric and auscultatory methods of recording indirect blood pressure regardless of whether manual or automatic measures are taken.

The AAMI recommends that for a blood pressure machine to be deemed acceptable, it must have a systematic bias of less than 5 mmHg and a standard deviation of less than 8 mmHg (95% confidence interval of ± 16 mmHg) [70]. In addition to the AAMI criteria, the British Hypertension Society (BHS) criteria [71] is also used to assess the validity of different blood pressure machines and a thorough review has been published indicating which automated blood pressure machines meet the established criteria for validation [4]. Importantly, and potentially problematic with respect to the validity of automated blood pressure machines, is the lack of agreement between manual auscultatory sphygmomanometry and that of directly measured intra-arterial pressure. After all, both the AAMI and BHS criteria establish the validity of automated blood pressure machines relative to manual sphygmomanometry as opposed to directly measured intra-arterial pressure. Thus, the validity of the automated blood pressure machine is being tested against manual sphygmomanometry, yet manual sphygmomanometry does not appear to be valid when compared to direct intra-arterial pressure. For example, when comparing the efficacy of cuff methods used in the present study, which did not differ with respect to systematic bias or random error across manual or automated measures, few studies met this very established criterion for validation. Specifically, only 49/103 (47.5%) cases for systolic blood pressure and 61/114 (53.5%) cases for diastolic blood pressure had means that differed by < 5 mmHg. With respect to random error, only 23/103 (22.3%) cases for systolic blood pressure and 42/114 (36.8%) cases for diastolic blood pressure had standard deviations < 8 mmHg.

Numerous factors may increase the magnitude of error present when comparing direct and indirect measurements (i.e., cuff size, deflation method, terminal digit bias) [72], and it should be mentioned that the error is not limited to human models as this disagreement has also been observed in simulated arteries [73]. Of importance, taking multiple measures to ensure that an individual is classified as hypertensive on several different occasions would not appear to solve this issue, since it is related to validity as opposed to reliability and is confounded by random error. Thus, a measure can be reliably invalid resulting in an improper blood pressure diagnosis. Nonetheless, it should be mentioned that there are various sources of error that can be attributed to the direct measure of intra-arterial blood flow as well, which may include catheter whipping, air bubbles in the fluid column, blood clotting, artifacts of respiration, and improper damping [74, 75].

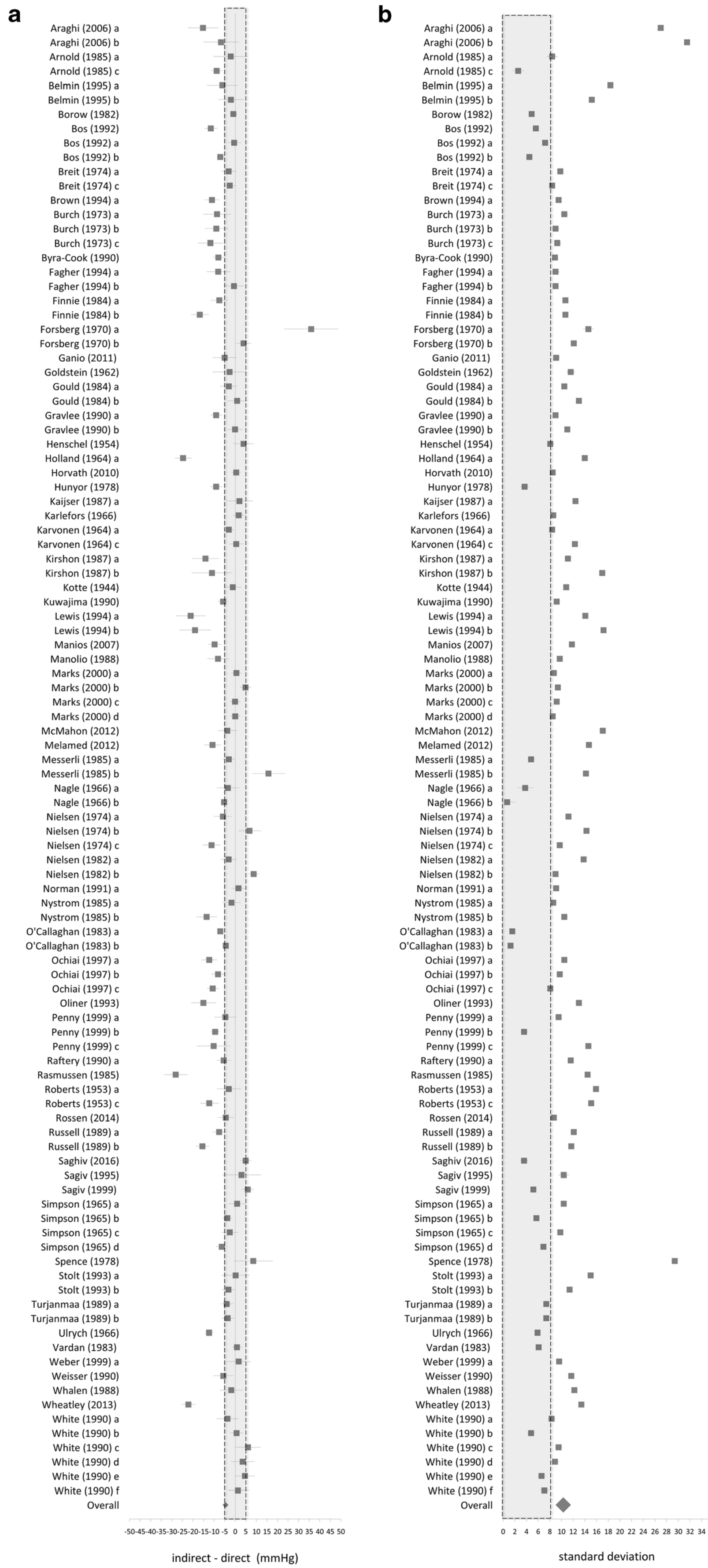

Fig. 2 Systolic blood pressure. The figure on the left details systematic bias calculated as the difference in blood pressure (indirect − direct). Values to the left of zero indicate an underestimation of systolic blood pressure using the cuff method and values to the right indicate an overestimation. Values in the light gray region illustrate those which met the acceptable standards set forth by the American Association for the Advancement of Medical Instrumentation (AAMI) (49/103; 47.5%). The figure on the right illustrates random error and is the standard deviation of the difference between the direct and indirect measures. Values in the light gray region indicate those meeting acceptable standards set forth by the AAMI (23/103; 22.3%)

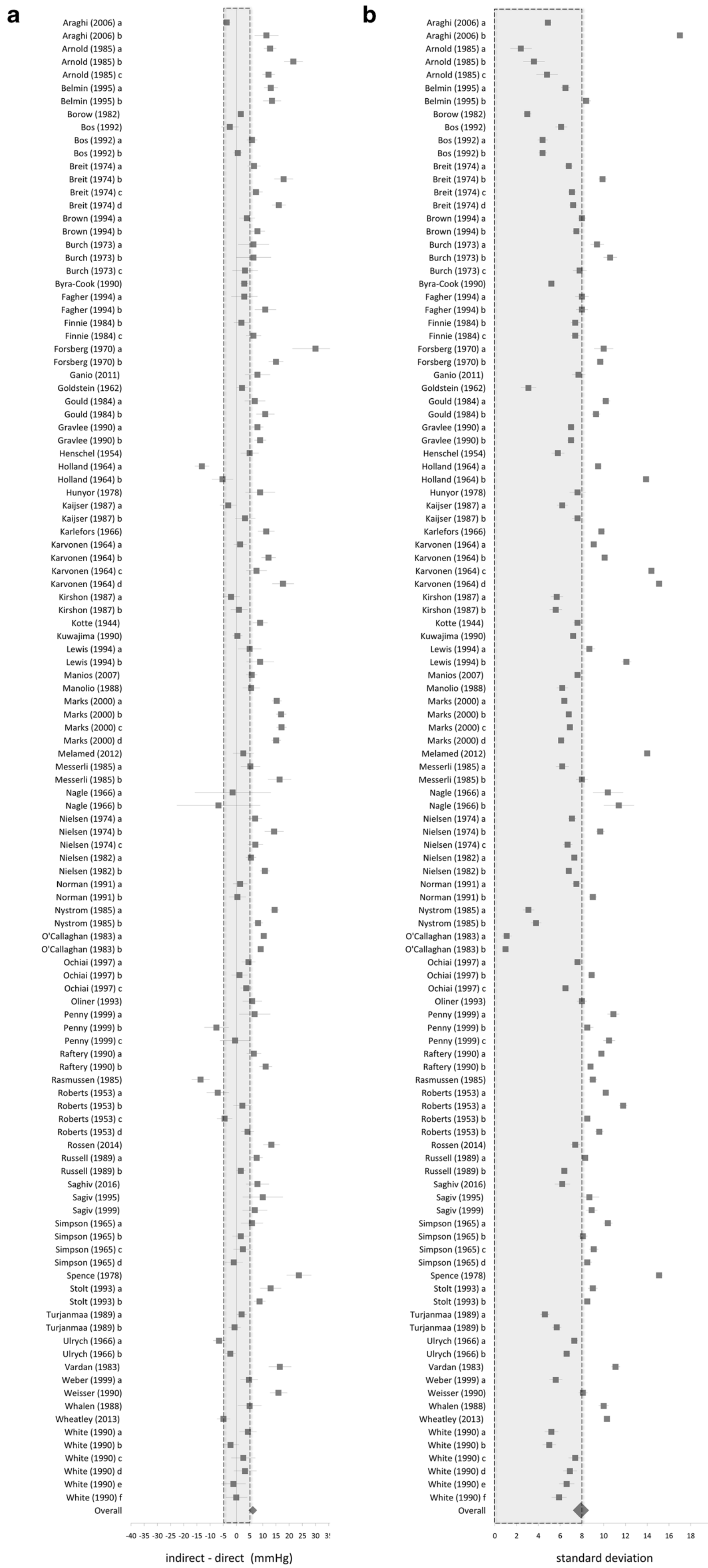

Fig. 3 Diastolic blood pressure. The figure on the left details systematic bias calculated as the difference in blood pressure (indirect – direct). Values to the left of zero indicate an underestimation of diastolic blood pressure using the cuff method and values to the right indicate an overestimation. Values falling in the light gray region illustrate those which met the acceptable standards set forth by the American Association for the Advancement of Medical Instrumentation (AAMI) (61/114; 53.5%). The figure on the right illustrates random error and is the standard deviation of the difference between the direct and indirect measures. Values in the light gray region indicate those meeting acceptable standards set forth by the AAMI (42/114; 36.8%)

We acknowledge that epidemiological studies clearly demonstrate strong correlations between blood pressure and various cardiovascular health related outcomes (i.e., myocardial infarction, stroke, cardiac failure, sudden death) [3], and we are in no way attempting to discredit these findings. When examining a large heterogeneous group of individuals, there will likely be numerous individuals falling on either end of the blood pressure spectrum to such an extent that we can be ≥ 95% confident they fall into a given category (e.g., even with the high minimal difference reported, several individuals will still have a high enough blood pressure such that the lower confidence limit still exceeds the threshold of to be classified as hypertensive). Therefore, it could be argued that the correlation between blood pressure and numerous cardiovascular health related outcomes is underestimated due to the degree of random error that is present, and it is possible that only those individuals who can truly be distinguished as normotensive or hypertensive are driving the association that is present.

Based on the 95% confidence interval in the present study our results indicate that traditional blood pressure machines will produce results within ± 20.2 mmHg for systolic blood pressure and ± 15.5 mmHg for diastolic blood pressure as compared to directly measured intra-arterial pressure. In other words, an individual with an indirect blood pressure measurement of 140/90 will have a directly measured intra-arterial pressure falling somewhere in the range from hypotensive to hypertensive, making it difficult to definitively conclude if an individual is hypertensive. Thus, prescribing hypertensive medication to individuals based on indirect blood pressure measurements may be problematic, as it is entirely possible that hypotensive individuals may be prescribed hypertensive medications. Of course, individuals with severe hypertension who exceed the level of random error above a clinical threshold, may still be safely prescribed hypertensive medications as it is unlikely this magnitude of difference would simply be by chance alone. Future studies may seek to explore alternative methods of indirectly measuring blood pressure that may reduce the magnitude of random error present.

Conclusion

The validity of both automated and manually administered indirect blood pressure methods is very poor when compared to that of directly measured intra-arterial pressure. While systolic blood pressure tends to be underestimated, diastolic blood pressure tends to be overestimated. More importantly, the limits of agreement between direct and indirect blood pressure measurements are very poor detailing a 95% confidence interval of ± 20.2 mmHg for systolic blood pressure and ± 15.5 mmHg for diastolic blood pressure. This makes it very difficult to obtain an accurate estimate of intra-arterial blood pressure using the cuff method, which is concerning because this is how individuals are medicated. Future technology is necessary to determine a more valid alternative to take noninvasive blood pressure.

Author Contributions JPL and TA designed the study. SJD extracted the data for analysis. SJD analyzed the data. SJD drafted the initial manuscript. SJD, JPL, TA, and MK revised the manuscript and contributed to the intellectual content.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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