Accuracy and Precision of Continuous Non-Invasive Arterial Pressure Monitoring in Critical Care

A systematic review and meta-analysis

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### Abstract

**Purpose**

Continuous non-invasive arterial pressure (CNAP) monitoring devices display non-invasive beat-to-beat arterial pressure measurements. The aim of this systematic review was to summarize the evidence regarding the agreement between CNAP and invasive arterial pressure measurements among patients admitted to an adult critical care unit.

**Methods**

Medline and EMBASE were searched for studies that included participants whose blood pressure was monitored concurrently using invasive and continuous non-invasive arterial pressure monitors in the intensive care unit. Two reviewers independently screened all studies and used the Revised Quality Assessment of Diagnostic Accuracy Studies tool (QUADAS-2) to complete the quality assessment. The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach was used to summarize the certainty of the evidence. Pooled estimates of the mean bias and limits of agreement with outer 95% confidence intervals (termed population limits of agreement because between-study heterogeneity and sampling error are accounted for in the estimates) were calculated.

**Results**

Population limits of agreement for systolic blood pressure were wide, spanning from -36.17 mmHg to 28.3mmHg (19 comparisons; 18 studies; 785 participants; 262,352 measurements). The accuracy of diastolic blood pressure measurements from CNAP devices were highly inconsistent across studies, resulting in extremely imprecise estimates for the population limits of agreement (-102.38 mmHg to 111.61mmHg; 18 comparisons; 17 studies; 760 participants; 262,235 measurements). Population limits of agreement for mean arterial pressure spanned from -40.63mmHg to 44.44mmHg (19 comparisons; 18 studies; 784 participants; 162,080 measurements). The evidence was rated as very low-quality evidence due to very serious concerns about heterogeneity and imprecision. Sensitivity analyses restricted to studies that were rated as low risk of bias across all domains of the QUADAS-2 revealed wider population limits of agreement than the primary analysis.

**Conclusion**

The range of uncertainty in the accuracy of blood pressure monitoring system should be considered when deciding on the appropriate situations in which CNAP devices can be used in clinical practice. In practice, systolic blood pressure measurements from a continuous non-invasive device should be estimated to be as much as about 30-40 mmHg lower or higher than an invasive measurement. Results of this meta-analysis suggest that blood pressure measurements using CNAP monitoring are not sufficiently accurate to substitute for invasive monitoring for adult patients in critical care settings who require close hemodynamic monitoring.

Clinical trial number: Not applicable

Keywords: arterial pressure, continuous non-invasive monitoring, critical care

## Declarations

Availability of data and material (data transparency): All data used in the meta-analyses is available [here](add%20link%20here).

Code availability: All data used in the meta-analyses is available [here](https://github.com/nkamboj06/cnap-review) .

Abbreviated title:

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**Glossary of terms:**

CNAP = Continuous Non-invasive Arterial Pressure

GRADE = Grading of Recommendations, Assessment, Development and Evaluations

QUADAS-2 = Revised Quality Assessment of Diagnostic Accuracy Studies tool

LoA = Limits of Agreement

CI = Confidence intervals

SD2 = Variance

τ2 = Tau-squared

## Introduction

Invasive arterial pressure monitoring is the standard of care for patients requiring continuous blood pressure monitoring. [1] Arterial cannulation is painful, time-consuming, needs to be done by a trained clinician, and is associated with rare complications such as infections, embolism, tissue and nerve damage. For these reasons, intermittent non-invasive blood pressure monitoring is a frequently used alternative. [1] However, monitoring blood pressure intermittently increases risk of late recognition and delayed correction of hemodynamic compromise. Continuous non-invasive arterial pressure (CNAP) monitoring allows for continuous blood pressure measurements without the risk of complications and inconvenience associated with arterial cannulation. CNAP monitoring devices display real-time, continuous arterial pressure waveforms and provide non-invasive beat-to-beat arterial pressure measurement.[2]

Continuous non-invasive monitoring of blood pressure can be achieved through the arterial applanation tonometry and volume clamp techniques (also called vascular unloading technique or finger cuff technologies).[1, 3, 4] Arterial applanation tonometry is based on the work of Pressman and Newgard, who discovered that a transducer strapped to an artery with a bone underneath, can obtain the arterial pulse wave. [1] A device that is automated and commercially available that uses this method is the T-Line system (Tensys Medical, San Diego, CA, USA). The volume clamp technique is based on the work by Penaz et al. (1976). [5] Blood pressure is measured at the finger using an inflatable cuff combined with a photodiode. [1] Devices using this technique include ClearSight system (Edwards Life-sciences, Irvine, CA, USA [formerly known as Nexfin; BMEye, Amsterdam, The Netherlands); and CNAP® monitor (CNSystems, Graz, Austria). Numerous studies have investigated the concordance between CNAP measurement and invasive arterial pressure measurement in critical care. Critical appraisal of the quality of evidence from these studies followed by synthesis of results in a meta-analysis would aid clinical decision-making regarding the appropriateness of substituting CNAP for blood pressure monitoring in the intensive care unit.

## Methods

A systematic review was conducted. The primary comparison for this review was blood pressure measured using a CNAP device versus blood pressure measured using an invasive device.

### Inclusion criteria

Studies that reported blood pressure from a CNAP device with a concurrent invasive measurement obtained from an arterial cannula were included. Due to the potential of overestimation of the intervention performance, case control designs were excluded. Studies were limited to human subjects who were 18 years of age or older and received care in a critical care setting (eg. Intensive Care Unit, Coronary Care Unit, Cardiothoracic Intensive Care Unit). No publication date or language restrictions were applied. Published conference abstracts were included if there was enough information reported to appraise the quality of the study.

### Data sources and searches

A comprehensive search of EMBASE and Medline was conducted. The search strategy is presented in the appendix.[6] Study characteristics (author, year of publication, country, design, sample size, clinical setting, numbers studied, and analyses for each outcome), population characteristics (inclusion and exclusion criteria) and blood pressure measurement characteristics (type of CNAP device and site of invasive measurements) were extracted. Outcomes were the mean bias (eg, accuracy) and variance (eg, SD, precision) for systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP). We also extracted information about how repeated measurements were handled. In particular we assessed whether studies: (1) analysed each pair of data separately; (2) treated each pair of data as independent; or (3) used either analysis of variance or a random effects model as a way to control for the dependent nature of the repeated measures data.[7]

Two reviewers independently completed risk of bias assessments using the revised Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2).[8] Risk of bias for patient selection, conduct of the CNAP measurements, conduct of the comparator invasive measurements, and timing and flow (eg, timing of CNAP and established invasive blood pressure measurements, dropouts) was rated as ‘high’, ‘low’ or ‘unclear’.

The Grading Quality of Evidence and Strength of Recommendation methodology was applied to rate the quality of evidence across studies.[9] Evidence was downgraded in accordance with study limitations, inconsistency, and imprecision. There were no circumstances in which evidence was downgraded for indirectness as this systematic review only included relevant studies. Although the possibility of publication bias was not excluded, this bias was not formally assessed as it was not considered sufficient enough to reason downgrading the quality of evidence.

### Data synthesis and analysis

A framework for meta-analysis of Bland-Altman method comparison studies based on limits of agreement approach was used.[10] One advantage of this method is that it incorporates sampling error into the estimate of the pooled limits of agreement (LoA). This ‘population LoA’ is wider than those typically reported in meta-analyses of Bland-Altman studies.[10]

Pooled limits of agreement were calculated using the formula , where is the average bias across studies, is the average within-study variation in differences and is the variation in bias across studies. We estimated and using a weighted least-squares model, which is similar to a random-effects approach. The associated estimations of their standard errors were made using robust variance estimation. As some studies used repeated-measures designs without accommodating for the correlation between measurements from the same participants, robust variance estimation was used instead of model-based standard errors. [11–13] The method-of-moments estimator from DerSimonian & Laird [14] was used for the parameter.

Outer 95% confidence intervals for pooled limits of agreement were calculated to determine the measures of uncertainty. If the individual studies did not account for repeated measurements, we calculated weights proportional to the number of participants and not the total number of measurements for use in the meta-analysis. All the analyses were conducted using the R statistical program.[15] All data and R code used in the meta-analyses is available [here](https://github.com/nkamboj06/cnap-review) and archived here.

A sensitivity analysis for the primary comparison (CNAP versus invasive arterial pressure monitoring systems) was performed based on risk of bias. Studies rated as ‘unclear risk of bias’ was treated as ‘high risk’ and ‘high risk of bias’ studies were excluded from analyses. We conducted subgroup analyses for the primary comparison according to the method of CNAP monitoring (volume clamp vs. arterial applanation tonometry), and arterial catheter site for invasive arterial pressure measurement (radial vs. femoral). As clinicians would be interested in the accuracy of specific CNAP devices, we conducted a subgroup analyses for the type of CNAP monitoring device (CNAP® monitor, ClearSight system, and T-Line), where a sufficient number of studies were available. Due to the lack of validated methods on statistical approaches for detecting reporting bias, this assessment was not performed. [16] Simulations have revealed that tests for detecting funnel plot asymmetry will result in publication bias often being identified incorrectly.[17]

Results from each study were converted into a standard format, with bias meaning CNAP minus the comparator invasive blood pressure monitoring system. One study used the femoral artery as the comparator for all 45 participants and also completed an additional analysis on 17 of the 45 participants using the radial artery for invasive MAP measurement. [18] Only the results from the femoral artery were reported. Another study reported results for multiple groups of participants.[19] Each of these groups was treated as a separate ‘comparison’ in the meta-analysis. Two studies used a mixture of radial and femoral artery for comparator measurements.[20, 21] The authors of these studies reported the combined results therefore these two studies were not included in the invasive arterial pressure measurement site sub-group analysis. We used the combined estimate in our primary analysis and the estimate for the different methods, and devices in a subgroup analysis. At present there are no minimal standards set for the accuracy of CNAP monitoring systems. Criteria developed by the Association for the Advancement of Medical Instrumentation (AAMI) for evaluating automatic sphygmanometers has been cited in other research to evaluate CNAP accuracy. [21–26] The AAMI defines acceptable limits for accuracy of an automatic sphygmanometer as no greater than 5 mmHg and precision not greater than 8 mmHg for SAP and DBP. [27]

## Results

### Study selection and description

Nineteen studies were included (Figure ). Twenty studies were conducted in the wrong setting (eg, outpatient, operating room) and were excluded. Seven studies were conducted with the wrong population (i.e <18 years of age, subjects were volunteers), and two studies reported the wrong outcome, therefore were excluded.

A summary of the characteristics of included studies is displayed in Table 1. The primary meta-analysis for systolic blood pressure consisted of 262,352 measurements, 785 participants, and 19 comparisons from 18 individual studies. The primary meta-analysis for diastolic blood pressure consisted of 262,235 measurements, 760 participants, and 18 comparisons from 17 individual studies . There were 162,080 measurements from 784 participants included in the primary meta-analysis for mean arterial pressure (19 comparisons; 18 studies).

The sensitivity analysis including only studies that were rated as having low risk of bias across all domains included 8 comparisons from 7 studies that enrolled 234 participants with 155,459 paired measurements for the systolic blood pressure outcome. Primary DBP comparison of low risk of bias studies included 8 comparisons from 7 studies that enrolled 234 participants with 155,459 paired measurements. Primary MAP comparison for low risk of bias studies included 7 comparisons from 6 individual studies of 214 participants with 155,459 paired measurements.

There were 7 studies that compared the SBP based on the arterial applanation tonometry method to invasive SBP, comprising 7 comparisons with 122,704 measurements from 180 participants. Arterial applanation tonometry method was used in 7 studies that compared to invasive DBP, comprising 7 comparisons with 122,704 measurements from 180 participants. For MAP measurement this method was used in 7 studies comprising 7 comparisons with 122,704 measurements from 180 participants. There were 11 studies that compared the SBP based on the volume clamp method to invasive arterial pressure, comprising 12 comparisons with 139,648 measurements from 605 participants. Volume clamp method was used in 10 studies that compared to invasive DBP, comprising 11 comparisons with 139,531 measurements from 580 participants. Volume clamp method for MAP measurement was used in 11 studies comprising 12 comparisons with 39,376 measurements from 604 participants.

ClearSight system was used in 6 studies that compared SBP to invasive SBP, comprising 7 comparisons with 15,466 measurements from 204 participants. There were 5 studies that compared ClearSight system DBP to invasive DBP, comprising 6 comparisons with 15,349 measurements from 179 participants. ClearSight system for MAP measurement was used in 6 studies comprising 7 comparisons with 15,466 measurements from 204 participants. There were 4 studies that compared the SBP based on the CNAP® monitor to invasive SBP, comprising 4 comparisons with 23,859 measurements from 381 participants. There were 4 studies that compared to CNAP® monitor and invasive DBP, comprising 4 comparisons with 23,859 measurements from 381 participants. CNAP® monitor for MAP measurement was used in 4 studies comprising 4 comparisons with 23,859 measurements from 381 participants. T-line was used in 6 studies that compared SBP to invasive SBP, comprising 6 comparisons with 122,404 measurements from 170 participants. T-line was used in 6 studies that compared to invasive DBP, comprising 6 comparisons with 122,404 measurements from 170 participants. T-line for MAP measurement was used in 6 studies comprising 6 comparisons with 122,404 measurements from 170 participants.

From the 19 studies, 7 used the femoral artery and 12 used the radial artery for direct invasive measurement. There were 5 studies that compared the SBP from the femoral site, comprising 5 comparisons with 89,323 measurements from 185 participants. DBP from the femoral site was used in 5 studies, comprising 5 comparisons with 89,323 measurements from 185 participants. Femoral site for MAP measurement was used in 5 studies comprising 5 comparisons with 89,323 measurements from 185 participants. As mentioned previously, one included study used the femoral site for all participants as the main comparison and included the radial site on 17 of the 45 participants for MAP measurements.[18] Only the femoral site comparison from that study were included in our meta-analysis. There were 11 studies that compared the SBP from the radial site, comprising 12 comparisons with 172,366 measurements from 393 participants. Radial site was used in 11 studies that compared DBP, comprising 12 comparisons with 172,366 measurements from 393 participants. MAP measurement from the radial site was used in 11 studies comprising 12 comparisons with 72,094 measurements from 392 participants.

The modified QUADAS-2 was used to conduct the quality assessment (presented in Figure ). In the patient selection domain, risk of bias was assessed as low in 17 studies, unclear in 1, and high in 1. In the index test domain, 14 studies were assessed as low risk, 3 as unclear risk, and 2 as high risk. In the reference standard domain, 13 studies were assessed as low risk, 2 as unclear risk, and 4 as high risk. In the flow and timing domains, 11 studies were low risk, 4 unclear risk, and 4 high risk. Overall, 7 studies were assessed as low risk and 12 as high risk. In 8 (42%) studies, the authors declared a receipt of funding.

### Primary meta-analysis

Table 2 presents the results of the primary, sensitivity, and all subgroup analyses. The pooled estimate for the mean bias between the CNAP and invasive arterial pressure measurements was -3.94 mmHg, 4.61 mmHg, and 1.91mmHg for systolic, diastolic, and mean arterial pressure, respectively. Population limits of agreement, which take into consideration the between-study heterogeneity and sampling error, were wide, spanning from -36.17 mmHg to 28.3mmHg for systolic blood pressure, -102.38 mmHg to 111.61 mmHg for diastolic blood pressure, and -40.63 mmHg to 44.44mmHg for mean arterial pressure. The amount of between-study heterogeneity is displayed graphically in the density plots in Figure . The quality of evidence for the primary meta-analysis was downgraded to very low quality due to concerns about imprecision, inconsistency, and study limitations.

### Sensitivity Analyses

Population limits of agreement for the sensitivity analysis restricted to studies rated as low risk across all domains of the QUADAS-2 were wider than the primary meta-analysis for all outcomes. The mean bias for systolic blood pressure was -3.89 mmHg with population limits of agreement spanning from -53.17 mmHg to 45.38mmHg. The mean bias for diastolic blood pressure was 4.75 mmHg with population limits of agreement of -213.98 mmHg to 223.48mmHg. The mean bias for mean arterial pressure was 1.54 mmHg, with population limits of agreement between -86.05 mmHg and 89.13mmHg. The quality of evidence for this sensitivity analysis was downgraded to very low quality due to concerns about imprecision and inconsistency. A sensitivity analysis excluding studies that received funding from device manufacturers revealed population limits of agreement that were wider than the primary analysis (-38.62 mmHg to 29.54mmHg for systolic blood pressure, -219.52 mmHg to 227.01mmHg for diastolic blood pressure, and -74.59 mmHg to 79.43mmHg for mean arterial pressure).The evidence rating for this sensitivity analysis was downgraded to very low, again, due to concerns about imprecision, inconsistency, and study limitations.

### Subgroup Analyses

We conducted three subgroup analyses based on the method of CNAP monitoring, types of CNAP device, and the anatomical site (femoral or radial artery) where the arterial catheter was placed for invasive blood pressure measurement. In the subset of studies conducted using a device based on the arterial applanation tonometry, the pooled mean bias (population limits of agreement) for systolic blood pressure was -3.12 mmHg (-39.23 mmHg to 32.99 mmHg). For diastolic blood pressure, mean bias was 5.54 mmHg (-31.22 mmHg to 25.89 mmHg). The pooled mean bias for mean aretial pressure was 2.15 mmHg (-21.59 mmHg to 25.89 mmHg). In the subset of studies conducted using a device based on the volume clamp method, the pooled mean bias (population limits of agreement) for systolic blood pressure was -4.36 mmHg (-39.13 mmHg to 30.42 mmHg). Pooled mean bias for diastolic blood pressure was 3.79 mmHg (-213.89 mmHg to 221.47 mmHg), and 1.46 mmHg (-66.25 mmHg to 69.16 mmHg) for mean aterial pressure. The GRADE rating for quality of evidence was downgraded to very low quality due to concerns about imprecision, inconsistency, and study limitations.

In the subset of studies conducted based on the type of monitoring device, the pooled mean bias (population limits of agreement) for the ClearSight system was -3.96 (-61.19 mmHg to 53.27 mmHg) for systolic blood pressure, 3.52 (-440.22 mmHg to 447.27 mmHg) for diastolic blood pressure, and 0.21 (-101.96 mmHg to 102.39 mmHg) for mean arterial pressure. The pooled mean bias (population limits of agreement) for the CNAP® monitor was -5.01 (-39.66 mmHg to 29.65 mmHg) for systolic blood pressure, 3.46 (-695.33 mmHg to 702.25 mmHg) for diastolic blood pressure, and 4.92 (-20.73 mmHg to 30.57 mmHg) for mean arterial pressure. In the subset of studies conducted based on the type of T-line monitoring device, the mean bias (population limits of agreement) was -3.47 (-45.58 mmHg to 38.64 mmHg) for systolic blood pressure, 6.31 (-30.88 mmHg to 43.51 mmHg) for diastolic blood pressure, and 2.55 (-25.43 mmHg to 30.53 mmHg) for mean arterial pressure. The GRADE rating for quality of evidence was downgraded to very low due to study limitations, imprecision, and inconsistency.

In the subset of studies conducted using the femoral site for invasive systolic blood pressure measurement, the pooled mean bias (population limits of agreement) was -6.21 mmHg (-64.75 mmHg to 52.32 mmHg), for diastolic blood pressure 6.31 mmHg (-15.93 mmHg to 19.9 mmHg), and for mean arterial pressure 1.21 mmHg (-17.48 mmHg to 19.9 mmHg). For the radial site, the estimates for pooled mean bias (population limits of agreement) were -3.39 mmHg (-35.19 mmHg to 28.4mmHg) for systolic blood pressure, 5.15 mmHg (-122.01 mmHg to 67.6 mmHg) for diastolic blood pressure, and 2.32 mmHg (-62.96 mmHg to 67.6 mmHg) for mean arterial pressure. We downgraded the quality of evidence to very low quality due to concerns about imprecision, inconsistency, and study limitations.

## Discussion

We found that systolic and mean arterial blood pressure measurements from CNAP monitoring devices could be as much as about 30-40 mmHg lower or higher than an invasive measurement recorded at the same time. Results for the diastolic blood pressure outcome suggest CNAP devices produce highly inaccurate measurements for this parameter. Based on these results, it is not appropriate to substitute blood pressure measurements from CNAP devices in place of those obtained from invasive arterial pressure monitoring in critical care settings when close hemodynamic monitoring is required. The evidence was downgraded to very low quality due to concerns about imprecision, inconsistency and risk of bias.

Pooled estimates for the accuracy of CNAP devices have been reported in previous meta-analyses.[2, 28] Our estimates for the population limits of agreement should be considered a better representation of the magnitude of discrepancy which should be expected between CNAP and invasive measurements if these devices were to be used in critical care settings for a number of reasons. First, in our review, we used the framework for meta-analysis of Bland-Altman method comparison studies based on limits of agreement approach. [10] This approach incorporates the magnitude of heterogeneity in results between studies as well as sampling error. Second, we applied repeated measures adjustments for several of the included studies, which did not account for the correlation between measurements taken from the same participants over time in their primary analyses. This adjustment was not undertaken in the prior meta-analyses, which may lead to more favourable estimates for pooled limits of agreement.[7] Third, by restricting the systematic review to the specific population of critical care patients, this systematic review provide direct evidence for this context. The previous meta-analyses included participants in the perioperative setting and did not conduct subgroup analysis.[2, 28] Another distinction is that we included both methods of CNAP monitoring (volume clamp and arterial applanation tonometry) in our meta-analyses. A recent meta-analysis only focused on the volume clamp method.[28] Our subgroup meta-analyses revealed important insights into the accuracy of specific types of CNAP devices in critical care.

The certainty of evidence was downgraded due to impresion arising from the fact that many included studies analysed a large number of blood pressure measurements from only a small number of participants. For example, one study analysed 8700 measurements from just 29 participants [29]). We used robust variance estimation to ensure that the pooled estimates were proportional to the number of patients, not the total number of measurements.[10] Therefore, studies with much larger sample sizes are required to increase confidence in the accuracy and precision of CNAP devices.

One obvious feature of the primary and sensitivity meta-analyses that requires discussion is that population limits of agreement for diastoloic blood pressure were far wider than the systolic and mean arterial pressure outcomes. This was primarily due to the greater heterogeneity across the studies included in the analysis, evidenced by high values for the τ2 parameter (reported in Table 2). The more pronounced variation in limits of agreement for diastolic blood pressure in comparison with systolic and mean arterial pressure is also clearly visible in the density plots presented in Figure 3. Close inspection of the subgroup analyses based on the type of CNAP device used, does provide some important additional insight. Population limits of agreement for the diastolic blood pressure outcome in the subgroup meta-analyis of studies that used the arterial applanation tonometry approach were not wider than systolic and mean arterial pressure and did not have high values for the τ2 parameter, meaning results between studies were not inconsistent. Based on these results, CNAP devices based on arterial applanation technology should be considered more reliable for use in clinical practice and, in particular, they should given preference over volume clamp devices for any situation where continuous non-invasive monitoring of diastolic blood pressure is required.

The sub-group analysis restricted to studies that used devices based on the arterial applanation tonometry technique was comprised primarily of studies that used only one specific device (T-line). From the seven included studies, six used the T-line and one used the NCAT. In contrast, the subgroup meta-analysis of devices based on the volume clamp approach included three different types of devices (Finapres, ClearSight, CNAP® monitor) across the 11 studies. Moreover, different models for the Finapres, ClearSight and CNAP® devices were used across the studies. It seems, though, that variation in the type of volume clamp device does not explain the large variation in estimates for the accuracy of diastolic blood pressure population limits of agreement. Population limits of agreement for diastolic blood pressure were wide in further subgroup meta-analyses restricted to studies that used the ClearSight and CNAP® devices.

### Limitations

Data on adverse events due to blood pressure monitoring with CNAP devices were not extracted. This meta-analysis focused on calculating population limits of agreement, which incorporate the variation in bias between studies into the estimates. Therefore, it was not appropriate to use meta-regression or tests for interaction between subgroups to investigate sources of heterogeneity. The possibility of publication bias cannot be ruled out, although the evidence suggests this may not be as serious of a problem for studies that are not randomized controlled trials.[16] Several different types of CNAP monitoring devices were combined in our primary meta-analysis. These devices are based on different technologies, namely the arterial applanation tonometry and volume-clamp methods. We performed a sub-group analysis of the different methods (arterial applanation tonometry and volume clamp), and of the different devices (CNAP® monitor, ClearSight system, and T-line). Different models of each device were not assessed individually. We did not undertake subgroup meta-analysis for specific CNAP devices where there was an insufficient number of studies. For example, only two studies used the Finapres device. One reported on the systolic and diastolic blood pressure outcomes [30], while the other reported results for only mean arterial pressure [31]. There was one study that explored the NCAT device.[32] This systematic review focused on estimating the absolute agreement between the CNAP and the invasive methods. We found that a blood pressure measurement at a certain point in time cannot be considered an accurate reflection of ‘true’ (i.e.invasive) blood pressure. As arterial pressure continuously changes overtime in response to a variety of factors, an alternative way that CNAP devices could potentially be useful in clinical practice is if the trends over time were accurate. We did not evaluate the trending ability CNAP devices because methods to meta-analyse results from individual studies are not available.

## Conclusion

Substantial differences between blood pressure measurements from continuous non-invasive and invasive monitoring for blood pressure measurements were identified in this meta-analysis. Population limits of agreement were wide, spanning from -36.17 mmHg to 28.3mmHg for SBP, -102.38 mmHg to 111.61 mmHg for DBP, and -40.63 mmHg to 44.44mmHg for MAP. Clinicians should consider this broad range of uncertainty of continuous noninvasive blood pressure monitoring if using these devices to inform clinical decision-making in critical care. More consistent population limits of agreement across systolic, diastolic and mean arterial pressure were identified in a subgroup meta-analysis of studies that evalauted CNAP devices based on arterial applanation tonometry, which was primarily the T-line device. Based on the evidence at hand, the T-line device should be considered the most accurate CNAP device in critical care settings.

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# Figure legend

Fig. PRISMA Flow Diagram.

Fig. Risk of bias assessments for included studies.

Fig. Comparisons between CNAP and invasive blood pressure measurement within and across studies. Blue curves are distributions of the differences between measurements from CNAP and invasive arterial blood pressure measurements in individual studies. The red curve is the distribution of the pooled estimate.

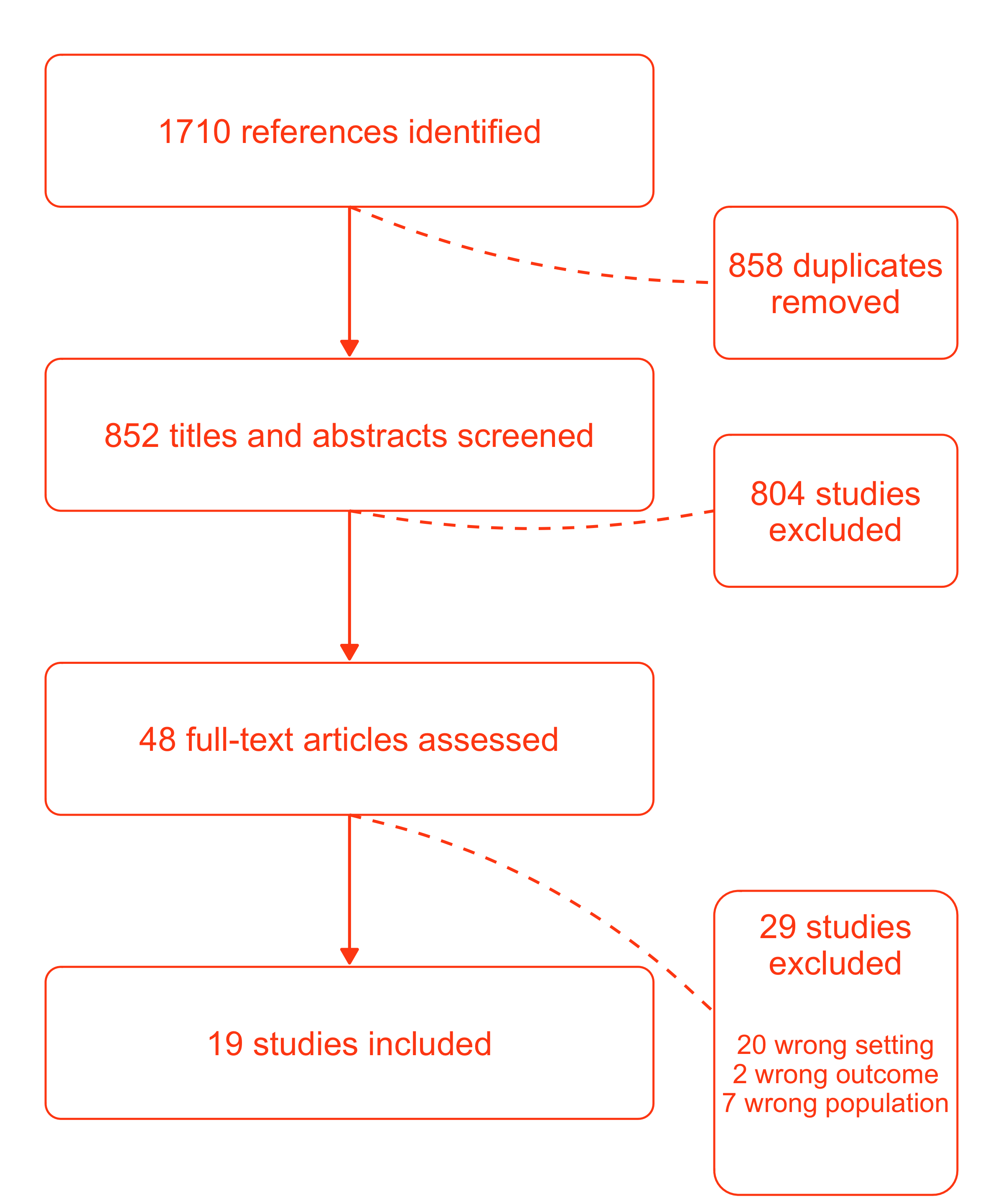


Figure : PRISMA Flow Diagram

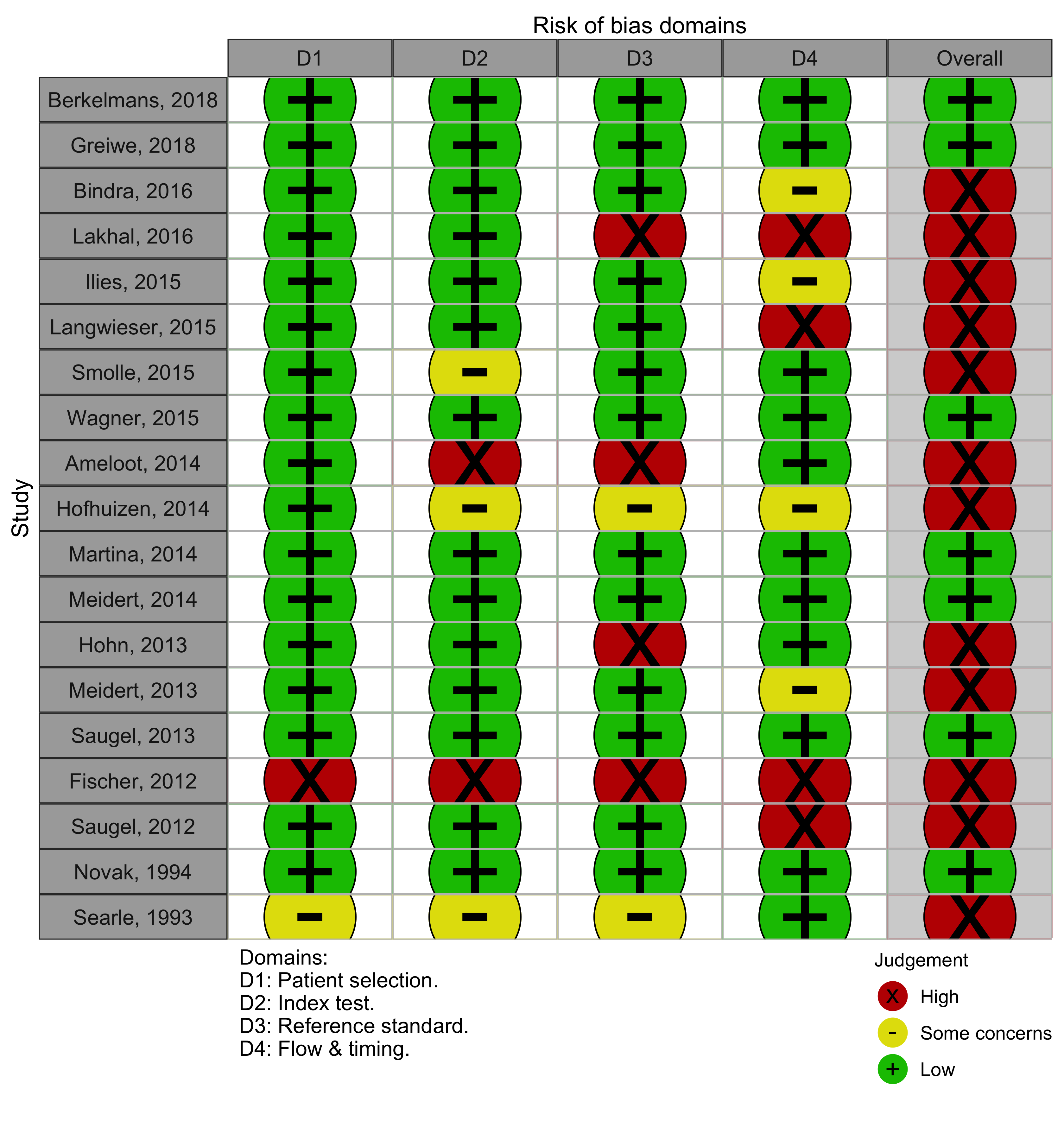


Figure : Risk of bias assessments for included studies

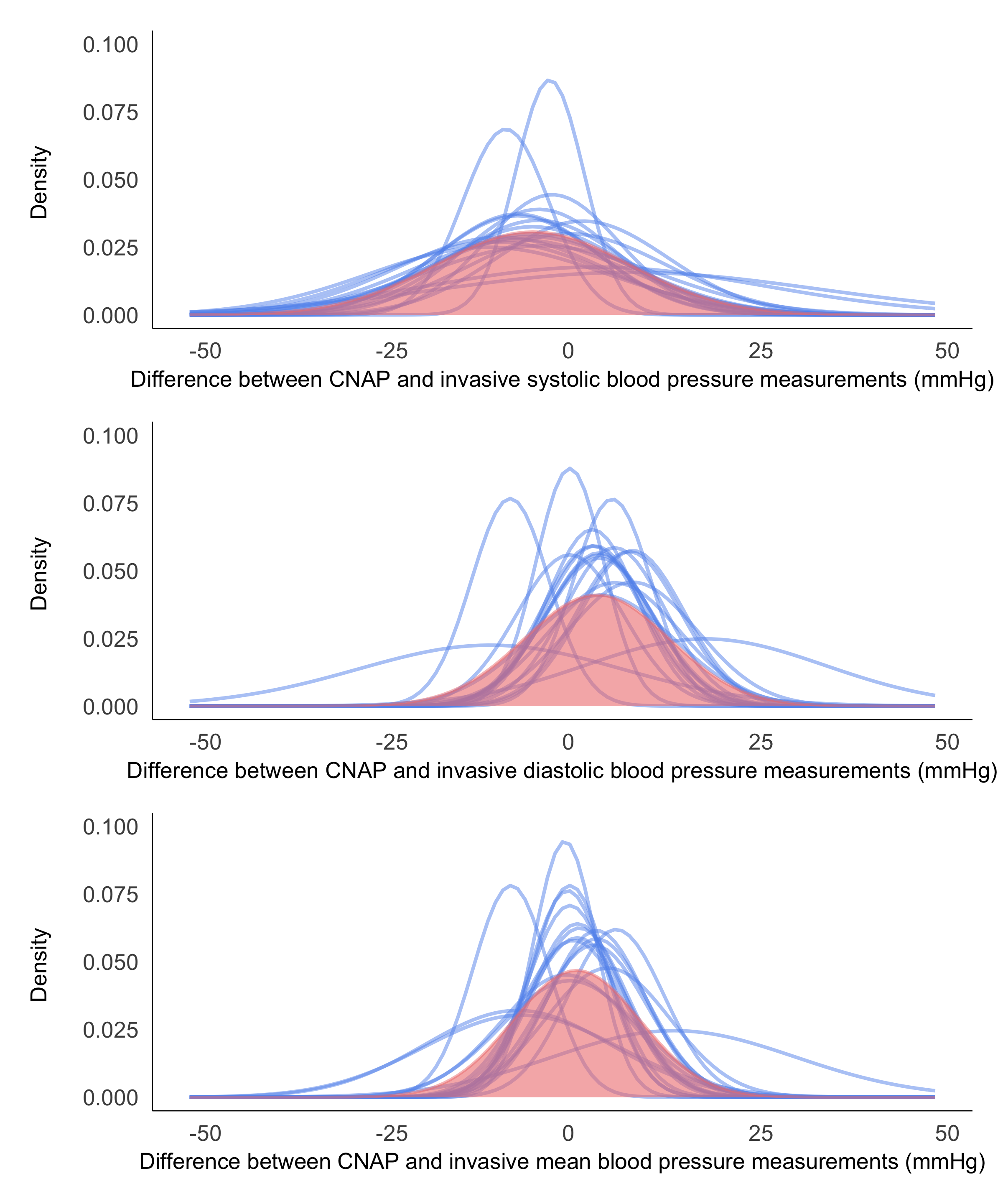


Figure : Comparisons between CNAP and invasive blood pressure measurement within and across studies. Blue curves are distributions of the differences between measurements from CNAP and invasive arterial blood pressure measurements in individual studies. The red curve is the distribution of the pooled estimate.)

# Appendix

## Medline search strategy

1. Blood pressure OR arterial pressure
2. ‘non invasive’ OR Noninvasive or non-invasive
3. 1 AND 2
4. Nexfin or ClearSight OR CNAP OR CNAPTM OR Finapres OR Tensys OR T-line OR TL-200 OR TL-300 OR Vasotrac
5. Penaz OR (Pressman and Newgard) OR Volume Clamp OR Arterial applanation tonometry OR Finger Cuff OR ‘vascular unloading’ OR ‘pulse transit time’
6. (Continuous OR continued OR continual OR continually OR continuing)
7. (Beat-to-beat OR real time OR real-time OR simultaneous OR simultaneously)
8. (Accuracy OR precision OR reliability OR validity OR validation OR standard deviation)
9. (Bias OR (mean adj1 difference) OR (limi\* adj2 agreement) OR (Bland adj1 Altman))
10. blood pressure monitors.sh.
11. 6 OR 7
12. 10 OR 11
13. 3 AND 11
14. 5 AND 13
15. 4 OR 12 OR 13 OR 14
16. 8 OR 9
17. 15 AND 16

## EMBASE search strategy

1. Blood pressure OR arterial pressure
2. ‘non invasive’ OR Noninvasive or non-invasive
3. 1 AND 2
4. Nexfin or ClearSight OR CNAP OR CNAPTM OR Finapres OR Tensys OR T-line OR TL-200 OR TL-300 OR Vasotrac
5. Penaz OR (Pressman and Newgard) OR Volume Clamp OR Arterial applanation tonometry OR Finger Cuff OR ‘vascular unloading’ OR ‘pulse transit time’
6. (Continuous OR continued OR continual OR continually OR continuing)
7. (Beat-to-beat OR real time OR real-time OR simultaneous OR simultaneously)
8. (Accuracy OR precision OR reliability OR validity OR validation OR standard deviation)
9. (Bias OR (mean adj1 difference) OR (limi\* adj2 agreement) OR (Bland adj1 Altman))
10. exp blood pressure monitor/
11. 6 OR 7
12. 10 OR 11
13. 3 AND 11
14. 5 AND 13
15. 4 OR 12 OR 13 OR 14
16. 8 OR 9
17. 15 AND 16

## Table 1: Study Characteristics

| Study | | | Participants | | | | Blood pressure measurements | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | Age (years)a |  |  | Device |  |  | Participants |  | Measurements |
| 2018 | Berkelmans |  |  | 74 (9) | Atrial fibrillation | ICU/CCU | ClearSight | Radial | 31 |  | 4650 |  |
|  | 64 (17) | Sinus Rhythm | 10 |  | 1500 |  |
| Greiwe |  |  | 71 [59, 76] |  | Cardiac Surgery ICU | T-line | Radial | 31 |  | 27900 |  |
| 2016 | Bindra |  |  | 62.2 (28 to 87)\* |  | ICU | Finapres | Radial | 19 |  | 51 |  |
| Lakhal |  |  | 64 (13) |  | Surgical ICU | CNAP® | Radial/Femoral | 182 |  | 546 |  |
| 2015 | Ilies |  |  | 68.8 (9.4) |  | Cardiac ICU | CNAP® | Radial | 104 |  | 11222 |  |
| Langwieser |  |  | 69 [60, 77) |  | Cardiac ICU | T-line | Radial | 30 |  | 7304 |  |
| Smolle |  |  | 66 [56, 72] |  | Medical ICU | CNAP® | Radial | 40 |  | 7200 |  |
| Wagner |  |  | 60 [52, 71] |  | ICU | CNAP® | Femoral | 55 |  | 4891 |  |
| 2014 | Ameloot |  |  | 57.6 (19.4) |  | Medical Surgical Burns ICU | ClearSight | Femoral | 45 |  | 225 |  |
| Radial | 17 |  | 85 |  |
| Hofhuizen |  |  | 67 (50 to 81)\* |  | ICU | ClearSight | Radial | 20 |  | 54 |  |
| Martina |  |  | 50 (11) |  | ICU | ClearSight | Radial | 29 |  | 8700 |  |
| Meidert |  |  | 67 [54 to 77]\* |  | ICU | T-line | Radial | 24 |  | 2993 |  |
| 2013 | Hohn |  |  | 63 (18 to 82)\* |  | ICU | ClearSight | Radial/Femoral | 25 |  | 117 |  |
| Meidert |  |  | 60 [55, 65] |  | ICU | T-line | Femoral | 23 |  | 2879 |  |
| Saugel |  |  | 63 [51, 74] |  | Medical ICU | T-line | Femoral | 34 |  | 4502 |  |
| 2012 | Fischer |  |  | 68 [22 to 85]\* |  | Cardiac Surgery ICU | ClearSight | Radial | 44 |  | 220 |  |
| Saugel |  |  | 68 [61.5, 73.5] |  | Medical ICU | T-line | Femoral | 28 |  | 76826 |  |
| 1994 | Novak |  |  | [20 to 78] |  | ICU | Finapres | Radial | 20 |  | 100323 |  |
| 1993 | Searle |  |  | 60.8 (11.7) |  | Cardiac ICU | NCAT | Radial | 10 |  | 300 |  |
| amean (standard deviation), mean(range)\*, mean(interquartile range), median[range]\*, or median [interquartile range] | | | | | | | | | | | | |

### Table 2: Results of meta-analyses

|  |  |  |  |  |  |  |  |  |  |  | Population LoA | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Analysis | Outcome | Studies | Comparisons | Participants | Measurements | Mean biasa | SD2ab | τ2ac | Lower 95% LoAad | Upper 95% LoAad | Outer CI for lower 95% LoAade | Outer CI for upper 95% LoAade |
| Primary | SBP | 18 | 19 | 785 | 262,352 | -3.94 | 162.06 | 6.97 | -29.94 | 22.06 | -36.17 | 28.30 |
| DBP | 17 | 18 | 760 | 262,235 | 4.61 | 60.67 | 33.77 | -14.82 | 24.05 | -102.38 | 111.61 |
| MAP | 18 | 19 | 784 | 162,080 | 1.91 | 55.75 | 16.78 | -15.13 | 18.94 | -40.63 | 44.44 |
| Low Risk Studies | SBP | 7 | 8 | 234 | 155,459 | -3.89 | 158.21 | 12.65 | -30.04 | 22.25 | -53.17 | 45.38 |
| DBP | 7 | 8 | 234 | 155,459 | 4.75 | 57.01 | 39.45 | -14.89 | 24.39 | -213.98 | 223.48 |
| MAP | 6 | 7 | 214 | 55,136 | 1.54 | 54.47 | 20.43 | -15.77 | 18.85 | -86.05 | 89.13 |
| Studies Not Funded | SBP | 11 | 12 | 504 | 135,671 | -4.54 | 142.94 | 7.99 | -29.11 | 20.03 | -38.62 | 29.54 |
| DBP | 11 | 12 | 504 | 135,671 | 3.74 | 67.06 | 47.87 | -17.70 | 25.18 | -219.52 | 227.01 |
| MAP | 11 | 12 | 504 | 135,671 | 2.42 | 51.49 | 22.97 | -14.84 | 19.68 | -74.59 | 79.43 |
| Arterial Applanation Tonometry | SBP | 7 | 7 | 180 | 122,704 | -3.12 | 145.51 | 4.84 | -27.64 | 21.40 | -39.23 | 32.99 |
| DBP | 7 | 7 | 180 | 122,704 | 5.54 | 65.27 | 9.78 | -11.79 | 22.87 | -31.22 | 42.30 |
| MAP | 7 | 7 | 180 | 122,704 | 2.15 | 51.28 | 5.05 | -12.86 | 17.16 | -21.59 | 25.89 |
| Volume Clamp | SBP | 11 | 12 | 605 | 139,648 | -4.36 | 169.61 | 7.39 | -30.97 | 22.25 | -39.13 | 30.42 |
| DBP | 10 | 11 | 580 | 139,531 | 3.79 | 58.16 | 45.17 | -16.54 | 24.12 | -213.89 | 221.47 |
| MAP | 11 | 12 | 604 | 39,376 | 1.46 | 57.54 | 21.19 | -16.29 | 19.20 | -66.25 | 69.16 |
| ClearSight | SBP | 6 | 7 | 204 | 15,466 | -3.96 | 161.42 | 14.32 | -30.47 | 22.55 | -61.19 | 53.27 |
| DBP | 5 | 6 | 179 | 15,349 | 3.52 | 45.88 | 52.30 | -16.29 | 23.34 | -440.22 | 447.27 |
| MAP | 6 | 7 | 204 | 15,466 | 0.21 | 48.70 | 22.42 | -16.65 | 17.08 | -101.96 | 102.39 |
| CNAP® | SBP | 4 | 4 | 381 | 23,859 | -5.01 | 180.32 | 2.85 | -32.08 | 22.06 | -39.66 | 29.65 |
| DBP | 4 | 4 | 381 | 23,859 | 3.46 | 98.50 | 60.83 | -21.78 | 28.71 | -695.33 | 702.25 |
| MAP | 4 | 4 | 381 | 23,859 | 4.92 | 58.73 | 4.85 | -11.03 | 20.86 | -20.73 | 30.57 |
| T-line | SBP | 6 | 6 | 170 | 122,404 | -3.47 | 186.54 | 7.19 | -31.31 | 24.37 | -45.58 | 38.64 |
| DBP | 6 | 6 | 170 | 122,404 | 6.31 | 74.82 | 9.10 | -12.01 | 24.64 | -30.88 | 43.51 |
| MAP | 6 | 6 | 170 | 122,404 | 2.55 | 58.54 | 6.13 | -13.53 | 18.64 | -25.43 | 30.53 |
| Femoral Site | SBP | 5 | 5 | 185 | 89,323 | -6.21 | 170.01 | 13.09 | -33.28 | 20.85 | -64.75 | 52.32 |
| DBP | 5 | 5 | 185 | 89,323 | 6.31 | 62.53 | 3.71 | -9.96 | 22.59 | -15.93 | 28.56 |
| MAP | 5 | 5 | 185 | 89,323 | 1.21 | 49.36 | -0.68 | -12.74 | 15.16 | -17.48 | 19.90 |
| Radial Site | SBP | 11 | 12 | 393 | 172,366 | -3.39 | 137.44 | 6.20 | -27.37 | 20.58 | -35.19 | 28.40 |
| DBP | 11 | 12 | 393 | 172,366 | 5.15 | 52.41 | 32.32 | -13.26 | 23.56 | -122.01 | 132.31 |
| MAP | 11 | 12 | 392 | 72,094 | 2.32 | 55.27 | 20.34 | -15.07 | 19.71 | -62.96 | 67.60 |
| aUnits are mmHg | | | | | | | | | | | | |
| bVariance | | | | | | | | | | | | |
| cMeasure of heterogeneity | | | | | | | | | | | | |
| dLoA = Limits of Agreement | | | | | | | | | | | | |
| eCI = Confidence Intervals | | | | | | | | | | | | |