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

A systematic review and meta-analysis

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### Abstract

**Purpose**

Continuous arterial pressure measurement is a mainstay of hemodynamic monitoring for critically ill patients. Continuous non-invasive arterial pressure (CNAP) monitoring allows for non-invasive beat-to-beat arterial pressure measurements using pulse wave analysis and can bridge the gap between continuous-invasive blood pressure monitoring and non-invasive intermittent oscillometric devices. However, the accuracy and precision of these devices remains unclear. Therefore, 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 intensive 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 -59.93 mmHg to 56.11mmHg (19 comparisons; 18 studies; 785 participants; 262,352 measurements).The evidence was rated as very low-quality. The accuracy of diastolic blood pressure measurements from CNAP devices was rated as very low-quality evidence due to very serious concerns about heterogeneity and imprecision. Population limits of agreement spanned from -216.7 mmHg to 219.72mmHg (18 comparisons; 17 studies; 760 participants; 262,235 measurements). The GRADE rating for mean arterial pressure was low-quality. Population limits of agreement spanned from -68.89mmHg to 71.87mmHg (19 comparisons; 18 studies; 784 participants; 162,080 measurements). Population limits of agreement in sensitivity analyses restricted to studies that were rated as low risk of bias across all domains of the QUADAS-2 revealed similar results.

**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. The SBP measurement from continuous non-invasive devices can be as much as 60 mmHg higher or lower. The 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 the intensive care unit.

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.

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

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

For patients requiring continuous blood pressure monitoring in critical care, invasive arterial pressure monitoring is the standard of care. [1] The cannulation of an artery 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 (NIBP) 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 is a promising solution because it allows for continuous blood pressure measurements without risk of the 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); 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 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 design studies were excluded. Studies were limited to human subjects who were 18 years of age or older and receiving care in a critical care setting (excluding operative room). 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

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.[6]

Two reviewers independently completed risk of bias assessments using the revised Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2).[7] 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’.

A comprehensive search of multiple databases and international clinical trial registry EMBASE and Medline was conducted to minimize the risk of publication bias (see appendix for search strategy). [8] Due to the lack of validated methods on statistical approaches for detecting reporting bias, this assessment was not performed. [begg2005systematic] Simulations have revealed that tests for detecting funnel plot asymmetry will result in publication bias often being identified incorrectly.[9]

The Grading Quality of Evidence and Strength of Recommendation methodology was applied to rate the quality of evidence.[10] 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

The objective for the meta-analysis was to estimate the population limits of agreement between blood pressure measurements from CNAP monitoring devices and established invasive monitoring. A framework for meta-analysis of Bland-Altman method comparison studies based on limits of agreement approach was used.[11] This method was selected because it mirrors the approach in primary Bland-Altman studies, providing an estimate of the pooled limits of agreement in the population (not just the samples studied). The ‘population LoA’ is wider than those typically reported in meta-analyses of Bland-Altman studies.[11] Pooled limits of agreement were calculated using , 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 (similar to a random-effects approach) and associated estimations of their SEs were made using robust variance estimation (RVE). As some studies included used repeated-measures designs without accommodating for the correlation between measurements, robust variance estimation was used instead to model-based standard errors. [12–14] The method-of-moments estimator from DerSimonian & Laird [15] was used for the parameter.

The 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, it was adjusted for in our study by using weights proportional to the number of participants and not the total number of measurements. All the analyses were conducted using the R statistical program.[16] All data and R code used in the meta-analyses is available [here](https://github.com/nkamboj06/cnap-review) and archived here.

Prior to conducting the meta-analyses, the results from each study were converted into a standard format, with bias meaning CNAP monitoring system 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. [17] Only the results from the femoral artery were reported. Another study reported results for multiple groups of participants, therefore in the meta-analysis each of these groups was treated as a separate ‘comparison’. [18] Two studies [19, 20] used a mixture of radial and femoral artery for comparator measurements.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.To the best of our knowledge there are no specific guidelines to evaluate CNAP monitoring systems, however the 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 measurement. [20–25] Therefore, for this review the criteria by AAMI for automatic sphygmanometers was used to evaluate CNAP monitoring. For SAP, DBP, and MAP, the defined acceptability for accuracy was no greater than 5 mmHg and precision not greater than 8 mmHg for SAP and DBP. [26] It was deemed that outer confidence bounds for 95% limits of agreement between CNAP and invasive monitoring systems (termed as ‘population limits of agreement’) outside of these bounds would be clinically unacceptable.

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 or AAT), 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.

## Results

### Study selection and description

Nineteen studies were included (Figure 1). Twenty studies were conducted in the wrong setting (eg, outpatient, operating room) and were excluded. Seven studies were on 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 SBP comparison of the CNAP versus invasive arterial pressure measurements consisted of 262,352 measurements, 785 participants, and 19 comparisons from 18 individual studies. Primary DBP comparison consisted of 262,235 measurements, 760 participants, and 18 comparisons from 17 individual studies . Primary MAP comparison consisted of 162,080 measurements, 784 participants, and 19 comparisons from 18 individual studies. The sensitivity analysis for the primary SBP comparisons with 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. 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.[17] 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 2). 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, seven studies were assessed as low risk and 12 as high risk. Risk of bias assessments are presented in Figure 2. In 8 (42%) studies, the authors declared a receipt of funding.

### Primary Comparison

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 -1.91 mmHg, 1.51 mmHg, and 1.49mmHg for SBP, DBP, and MAP, respectively. Population limits of agreement, which take into consideration the between-study heterogeneity and sampling error, were wide, spanning from -59.93 mmHg to 56.11mmHg for SBP, -216.7 mmHg to 219.72 mmHg for DBP, and -68.89 mmHg to 71.87mmHg for MAP. The amount of between-study heterogeneity is displayed graphically in the density plot in Fig.3. The quality of evidence for the primary comparison 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 similar to the primary analysis for SBP, DBP, and MAP. The mean bias for SBP was -3.89 mmHg with population limits of agreement spanning from -53.17 mmHg to 45.38mmHg. The mean bias for DBP was 4.75 mmHg with population limits of agreement of -213.98 mmHg to 223.48mmHg. The mean bias for MAP was 1.54 mmHg with population limits of agreement -86.05 mmHg to 89.13mmHg. The quality of evidence for this sensitivity analysis was downgraded to low quality due to concerns about imprecision and inconsistency. A further sensitivity analysis excluding studies that received funding from device manufacturers revealed population limits of agreement that were wider than the primary analysis (-73.53 mmHg to 68.28mmHg for SBP, -274.81 mmHg to 279.12mmHg for DBP, and -88.24 mmHg to 92.39mmHg for MAP).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 arterial catheter site of invasive arterial pressure measurement. In the subset of studies conducted using a device based on the arterial applanation tonometry the mean bias (population limits of agreement) for SBP was -2.41 mmHg (-54.74 mmHg to 49.91 mmHg), DBP 5.54 mmHg (-31.22 mmHg to 25.89 mmHg), and MAP 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 mean bias (population limits of agreement) for SBP was -1.63 mmHg (-97.44 mmHg to 94.17 mmHg), DBP -1.3 mmHg (-320.25 mmHg to 317.65 mmHg), and MAP 0.83 mmHg (-137.63 mmHg to 139.28 mmHg). The GRADE rating for quality of evidence was downgraded to 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 mean bias (population limits of agreement) for the ClearSight system was -1.09 (-295.59 mmHg to 293.42 mmHg) for SBP, -2.71 (-221.51 mmHg to 216.09 mmHg) for DBP, and -0.41 (-58.24 mmHg to 57.42 mmHg) for MAP. The mean bias (population limits of agreement) for the CNAP® monitor was -3.15 (-155.61 mmHg to 149.32 mmHg) for SBP, -1.28 (-1430.91 mmHg to 1428.36 mmHg) for DBP, and 1.68 (-501 mmHg to 504.36 mmHg) for MAP. 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 SBP, 6.31 (-30.88 mmHg to 43.51 mmHg) for DBP, and 2.55 (-25.43 mmHg to 30.53 mmHg) for MAP. The GRADE rating for quality of evidence was downgraded to low, again due to study limitations, imprecision, and inconsistency.

In the subset of studies conducted using the femoral site for invasive SBP measurement, the mean bias (population limits of agreement) was -2.98 mmHg (-311.89 mmHg to 305.93 mmHg), for DBP 2.38 mmHg (-588.85 mmHg to 18.89 mmHg), and fpr MAP 0.09 mmHg (-18.71 mmHg to 18.89 mmHg). For the radial site the mean bias (population limits of agreement) were -0.92 mmHg (-70.03 mmHg to 68.19mmHg) for SBP, 2.09 mmHg (-285.69 mmHg to 82.67 mmHg) for DBP, and 1.16 mmHg (-80.36 mmHg to 82.67 mmHg) for MAP. The population limits of agreement were much wider for the radial site results of SBP, DBP, and MAP compared to femoral site. We downgraded the quality of evidence to very low quality due to concerns about imprecision, inconsistency, and study limitations.

## Discussion

This systematic review showed that blood pressure measurement from CNAP monitoring devices could have a MAP as much as about 70 mmHg higher or lower than invasive MAP. On the basis of these results, these devices would not satisfy the standards of the AAMI guidelines. It was reassuring that results of our sensitivity analysis restricted to studies rated to be at low risk of bias using the QUADAS-2 tool were similar. These results have important implications for practice where continuous blood pressure monitoring is essential for timely clinical decision making. It is not appropriate to substitute CNAP devices in place of invasive arterial pressure monitoring in critical care.

We found that the accuracy of blood pressure measurements from CNAP devices compared to invasive arterial pressure measurements has been evaluated using various devices and methods. A sub-group analysis restricted to studies that used devices based on the arterial applanation tonometry technique consisted of six studies with the T-line device and one with the NCAT. Two of the authors who conducted the studies using T-line completed another study in the same clinical setting with a different model of the T-line device. [27] Whereas, the volume clamp included three different types of devices (Finapres, ClearSight system, and CNAP® monitor) and each device had various models. As a result, there were more factors to incorporate into the volume clamp subgroup analysis, which may potentially be contributing to the broader population limits of agreement. Additional studies are required to evaluate the accuracy of both the volume clamp and arterial applanation tonometry methods.

Our estimates of the limits of agreement from CNAP monitoring are similar to results from a previous meta-analysis that compared it to invasive measurements.[2] In our study, we used the framework for meta-analysis of Bland-Altman method comparison studies based on limits of agreement approach, as it provides an estimate of the pooled limits of agreement in the population and not just the samples studied. [11] This allowed for us to incorporate the magnitude of heterogeneity in results between studies and sampling error resulting in limits of agreement that are wider, which was not included in previous meta-analyses.

Many studies in this review analysed a large number of measurements of blood pressure with relatively small sample sizes (ie. one study had 29 participants and 8700 measurements [32]). Importantly, our approach to the meta-analysis takes this into account and by using robust variance estimation, weights for pooling estimates in the meta-analysis become proportional to the number of patients, not the total number of measurements. [11]

Our meta-analysis focused strictly on critical care patients, whereas other meta-analyses also included participants in perioperative setting. [2, 31] We included both methods of CNAP monitoring (volume clamp and arterial applanation tonometry) in our meta-analysis, whereas, other meta-analysis only focused on the volume clamp method. [31]

The trending ability of continuous non-invasive monitors is important information for clinicians to consider when using CNAP devices in practice. In our meta-analysis we focused on the absolute agreement between the CNAP and the invasive methods and 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, even though we know that point estimates are not accurate, if the trends over time were accurate. This trending ability was not analyzed in our meta-analysis.

### Limitations

Our meta-analysis assesses the accuracy of blood pressure measurements from CNAP devices and does not assess the clinical utility of this monitoring system. The evidence of this review should be considered in the context of additional information about the reliability of this device to guide decision-making. Data on adverse events due to blood pressure monitoring with CNAP devices was not extracted. This meta-analysis focused on calculating population limits of agreement, which incorporate the variation in bias between studies into the estimates. Therefore, we did not 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.[33]

As the purpose of this meta-analysis was to have an understanding of the overall accuracy of these technologies, several different types of continuous non-invasive blood pressure monitoring devices were combined in our primary meta-analysis. However, these devices are based on different technologies, for instance, the T-line device is based on the AAT method that uses the radial artery for blood pressure measurement, whereas the CNAP is calibrated on an oscillometric blood pressure cuff, whereas the Clearsight system is not. 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), which showed very similar results for bias and precision. Different models of each device were not assessed individually.

## Conclusion

Substantial differences between blood pressure measurements from continuous non-invasive and invasive monitoring for blood pressure measurements were identified in this meta-analysis. The results of this meta-analysis show that the population limits of agreement were wide, spanning from -59.93 mmHg to 56.11mmHg for SBP, -216.7 mmHg to 219.72 mmHg for DBP, and -68.89 mmHg to 71.87mmHg for MAP. Clinicians should consider the range of uncertainty of continuous noninvasive blood pressure monitoring when using these devices to inform their decision-making for patients in critical care.

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# Figure legend

Fig. 1 PRISMA Flow Diagram

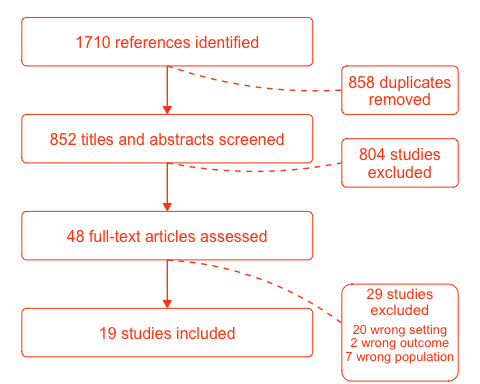


Fig. 2 Risk of bias assessments for included studies

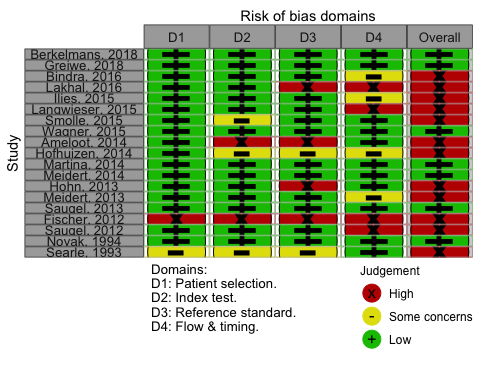


Fig. 3 Comparisons between invasive and CNAP blood pressure measurement within and across studies

## [1] NA

# 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) |  |  | CNAP | Comparator |  | participants | Participants | measurements | Measurements |
| 2018 | Berkelmans |  |  | 74 (9) | Atrial fibrillation | ICU, Medium care unit or Coronary care unit | ClearSight | invasive | radial | 31 |  | 4650 |  |
|  | 64 (17) | Sinus Rhythm | 10 |  | 1500 |  |
| Greiwe |  |  | 71 [59, 76) |  | Cardiological or Cardio-Surgical ICU | T-line | invasive | radial | 31 |  | 27900 |  |
| 2016 | Bindra |  |  | 62.2 [28 to 87] |  | ICU | Finapres | invasive | radial | 19 |  | 51 |  |
| Lakhal |  |  | 64 (13) |  | Surgical ICU | CNAP® | invasive | radialfemoral | 182 |  | 546 |  |
| 2015 | Ilies |  |  | 68.8 (9.4) |  | Cardiovascular ICU | CNAP® | invasive | radial | 104 |  | 11222 |  |
| Langwieser |  |  | 69 [60, 77) |  | Cardiac ICU | T-line | invasive | radial | 30 |  | 7304 |  |
| Smolle |  |  | 66 [56, 72) |  | Medical ICU | CNAP® | invasive | radial | 40 |  | 7200 |  |
| Wagner |  |  | 60 [52, 71) |  | ICU | CNAP® | invasive | femoral | 55 |  | 4891 |  |
| 2014 | Ameloot |  |  | 57.6 (19.4) |  | Medical-­Surgical-­Burns ICU | ClearSight | invasive | femoral | 45 |  | 225 |  |
| invasive | radial | 17 |  | 85 |  |
| Hofhuizen |  |  | 67 [50 to 81] |  | ICU | ClearSight | invasive | radial | 20 |  | 54 |  |
| Martina |  |  | 50 (11) |  | ICU | ClearSight | invasive | radial | 29 |  | 8700 |  |
| Meidert |  |  | 67 [54 to 77] |  | ICU | T-line | invasive | radial | 24 |  | 2993 |  |
| 2013 | Hohn |  |  | 63 [18 to 82] |  | ICU | ClearSight | invasive | radialfemoral | 25 |  | 117 |  |
| Meidert |  |  |  |  | ICU | T-line | invasive | femoral | 23 |  | 2879 |  |
| Saugel |  |  | 63 [51, 74) |  | Medical ICU | T-line | invasive | femoral | 34 |  | 4502 |  |
| 2012 | Fischer |  |  | 68 [22 to 85] |  | Post-operative cardiac surgery ICU | ClearSight | invasive | radial | 44 |  | 220 |  |
| Saugel |  |  | 68 [61.5, 73.5) |  | Medical ICU | T-line | invasive | femoral | 28 |  | 76826 |  |
| 1994 | Novak |  |  | [20 to 78] |  | ICU | Finapres | invasive | radial | 20 |  | 100323 |  |
| 1993 | Searle |  |  | 60.8 (11.7) |  | Cardiac ICU | NCAT | invasive | radial | 10 |  | 300 |  |

### Table 2: Results of meta-analyses

|  |  |  |  |  |  |  |  |  |  |  | Population LoA | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 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 | -1.91 | 155.88 | 22.09 | -28.59 | 24.77 | -59.93 | 56.11 |
| Primary | DBP | 17 | 18 | 760 | 262,235 | 1.51 | 60.57 | 53.66 | -19.87 | 22.89 | -216.70 | 219.72 |
| Primary | MAP | 18 | 19 | 784 | 162,080 | 1.49 | 54.34 | 25.14 | -16.34 | 19.32 | -68.89 | 71.87 |
| Low risk studies | SBP | 7 | 8 | 234 | 155,459 | -3.89 | 158.21 | 12.65 | -30.04 | 22.25 | -53.17 | 45.38 |
| Low risk studies | DBP | 7 | 8 | 234 | 155,459 | 4.75 | 57.01 | 39.45 | -14.89 | 24.39 | -213.98 | 223.48 |
| Low risk studies | 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 | -2.63 | 133.04 | 22.84 | -27.59 | 22.34 | -73.53 | 68.28 |
| Studies not funded | DBP | 11 | 12 | 504 | 135,671 | 2.15 | 67.06 | 54.75 | -19.92 | 24.23 | -274.81 | 279.12 |
| Studies not funded | MAP | 11 | 12 | 504 | 135,671 | 2.08 | 49.42 | 25.55 | -15.24 | 19.39 | -88.24 | 92.39 |
| AAT | SBP | 7 | 7 | 180 | 122,704 | -2.41 | 127.48 | 12.90 | -26.11 | 21.28 | -54.74 | 49.91 |
| AAT | DBP | 7 | 7 | 180 | 122,704 | 5.54 | 65.27 | 9.78 | -11.79 | 22.87 | -31.22 | 42.30 |
| AAT | 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 | -1.63 | 170.35 | 30.00 | -29.94 | 26.68 | -97.44 | 94.17 |
| Volume Clamp | DBP | 10 | 11 | 580 | 139,531 | -1.30 | 58.01 | 57.19 | -22.77 | 20.17 | -320.25 | 317.65 |
| Volume Clamp | MAP | 11 | 12 | 604 | 39,376 | 0.83 | 55.40 | 34.46 | -18.13 | 19.78 | -137.63 | 139.28 |
| ClearSight | SBP | 6 | 7 | 204 | 15,466 | -1.09 | 162.52 | 50.88 | -30.30 | 28.13 | -295.59 | 293.42 |
| ClearSight | DBP | 5 | 6 | 179 | 15,349 | -2.71 | 45.72 | 33.86 | -20.55 | 15.13 | -221.51 | 216.09 |
| ClearSight | MAP | 6 | 7 | 204 | 15,466 | -0.41 | 45.49 | 14.84 | -15.95 | 15.12 | -58.24 | 57.42 |
| Tline | SBP | 6 | 6 | 170 | 122,404 | -3.47 | 186.54 | 7.19 | -31.31 | 24.37 | -45.58 | 38.64 |
| Tline | DBP | 6 | 6 | 170 | 122,404 | 6.31 | 74.82 | 9.10 | -12.01 | 24.64 | -30.88 | 43.51 |
| Tline | MAP | 6 | 6 | 170 | 122,404 | 2.55 | 58.54 | 6.13 | -13.53 | 18.64 | -25.43 | 30.53 |
| CNAP | SBP | 4 | 4 | 381 | 23,859 | -3.15 | 180.72 | 26.90 | -31.97 | 25.67 | -155.61 | 149.32 |
| CNAP | DBP | 4 | 4 | 381 | 23,859 | -1.28 | 98.20 | 92.08 | -28.87 | 26.31 | -1430.91 | 1428.36 |
| CNAP | MAP | 4 | 4 | 381 | 23,859 | 1.68 | 58.53 | 46.40 | -18.80 | 22.17 | -501.00 | 504.36 |
| Femoral | SBP | 5 | 5 | 185 | 89,323 | -2.98 | 170.01 | 45.98 | -32.37 | 26.42 | -311.89 | 305.93 |
| Femoral | DBP | 5 | 5 | 185 | 89,323 | 2.38 | 62.53 | 58.83 | -19.65 | 24.41 | -588.85 | 593.61 |
| Femoral | MAP | 5 | 5 | 185 | 89,323 | 0.09 | 44.96 | 1.01 | -13.47 | 13.65 | -18.71 | 18.89 |
| Radial | SBP | 11 | 12 | 393 | 172,366 | -0.92 | 128.06 | 22.07 | -25.43 | 23.59 | -70.03 | 68.19 |
| Radial | DBP | 11 | 12 | 393 | 172,366 | 2.09 | 52.28 | 54.32 | -18.56 | 22.74 | -285.69 | 289.87 |
| Radial | MAP | 11 | 12 | 392 | 72,094 | 1.16 | 55.27 | 23.92 | -16.64 | 18.95 | -80.36 | 82.67 |
| aUnits are mmHg | | | | | | | | | | | | |
| bVariance | | | | | | | | | | | | |
| cMeasure of heterogeneity | | | | | | | | | | | | |
| dLoA = Limits of Agreement | | | | | | | | | | | | |
| eCI = Confidence Intervals | | | | | | | | | | | | |