Accuracy and Precision of Continuous Non-Invasive Arterial Pressure Monitoring Compared with Invasive or Non-Invasive Blood Pressure Monitoring

A systematic review and meta-analysis

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### Abstract

**Purpose**

Arterial blood pressure monitoring is vital to clinical decision making. Both the gold standard for monitoring, which is invasive arterial pressure measurement, and the most common modality of blood pressure modality, non-invasive blood pressure monitoring present with limitations that can be resolved with continuous non-invasive arterial pressure (CNAP) monitoring. The aim of this systematic review is to summarize the evidence regarding the concordance between CNAP and invasive arterial pressure monitoring.

**Methods**

Medline and EMBASE were searched for studies published using commercially available CNAP monitoring systems that reported on a measurement of the invasive or non-invasive arterial pressure that coincided with a measurement of CNAP. Study selection and quality assessment using the Revised Quality Assessment of Diagnostic Accuracy Studies tool (QUADAS-2) was performed independently by two reviewers.The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach was used to summarize the strength of the evidence. Pooled estimates of the mean bias and limits of agreement with outer 95% confidence intervals (population limits of agreement) were calculated.

**Results**

The primary meta-analysis of CNAP versus invasive arterial pressure monitoring consisted of 19 comparisons from 18 individual studies, with data from 785 participants with 262,352 paired measurements for SBP were included. For DBP 18 comparisons from 17 individual studies, with data from 760 participants with 262,235 paired measurements were included. For MAP 19 comparisons from 18 individual studies, with data from 784 participants with 162,080 paired measurements for MAP were included. The pooled estimate for the mean bias was -1.91mmHg, 1.51mmHg, 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 219.72mmHg for DBP, and -68.89mmHg to 71.87mmHg for MAP. Population limits of agreement for the sensitivity analysis included studies that were rated as having low risk of bias across all domains of the QUADAS-2 and revealed similar results to the primary analysis.

**Conclusion**

The range of uncertainty in the accuracy of blood pressure monitoring system should be considered when deciding to use these device in clinical settings. The SBP measurement from continuous non-invasive devices can be as much as 60 mmHg higher or lower. Therefore, these devices should be used with caution in clinical setting where hemodynamic measurements dictate clinical decision making.

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:**

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

Blood pressure monitoring is a mainstay of hemodynamic monitoring and is a requirement for patients in critical care settings [1] For patients requiring continuous blood pressure monitoring, invasive arterial pressure monitoring is often used as the standard of care and involves arterial cannulation. [1] The cannulation of an artery is painful, time-consuming, needs to be done by a trained clinician, and is associated-although very rarely- with complications such as infections, embolism, tissue and nerve damage. [1] In addition, specialized equipment is required in order to analyse arterial pressure continuously. For these reasons, non-invasive blood pressure (NIBP) monitoring is frequently used. [1] While there are many benefits of NIBP monitoring, the devices using this method are unable to provide continuous blood pressure measurements and may leave blood pressure fluctuations undetected or may lead to late recognition and delayed correction. For this reason, continuous non-invasive arterial pressure (CNAP) monitoring is fast gaining importance as it addresses the complications associated with the invasive monitoring and the limitations of NIBP monitoring.

CNAP monitoring is based on the arterial applanation tonometry (AAT) and volume clamp. Both techniques enable the arterial waveform and BP values to be obtained continuously. [2] AAT 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). Volume clamp is based on the work by Penaz et al. (1976). [3] and measure blood pressure at the finger using an inflatable cuff combined with a photodiode. [1] Devices using this technique include Nexfin (BMEYE B.V., Amsterdam, The Netherlands); CNAP (CNSystems, Graz, Austria). CNAP monitoring devices display real-time, continuous arterial pressure waveforms and provide non-invasive beat-to-beat arterial pressure measurement. Numerous studies have investigated the concordance between CNAP measurement and invasive arterial pressure measurement across a variety of clinical populations. 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 clinical practice.

## Methods

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

### Inclusion criteria

Studies that reported blood pressure measurements using CNAP technique and comparator invasive were included. Due to the potential of overestimation of the intervention performance, case control design studies were excluded. Studies were limited to human subjects admitted on an in-patient clinical healthcare setting (not including 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

The information extracted included 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). The outcomes that were extracted included the mean bias (eg, accuracy) and variance (eg, SD, precision) in SBP, DBP, and MAP measurement between the invasive and CNAP devices. 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.[4]

Two reviewers independently completed the risk of bias assessment for the included studies using the revised Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2).[5] 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’ risk of bias by the reviewers.

A comprehensive search of multiple databases and international clinical trial registry was conducted to minimize the risk of publication bias. [6] 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 being frequently identified incorrectly. [7]

The Grading Quality of Evidence and Strength of Recommendation methodology was applied to rate the quality of evidence.[8] 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 the devices using the 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.[9] 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.[9] 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. [10–12] The method-of-moments estimator from DerSimonian & Laird [13] 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.[14] 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 compartor for all 45 participants and also completed an additional analysis on 17 of th 45 participants using both the radial and femoral artery for invasive MAP measurement. [15] Only the results from the femoral artery for SBP, DBP, and MAP 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’. [16] Two studies [17] [18] 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 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. [18] 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. [24] 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 measurement site of invasive arterial pressure (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, Nexfin, and T-Line).

## Results

### Study selection and description

Ninteen studies were included (Figure 1). Twenty studies were conducted in the wrong setting (eg, outpatient, OR) and were excluded. 7 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 comaprison for low risk of bias sutdies included 7 comparisons from 6 individual studies of 214 participants with 155,459 paired measurements.

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. There were 7 studies that compared the SBP based on the AAT method to invasive SBP, comprising 7 comparisons with 122,704 measurements from 180 participants. AAT method was used in 7 studies that compared to invasive DBP, comprising 7 comparisons with 122,704 measurements from 180 participants. AAT method for MAP measurement was used in 7 studies comprising 7 comparisons with 122,704 measurements from 180 participants.

Nexfin device 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 Nexfin DBP to invasive DBP, comprising 6 comparisons with 15,349 measurements from 179 participants. Nexfin 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 device to invasive SBP, comprising 4 comparisons with 23,859 measurements from 381 participants. There were 4 studies that compared to CNAP and invasive DBP, comprising 4 comparisons with 23,859 measurements from 381 participants. CNAP 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, seven used the femoral artery and 12 used the radial artery for 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. 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. For this study, only the femoral site comparison 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 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, 1.51, 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 similair to the primary analysis for SBP, DBP, and MAP. The mean bias for SBP was -3.89 mmHg with population limits of agreement -53.17 mmHg to 45.38mmHg. The mean bias for DBP was 4.75 mmHg with population limits of agreement -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, inconsistency, and study limitations. A further sensitivity analysis excluding studies that received funding revealed population limits that were wide 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 low, again due to concerns about imprecision, inconsistency, and study limitations.

### Subgroup Analyses

We conducted three subgroup analyses for the primary comparison according to the method of CNAP monitoring, type of CNAP device, and measurement site of invasive arterial pressure.In the subset of studies conducted using a device based on the volume clamp method, the mean bias and population limits of agreement for SBP was -1.63mmHg (-97.44 mmHg to 94.17mmHg), DBP -1.3mmHg (-320.25 mmHg to 317.65mmHg), and MAP 0.83mmHg (-137.63 mmHg to 139.28mmHg). In the subset of studies conducted using a device based on the AAT method, the mean bias and population limits of agreement for SBP was -2.41mmHg (-54.74 mmHg to 49.91mmHg), DBP 5.54mmHg (-31.22 mmHg to 25.89mmHg), and MAP 2.15mmHg (-21.59 mmHg to 25.89mmHg). 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 CNAP monitoring device, the mean bias and population limits of agreement for Nexfin was -1.09 (-295.59 mmHg to 293.42mmHg) for SBP, -2.71 (-221.51 mmHg to 216.09mmHg) for DBP, and -0.41 (-58.24 mmHg to 57.42mmHg) for MAP. The mean bias and population limits of agreement for the CNAP system was -3.15 (-155.61 mmHg to 149.32mmHg) for SBP, -1.28 (-1430.91 mmHg to 1428.36mmHg) for DBP, and 1.68 (-501 mmHg to 504.36mmHg) for MAP. In the subset of studies conducted based on the type of T-Line monitoring device, the mean bias and population limits of agreement was -3.47 (-45.58 mmHg to 38.64mmHg) for SBP, 6.31 (-30.88 mmHg to 43.51mmHg) for DBP, and 2.55 (-25.43 mmHg to 30.53mmHg) 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 and population limits of agreement was -2.98mmHg (-311.89 mmHg to 305.93mmHg), DBP 2.38mmHg (-588.85 mmHg to 18.89mmHg), and MAP 0.09mmHg (-18.71 mmHg to 18.89mmHg).For the radial site it was -0.92mmHg (-70.03 mmHg to 68.19mmHg), DBP 2.09mmHg (-285.69 mmHg to 82.67mmHg), and MAP 1.16mmHg (-80.36 mmHg to 82.67mmHg). The GRADE rating for quality of evidence was downgraded to very low quality due to concerns about imprecision, inconsistency, and study limitations.

## Discussion

The overall pooled bias for SBP, DBP, and MAP was -1.91, 1.51, and 1.49mmHg, respectively.  
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 CNAP devices would not satisify 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, and the studies not funded were similar to the primary analysis. These results may have important implications for practice where blood pressure monitoring is essential in clinical decision making, therefore it may not be appropriate to substitute CNAP devices in place of invasive arterial pressure. The evidence derived from this systematic review should only be considered within the context of other information about the clinical utility of these devices.

The accuracy of CNAP compared to invasive arterial pressure measurements has been evaluated using various devices and methods. The AAT sub-group analysis consisted of six studies based on the T-line device and one based on the NCAT. Two of the authors who conducted the studies using T-line completed another study in the same clinical setting but using a different model of the T-line device. [25] Whereas, the volume clamp included three different types of devices (Finapres, Nexfin, and CNAP), and each device had various models. As a results, there was more factors to incorporate into the volume clamp analysis subgroup, which may potentially be contributing to the broader population limits of agreement. Additional studies are required to evaluate the accuracy of the AAT and volume clamp methods.

The trending ability of CNAP monitors is important information for clinicians to consider when using CNAP devices in practice. This is because arterial pressure continuously changes in response to a variety of factors. In addition, evaluating trends in CNAP may be useful in clinical practice for evaluating the effectiveness of interventions employed to improve hemodynamic status. Conclusions about trending ability can be drawn from the accuracy and precision of absolute measurements. For example, the mean deviation between absolute measurements of CNAP and invasive (i.e. the accuracy) would be fixed if the monitor is highly precise providing an indication of trending ability. Alternatively, if the device is highly imprecise, the deviation between CNAP and invasive or non-invasive blood pressure will be variable making trending unreliable. As there are no agreed standards for the accuracy and precision of CNAP monitors, evaluation of trending ability is therefore ultimately a qualitative judgment about whether or not the index test is sufficiently precise, and our study did not measure the trending ability.

Our estimates of the accuracy of measurements from CNAP monitoring are similar to results from a previous meta-analysis that compared it to invasive measurements.[29] However, this previous meta-analysis used a statistical approach that did not incorporate the magnitude of heterogeneity in results between studies or sampling error. As such, it is possible that the CNAP monitoring may still be more precise.

A central concern for any systematic review is the validity of the original analyses. In this regard, it is important to note that it has been reported that the traditional Bland-Altman technique for assessing the concordance between two measurements has frequently been performed inappropriately in situations where repeated measurements are taken from the same research participant. Although there are ways to account for the dependent nature of the repeated measurements, multiple paired measurements from the same participants are often analysed as though they are independent. For this reason, framework for meta-analysis of Bland-Altman method comparison studies based on a LoA approach was used in our study, as it provides an estimate of the pooled LoAs in the population and not just the samples studied. Also, many studies in this review analysed a large number of measurements of blood pressure with relatively small sample sizes. 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.[9]

### Limitations

Our meta-analysis assesses the reLative accuracy of CNAP monitoring systems 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.[**???**]

Another limitation is that the all CNAP monitoring systems were mixed in our primary analysis. The T-line device 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 and the Nexfin is calibrated. As the purpose of this meta-analysis was to have an understanding of the overall accuracy of these technologies, we decided to mix the different devices. However, we performed a sub-group analysis of the different methods (AAT and Volume Clamp), and of the different devices (CNAP, Nexfin, and T-line), which showed very similar bias and precision. It is important to note the different models of each device were not assessed individually.

Finally, our initial protocol was focused on the accuracy of CNAP monitoring systems in concordance with invasive and non-invasive arterial pressure monitoring. However, we were only able to find two studies comparing CNAP and non-invasive blood pressure monitoring that met our inclusion criteria. A decision was made to include only studies that reported on the accuracy of the CNAP Monitoring System compared to invasive monitoring for this particular report. As patients in critical care setting require beat to beat arterial pressure monitoring, this decision permitted a more focused evaluation on this topic with this specific population.

## Conclusion

Substantial differences between blood pressure measurements from CNAP and invasive measuring systems were identified in this meta-analysis. Clinicians should consider the range of uncertainty in the accuracy of the CNAP monitoring when using these devices to inform their decision-making. As such, in many circumstances the use of these device would not be appropriate because a difference in SBP of about 60 mmHg is important to detect and manage clinical situations.

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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

# 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 device | Comparator |  |  | Participants |  | Measurements |
| 2018 | Berkelmans |  |  | 74 (9) | Atrial fibrillation | ICU, Medium care unit or Coronary care unit | nexfin | invasive | radial | 31 |  | 4650 |  |
|  | 64 (17) | Sinus Rhythm | 10 |  | 1500 |  |
| Greiwe |  |  | 71 [59, 76) |  | Cardiological or Cardio-Surgical ICU | tline | 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 |  |
| noninvasive | brachialopposite |
| noninvasive | brachial |
| 2015 | Ilies |  |  | 68.8 (9.4) |  | Cardiovascular ICU | cnap | invasive | radial | 104 |  | 11222 |  |
| Langwieser |  |  | 69 [60, 77) |  | Cardiac ICU | tline | 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 | nexfin | invasive | femoral | 45 |  | 225 |  |
| invasive | radial | 17 |  | 85 |  |
| noninvasive | brachial | 45 |  | 225 |  |
| Hofhuizen |  |  | 67 [50 to 81] |  | ICU | nexfin | invasive | radial | 20 |  | 54 |  |
| Martina |  |  | 50 (11) |  | ICU | nexfin | invasive | radial | 29 |  | 8700 |  |
| Meidert |  |  | 67 [54 to 77] |  | ICU | tline | invasive | radial | 24 |  | 2993 |  |
| 2013 | Hohn |  |  | 63 [18 to 82] |  | ICU | nexfin | invasive | radialfemoral | 25 |  | 117 |  |
| Meidert |  |  |  |  | ICU | tline | invasive | femoral | 23 |  | 2879 |  |
| Saugel |  |  | 63 [51, 74) |  | Medical ICU | tline | invasive | femoral | 34 |  | 4502 |  |
| 2012 | Fischer |  |  | 68 [22 to 85] |  | Post-operative cardiac surgery ICU | nexfin | invasive | radial | 44 |  | 220 |  |
| Saugel |  |  | 68 [61.5, 73.5) |  | Medical ICU | tline | 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 | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 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 |
| Clinically Available Devices SBP | 16 | 17 | 755 | 161,729 | -2.32 | 174.79 | 24.09 | -30.52 | 25.89 | -67.64 | 63.01 |
| Clinically Available Devices DBP | 15 | 16 | 730 | 161,612 | 1.22 | 66.63 | 56.01 | -20.93 | 23.37 | -242.53 | 244.97 |
| Clinically Available Devices MAP | 16 | 17 | 755 | 161,729 | 1.38 | 53.17 | 26.35 | -16.45 | 19.22 | -77.23 | 79.99 |
| 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 |
| 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 |
| Nexfin SBP | 6 | 7 | 204 | 15,466 | -1.09 | 162.52 | 50.88 | -30.30 | 28.13 | -295.59 | 293.42 |
| Nexfin DBP | 5 | 6 | 179 | 15,349 | -2.71 | 45.72 | 33.86 | -20.55 | 15.13 | -221.51 | 216.09 |
| Nexfin 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 | | | | | | | | | | | |